Mood Disorders and the GI Tract | Nutrition and Epigenetics | Preventing Type 2 Diabetes and Metabolic Syndrome | Diagnosing "Leaky Gut"

TOWNSENDLETTER.COM

Townsend Letter

The Examiner of Alternative Medicine

JANUARY 2019
ISSUE #426
$8.25

Pathfinder Bioinformatics Scholars, Center of Excellence in Generative Medicine University of Bridgeport, College of Naturopathic Medicine

JUMP TO TABLE OF CONTENTS

Peter D'Adamo, ND

New Genetic Database for Individualized Health Care

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 86 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

DNA CONNEXIONS

DNA Connexions is a sophisticated laboratory specializing in the detection of microbial DNA. Polymerase chain reaction technology (PCR), with its high specificity and sensitivity, is the cornerstone of our testing methodology.

The Lyme Panel tests for four unique gene sequences found in *Borrelia burgdorferi*, in addition to 10 common tickborne co-infectors.

Visit link below to receive a free Patient Information brochure.

www.DNAConnexions.com/Townsend

Jarrow FORMULAS®

Clinically Tested & Patent Protected Strains of the Predominant Vaginal Microflora

1. *L. crispatus* LbV 88
2. *L. jensenii* LbV 116
3. *L. gasseri* LbV 150N
4. *L. rhamnosus* LbV 96

Unlike the intestinal flora, the predominant vaginal microbiome are confined to much fewer species. Accordingly, only a few such vaginal specific *Lactobacillus* strains have been clinically tested for their ability to support vaginal health.*

Jarro-Dophilus® Women contains the four predominant *Lactobacillus* strains of the healthy vaginal tract known as the "Astarte" strains. All four Astarte strains were originally isolated from the vaginal tracts of young, healthy women in their third month of pregnancy. The samples were enumerated for the predominant strains and then screened for efficacy. The Astarte strains have been clinically documented to promote vaginal microflora and urinary tract health.*

Clinical Study #1 (1999)

In a study of 319 women visiting three medical clinics, most women's normal vaginal bacterial residents included *L. crispatus* (32%), followed by *L. jensenii* (23%), *L.* 1086V (15%), *L. gasseri* (5%), *L. fermentum* (0.3%), *L. oris* (0.3%), *L. reuteri* (0.3%), *L. ruminis* (0.3%), and *L. vaginalis* (0.3%).*

Antonio MAD, *et al. Journal of Infectious Diseases* 1999;180:1950–6.

Clinical Study #2 (2007)

In another study involving 126 healthy pregnant women, *L. crispatus* and *L. gasseri* were the most dominant species found, followed by *L. jensenii* and *L. rhamnosus*.*

Kiss H, *et al. BJOG: An International Journal of Obstetrics & Gynaecology* 2007;114: 1402-1407.

Clinical Study #3 (2014)

In a double-blind, randomized placebo-controlled trial, 1-week of oral supplementation with the four Astarte strains significantly enriched *Lactobacilli* in the vaginal tract and reduced Nugent score in the neo-vagina of post-operative transsexual women, an environment typically resistant to colonization by *Lactobacilli.*

Kaufmann U, *et al. Eur J Obstet Gynecol Reprod Biol.* 2014 Jan;172:102-5.

Clinical Study #4 (2016)

In immunosuppressed pregnant women with herpes infection, oral supplementation with the four Astarte strains significantly reduced undesirable microbes in the intestines and vagina, and simultaneously increased vaginal *Lactobacilli* 3-fold compared to placebo.* This was accompanied by reduced incidence of placental insufficiency, pre-eclampsia and fetal distress in the probiotic supplemented women.

Anoshina TM, *et al. Perinatologiya I Pediatriya* 2016;4(68):22-25.

ASTARTE

Protected by U.S. Patent 8,846,027 and European Patent 2,509,610, which are owned by HSO Health Care GmbH, Vienna, Austria, and licensed in the U.S. to Jarrow Formulas, Inc. Other international patents pending. Sold worldwide as Astarte.

Health care practitioners, please find Jarrow Formulas' products at:

emerson ECOLOGICS delivering to improve health™ — emersonecologics.com

natural partners — naturalpartners.com

***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.**

Visit us at www.jarrow.com for more product information.

NutriClear® *Plus*

Clearly a superior cleanse program.

NutriClear® *Plus*
15-Day Metabolic Cleanse Program

NutriClear® Plus is a science-based metabolic cleanse program that supports the body's detoxification processes. By supplying key nutrients in a delicious-tasting powder, **NutriClear® Plus** provides the ideal nutritional foundation for those in need of metabolic clearing, while also supporting hepatic function, energy production and intestinal balance. This powerful combination of micronutrients, **NitroGreens®**, fiber, fruit and vegetable extracts supports safe and effective detoxification to start you on a path of lifelong health.

Kit Includes:

- 30 Drink Mix Pouches
- 30 Supplement Packets
- Program Guidebook
- Biotics Research Shaker Cup

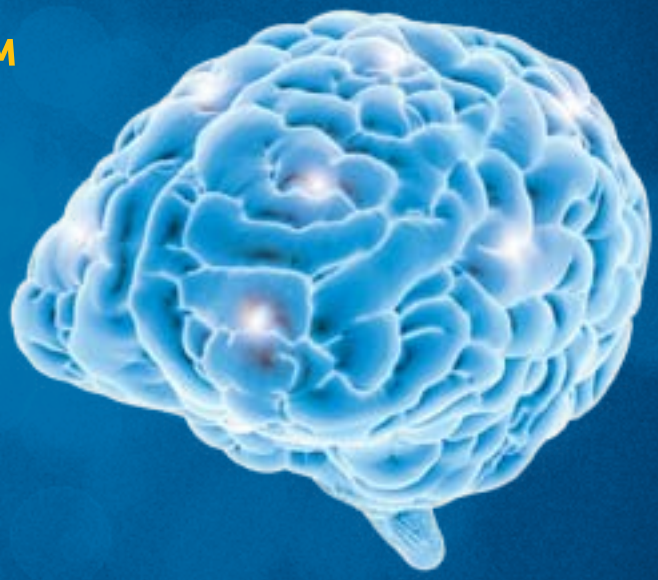
BIOTICS® RESEARCH CORPORATION

800-231-5777 • www.bioticsresearch.com

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.

BDNF Essentials™

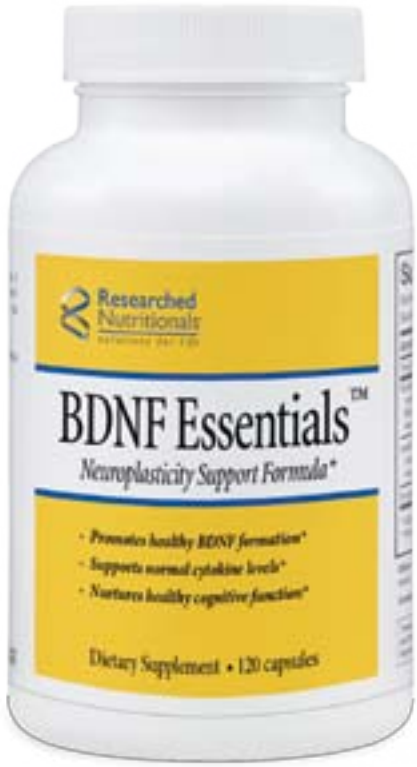
Promote Healthy Brain Function



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.

Sovereign Laboratories

Once Tests Show a Diagnosis of Intestinal Hyperpermeability ("Leaky Gut"), the Only Clinically-Proven Solution is

PRO Colostrum-LD®

When Combined with a Healthy Lifestyle, PRO-Colostrum-LD® Helps Begin the Body's Natural Healing Process

For additional information about the key metabolic and inflammatory markers used to assess leaky gut and how PRO Colostrum-LD® can help your patients, visit ColostrumTherapy.com/townsend

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.

A **COMPLETE** line of products to make your own.

Build your own line of uniquely branded Private Label supplements, with the same quality and cutting-edge products you know and trust from Allergy Research Group.

250+
products to choose from

only 12
bottle minimum order

0 cost
for label design and printing

8
customizable design options

3 day
turnaround on reorders

2 week
turnaround on new orders

All our Essential-Biotic™ probiotics are available for Private Labeling.

Use our customizable label design templates or supply your own.

www.allergyresearchgroup.com/private-label

AllergyResearchGroup®
Innovative Nutrition

800.545.9960
info@allergyresearchgroup.com
www.allergyresearchgroup.com

NSF GMP Registered

DRcaps

From the Publisher

Whitaker Debunks Food and Diet Myths

Julian Whitaker, MD's November 2018 issue of *Health & Healing*, a newsletter, headlined the issue with "Debunking Food and Diet Myths." Whitaker's monthly provides easy-to-understand writing palatable for the consumer. Much of what he writes about takes aim at big medicine. His clinic in southern California oftentimes recommends patients discontinue prescription medications thought to pose more risk than benefit. Dr. Whitaker is a dedicated nutritional interventionalist, advising healthy dietary and lifestyle change and use of supplementation. He is an advocate of doctors involved in integrative and functional medicine and has promoted chelation as a treatment for cardiovascular disease. However, some of the headlined myths he was debunking in the recent issue gave me pause – was he advocating for conventional dietitian menus or whole food nutrition?

continued on page 8 ➤

Improve Body Immune System

Scandinavian Formulas' Shark Liver Oil is a trusted product, having the highest known concentration of Alkylglycerols that affect the body's natural defense mechanisms. Harvested from cold water, deep-sea Greenland sharks.

Shark Liver Oil may aid in improving the body's immune system and may reduce side effects related to chemotherapy and radiation treatments.

- Scandinavian Formulas' Shark Liver Oil is a trusted name and product recognized and sold world-wide
- Clinically studied since 1962
- The only oil containing valuable Alkylglycerols
- All-natural and carefully controlled
- Contains no unwanted fats or impurities

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

From the Publisher

➤ *continued from page 6*

Here is a listing of some of the food and diet myths his newsletter claimed to have been "debunked" that I hesitated to agree with:

1. "HFCS (high-fructose corn syrup) is worse than sugar."
2. "Carbohydrates make you fat."
3. "Gluten should be avoided."
4. "Fresh food is better than frozen."
5. "Organic foods are more nutritious."
6. "Processed foods are bad."
7. "Microwaves kill nutrients in food."

Other myths that had been debunked seemed more reasonable to me:

1. "Salt is bad for you."
2. "Eggs raise cholesterol."
3. "Saturated fat causes heart disease."
4. "Chocolate causes acne."
5. "Soy has no place in a healthy diet."
6. "Diet soda helps with weight loss."
7. "Turkey makes you sleepy."

The chief concern I had with his myth-busting list was the tacit approval given to HFCS, a chemical that we are consuming in ever greater quantities in our processed foods and beverages. His two-paragraph explanation makes the point that the fructose in HFCS is not directly comparable to the fructose in fruit. The two do not have an identical effect on our metabolism and cellular functioning. The former is a chemical and must be considered as such physiologically while the latter isn't. To treat a chemical and natural compound identically may be okay from the food manufacturer's viewpoint, but it certainly is not from a nutritionist's.

Furthermore, many health problems can be attributed to eating or drinking foods and beverages processed with HFCS.[1] We have greatly increased our consumption of HFCS while decreasing table sugar over the past thirty years. Food manufacturers found that using the liquid sweetener facilitated a much greater diversity of food products compared to using cane or beet sugar, not to mention a reduction in costs. Farmers benefited with the limitless growth and harvesting of genetically modified corn (GMO) needed to manufacture HFCS. Fructose, as compared to glucose, impairs the affinity of insulin for its cell receptor, causing metabolic dysfunctioning leading to pre-diabetes.

Nancy Appleton, PhD, has detailed in her articles and popular books, such as *Lick the Sugar Habit*, the deleterious

continued on page 10 ➤

MUSHROOM WISDOM®

SCIENCE COMPLEMENTING ANCIENT WISDOM

Unique, Research-Based Mushroom Extracts

Super Mushroom and Mushroom Extracts

Townsend Letter Practitioner & Patient 15% Intro deal: Code TL1218
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.

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

Mushroom Wisdom has been offering mushroom products combining the best knowledge of nature with the latest science for over 25 years.

- Grown mirroring nature on their natural food source.
- Our mushrooms are extracted, making them more bioavailable to your patients.
- MW has been in the forefront of research on mushrooms and health.

From the Publisher

➤ *continued from page 8*

effects of fructose. Fructose readily converts into fat, leading to excess circulating triglycerides and obesity. Daily consumption of HFCS damages cellular liver functioning and leads to the development of non-alcoholic fatty liver disease. Other physiologic disturbances such as excess mineral losses and increased uric acid production have been observed with increased consumption. An increased risk of developing hypertension, heart and cardiovascular disease, gastrointestinal permeability, and cancer have also been associated with its use. Some studies have found unacceptably higher amounts of mercury in the sweetener.

There is a definite difference between HFCS and table sugar. Excesses of both can cause the aforementioned pathology but the former is more damaging. Unfortunately, our diets now are laden with it.

"HFCS is worse than table sugar" is not a myth and has not been debunked.

1. Price, A. High fructose corn syrup dangers and healthy alternatives. *Dr. Axe Food is Medicine.* www.draxe.com. Sept. 29, 2016.

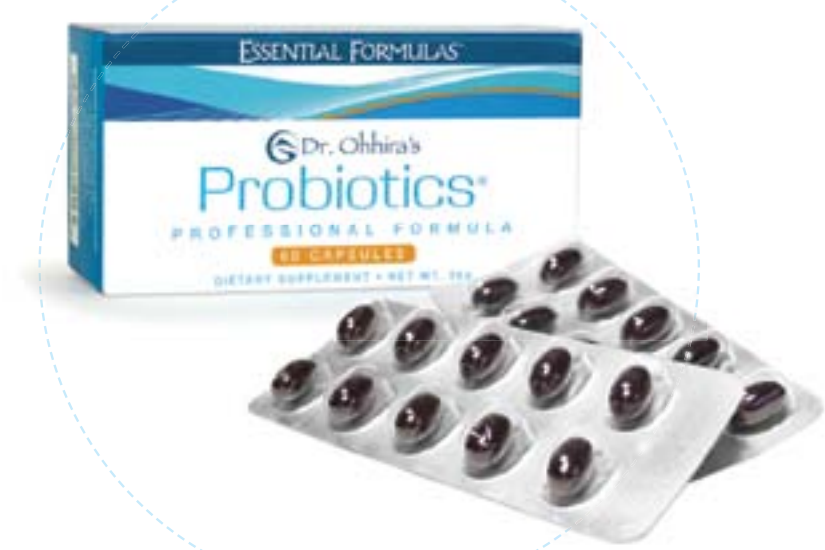
David Quig, PhD, on the Gastrointestinal Barrier System

How do we diagnose gastrointestinal permeability or, colloquially, leaky gut syndrome? Dr. David Quig, Vice President of Scientific Support at Doctor's Data Laboratory, makes the case in this issue that the GI barrier system is complex – that there can be many different aspects of permeability allowing the unwelcome absorption of antigenic, inflammatory, and undigested foods, chemicals and microorganisms. Quig refers to the passage of these materials through the GI barrier as breaches. (One cannot help visualizing openings permitting easy access for invasive organisms or entry of toxic chemicals and metals.)

Assessment of gastrointestinal permeability is best accomplished with the comprehensive stool analysis. This laboratory test not only diagnoses "abnormal" bacterial dysbiosis but also determines "insufficiency dysbiosis" meaning that the "good" microorganisms needed for intact barrier functioning are missing and gut permeability ensues. Butyrate, a short-chain fatty acid, is critical for "microorganism-host cross-talk." A low butyrate level will contribute significantly to leaky gut syndrome. Secretory IgA is a vital component of the mucus barrier; a low sIgA not only is a marker suggesting inadequate mucus in the mucosa but may represent overgrowth of Candida organisms. The stool analysis is a tool that we should implement more routinely in our practices.

continued on page 12 ➤

Discover the Dr. Ohhira Difference!™



While many digestive health formulas only contain probiotics, **Dr. Ohhira's Probiotics**® contains all the pieces your patient's need for optimal health, digestion and immune support: **PRE**biotics, **PRO**biotics, and **POST**biotics.* Dr. Ohhira's award-winning, professional strength formula is **fermented for five years** which results in a truly unique probiotic supplement with three advanced components:

PREbiotics—fermented fruits & vegetables that cultivate the existing good bacteria in the gut*

PRObiotics—numerous strains of living probiotics including *Bifidobacterium* and *Lactobacillus* that promote healthy digestion and immune response*

POSTbiotics—amino acids, vitamins, minerals, and natural organic acids that are produced by the fermentation process and are essential for whole health*

Help your patients Discover the Dr. Ohhira Difference!™

ESSENTIAL FORMULAS®
PROFESSIONAL

DISTRIBUTED BY emerson ECOLOGICS®

For More Information visit: www.essentialformulas.com/professionalformula • (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.

From the Publisher

➤ *continued from page 10*

Cover: Peter D'Adamo, ND, Invites *Townsend Letter* Readership to Use University of Bridgeport College of Naturopathic Medicine's Genomic Database

Doctor Peter D'Adamo is well known to our readership as well as health professionals and consumers through the US and internationally; he is the author of *Eat Right 4 Your Type*. While there has been criticism of his book, D'Adamo maintains that limiting the diet based on one's blood type is a sound approach to one's personal nutrition. His current work lies in the development of clinical "bioinformatics," which may transform naturopathic diagnosis and treatment into precision medicine. He is Distinguished Professor of clinical medicine and bioinformatics at the Center of Excellence in Generative Medicine (COEGM) at the University of Bridgeport, College of Naturopathic Medicine. In August the COEGM released "Circuits," which he describes as "a gene-based open source platform combining genomic data in a variety of robust dimensions. Circuits is web-based, has an imaginative and intuitive user interface, and is free to use." So, for readers seeking to know more about what their patient's genetic testing means, it may be an invaluable tool to expand diagnostic and therapeutic understanding.

D'Adamo explains that the COEGM has been in partnership during the past five years with Datapunk Bioinformatics LLC. The collaboration has led to development of "computational tools for precision medicine using generative-based algorithms." These include the proprietary "genomic development platform, Opus23" as well the "analytic modules, Utopia, for the microbiome, and Icarus, for the metabolome." These computational databases are open-source and without charge, enabling practitioners and public to use them for research and clinical exploration.

D'Adamo encourages readers to "surf Circuits and explore target genes that seem more interesting." As he was the primary individual who coded it, he is planning to expand the platform to permit exploring microbiota data to optimize organism applications and therapeutics. He looks forward to hearing about reader investigations using Circuits.

Jonathan Collin, MD

Happy 2019
from the staff of the
Townsend Letter

John Parks Trowbridge, MD, Presented with the Albert Nelson Marquis Lifetime Achievement Award by Marquis Who's Who

Marquis Who's Who, the world's premier publisher of biographical profiles, is proud to present John Parks Trowbridge, MD, with the Albert Nelson Marquis Lifetime Achievement Award. Dr. Trowbridge has been endorsed by Marquis Who's Who as a leader in the healthcare industry. An accomplished listee, Dr. Trowbridge celebrates 40 years' experience in his professional network and has been noted for achievements, leadership qualities, and the credentials and successes he has accrued in his field. As in all Marquis Who's Who biographical volumes, individuals profiled are selected on the basis of current reference value. Factors such as position, noteworthy accomplishments, visibility, and prominence in a field are all taken into account during the selection process.

One of America's leading stem cell physicians, Dr. Trowbridge has maintained his private practice, Life Celebrating Health, consisting of a health recovery unit, pain relief unit, and life-long health unit, in Humble, Texas, since 1978. He and his devoted support staff of many years are committed to a simple slogan: "Find it *now* – Fix it *right!*" Insistent on finding a *cause* where one is suspected through detailed history taking, hands-on physical exam, emerging tests, and novel reasoning, he cautions against assuming that drugs or surgery are the only real choices. He attributes his practice success to a simple unwavering devotion: pose challenging questions and *actively* seek out practical answers.

An Eagle Scout, National Merit Scholar, and California State Scholar, Dr. Trowbridge earned a Bachelor of Arts in biological sciences at Stanford University in 1970 and Doctor of Medicine at Case Western Reserve University in 1976. He studied at the National Institutes of Health and wrote and produced a teaching series of 12 videotapes on congenital heart disease. He trained in general surgery at Mount Zion Medical Center in San Francisco, urological surgery at the University of Texas-

➤

Lise Alschuler, ND, Joins UA Center for Integrative Medicine Faculty

The University of Arizona Center for Integrative Medicine (UACIM) announced that Lise Alschuler, ND, has joined the Center's faculty. In practice since 1994, Dr. Alschuler is board certified in naturopathic oncology.

Dr. Alschuler brings extensive experience to UACIM. She is the executive director of TAP Integrative, a nonprofit educational resource for integrative practitioners. She also maintains a naturopathic oncology practice in Scottsdale, Arizona, and co-hosts the *Five to Thrive* live radio show on the Cancer Support Network. She has been an invited speaker at more than 100 scientific and medical conferences.

"I am honored to join the faculty of the Center for Integrative Medicine," Dr. Aslchuler said. "The Center has been, and continues to be, at the forefront of health-care transformation. Through its programs, faculty and alumni, UACIM is securing a place in health care for whole-person-focused, integrative thought and practice. I am thrilled to add my contributions as an educator, naturopathic doctor and business woman to the already rich offerings of the Center."

Dr. Alschuler is a graduate of Bastyr University and a past-president and board member of the American Association of Naturopathic Physicians. She also is a board member and immediate past president of the Oncology Association of Naturopathic Physicians.

About the University of Arizona Center for Integrative Medicine

The University of Arizona Center for Integrative Medicine (UACIM) is leading the transformation of health care by creating, educating, and actively supporting a community that embodies the philosophy and practice of healing-oriented medicine. UACIM is internationally recognized for its evidence-based clinical practice, innovative educational programs and research that substantiates the field of integrative medicine and influences public policy. Since its creation in 1994, UACIM's vision of making integrative care available to all is being realized worldwide: UACIM graduates now are guiding more than 1 million patients to take a greater role in their health and healing. To learn more about UACIM, please visit azcim.org or connect with us on Facebook or Twitter.

◆

Lifetime Achievement Award

➤

Houston/Texas Medical Center, and master's studies in nutrition through the Florida Institute of Technology/Medical Research Institute, earning a Diplomate in Preventive Medicine in 1985. Having gained a broad background studying under leading professors in both medicine and surgery equipped him to step back and see "the big picture," where complex patient issues become easier to understand and effectively treat.

Dr. Trowbridge's 1976 Bantam Books bestseller, *The Yeast Syndrome*, is acknowledged worldwide as explaining confusing clinical presentations, especially those encountered in younger adults and also those in aging adults with *unexplained* illnesses. More recently, fungal markers identified in blood samples from patients suffering with dramatic, puzzling, often life-threatening illnesses have led Dr. Trowbridge to discover and develop treatments providing considerable recovery. Examples include severe skin sores, leukemia, bile duct cancer, elevated prostate PSA levels, lingering infections, immune deficiencies, all treated without conventional cortisone or chemotherapy. Fungal markers discovered in plaque-blocked heart arteries suggest an evolving dimension in treating deadly cardiovascular diseases.

Believing that people should get out of their pain and on with their lives, since 1990 Dr. Trowbridge's non-surgical treatments have helped people suffering with arthritis, neck and back pains, joint pains, and sports injuries. Recognized for his expertise in the blossoming field of regenerative medicine, he has coached over three dozen physicians to perform stem cell treatments for delightful recovery after years of suffering. Intent on sharing his innovative diagnostic and treatment perspectives, Dr. Trowbridge has been honored as an invited lecturer in Taiwan, Brazil, Canada, Mexico, and across the States. His patients travel from far and wide, frustrated with still feeling sick and tired despite the best of conventional care.

John Parks Trowbridge, MD

Expounding on his passion to discover or develop effective treatments for desperate patients has led to Editor's Choice awards for chapters in books co-authored with luminaries Jack Canfield, Brian Tracy, and Larry King. An expert in heavy metal toxicology, Dr. Trowbridge's innovative "chelation therapy" programs remove lead, mercury and more, to revitalize the lives of patients with assorted degenerative conditions … even having had two patients removed from the heart transplant list as they recovered. While "detox" is now a popular theme in modern culture, his career-long strategies have given a powerful definition to the recovery of vibrant health.

A recent book, *Failure is Not an Option,* clarifies the confusions surrounding how unique stem cell treatments can restore joint tissue structure and function, relieving pains even for those who have suffered for years. Among several other books by Dr. Trowbridge is *Sick and Tired,* which provides a welcome update to latest treatments for the yeast syndrome. Beyond articles and brochures, he has produced dozens of CDs and DVDs on integrative medicine topics, many derived from his earlier radio show, "Finally Feeling Better … Naturally, with Dr. John Trowbridge." He has planned numerous professional meetings for organizations where he has served as president or director.

Not wanting to be for his patients "one more in the long line of doctors who promised to help you and *didn't*," Dr. Trowbridge continues his persistent curiosity into the fundamental mechanisms of disease and health. His continuing contributions are recognized by the 2014 Distinguished Lifetime Achievement Award from the International College of Integrative Medicine and being named a Fellow of the American College for Advancement in Medicine. A natural educator, he insists that people know that they *do* have health choices now – otherwise, they don't have *any*.

Son of an Air Force bomber pilot, Dr. Trowbridge has had a particular enthusiasm for private piloting for over 40 years. He is the proud father of two delightful, accomplished daughters and beams with joy over his infant grandson.

Notably, Dr. Trowbridge has been cited in more than 60 volumes of *Who's Who*, including *Who's Who in America*, *Who's Who in Medicine and Healthcare*, and *Who's Who in the World*. In recognition of outstanding contributions to his profession and the Marquis Who's Who community, John Parks Trowbridge, MD, has been featured on the Albert Nelson Marquis Lifetime Achievement website. Please visit www.ltachievers.com for more information about this honor.

◆

The Most Effective Infrared Sauna for Raising Core Temperature !

46" tall
32" wide
33" deep

The Relax® Sauna

Advanced Semi-conductor Chip Technology raises core Temp 2.7° – 4.2° in 25-60 min

The Relax Sauna is used in Cancer Clinics while doing IV Therapy !

A cancer clinic in Washington uses the Relax Sauna while doing IV therapy on many of their patients. They do increase the core temperature to 102.8 degrees in 1 hour. Other clinics use the Relax Sauna for 5-7 minutes before doing IV Therapy when they have trouble getting the needles into the veins. The 20 second Relax Sauna heat-up time makes this very practical.

No Sweat? Know Sweat! the Definitive Guide to Reclaim Your Health

Book by Bill Akpinar, M.D. OMD, Chi Gong Master, Holistic Dentist

On the internet a Hypothermia Enthusiast posts: ***"The Relax Sauna is probably the best and only realistic option to do hyperthermia heat stress training at home that can replicate (or actually exceed based on my results) the benefits found in studies due to it cheaper competitors being underpowered."***

Increasing Core temperature to 104.5 degrees can kill Lyme Spirochetes. We have 13 testimonials on YouTube about the Relax Sauna and abating symptoms.

Effective, Safe, Durable & Convenient to use !

Using advanced technology, the Relax Sauna radiators shine 1500 watts of FIR energy against the back wall of the silver tent, which acts as a mirror. At 186,000 miles per second, within 1 second, the Relax Sauna light energy creates a feeling of being immersed in a healing FIR Light box with NO EMF (no electricity) Any damage to neutral EMF coming from the radiator is antidoted by the powerful healing effects of the Relax Far infrared Energy.

Relax® Far Infrared Energy Penetrates deeper than Near-Infrared Saunas !

Study also shows Relax Sauna Energy far more effective in Increasing Microcirculation

BEWARE ! - Almost All quoted Research on Near infrared (LEDS) has nothing to do with Near Infrared Saunas ! - Wow !

Research (on pubmed.com) compares the Relax Far infrared 200 watt Table Lamp to a 250 Watt Phillips Near Infrared Heat Lamp. They concluded Far Infrared was FAR MORE EFFECTIVE in increasing Microcirculation & Penetrating DEEPLY into Human Tissue. See: www.relaxsaunas.com/townsend.html to view this Study presented in 2004 at the Pacific Rim Biophotonic Conference in Taiwan.

ONLY Resonating Far Infrared Energy Pulsates the Water Molecules in your Body

Your Body resonates (as do all mammals and birds) at about 9400 nanometers (9.4 microns), water at 8000 nanometers Our Semi-conductor Chip technology allows no wiggle room, and filters out all energies that do not resonate with our cells This includes Near Infrared, Mid Infrared, and non-resonating Far Infrared greater than 14 microns (14,000 nanometers).

Pulsating the water molecules in your body creates a Dynamic Cascading effect of...

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

Search for "Relax Sauna Testimonials" on YouTube.

There are over 800 Video Testimonials on YouTube on how the Relax Sauna has transformed people's lives, How it has instantly reduced their pain, how it has given them a special feeling of upliftment, and much more.

CALL 626.200.8454 **www.relaxsaunas.com** **moment98@aol.com**

GO TO www.relaxsaunas.com/townsend.html Use code townsend19 to get $120 off the cost of a Relax Sauna until Jan 31, 2019

BioDisrupt™

Triple Action Support

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*

In this Issue

January 2019 | #426

On the cover: Pathfinder Bioinformatics Scholars, Center of Excellence in Generative Medicine, University of Bridgeport, College of Naturopathic Medicine
Front row (L-R) Far Rahman, Peter D'Adamo, Sara Zara; Middle row (L-R) Jessie Tommie, Katelyn Leib, Ashlund Zikmund, Frank Song, Robert Boyd;
Back Row (L-R) Emily D'Adamo, MacKenzie Mitchell, Anthony Pascucci, Thea Marx

Peter D'Adamo, ND – New Genetic Database for Individualized Health Care (pg. 57); Mood Disorders and the GI Tract (pgs. 25 and 28); Nutrition and Epigenetics (pgs. 78 and 84); Preventing Type 2 Diabetes and Metabolic Syndrome (pg. 34); Diagnosing "Leaky Gut" (pg. 38)

Coffee Aids Metabolism and Weight Management

by Steven M. Helschien, DC

"Coffee Aids Metabolism and Weight Management" is one in a series of articles, written to educate the healthcare community about the science behind the healthy benefits of coffee.

Introduction

One thing that proponents of healthy eating love about organic premium coffee, besides its high antioxidant content, is its low-calorie count. In fact, black coffee without added cream or sugar has next to zero calories. Frappes or creamy lattes withstanding, there is very little to account for in daily meal-tracking and calorie counting. It's a choice people can feel good about, and there is an added benefit to drinking coffee that will make you feel even better – literally. There may be weight-control benefits to drinking coffee in addition to its low-calorie properties, due to its boost in metabolism.

Metabolic Syndrome

Heart disease, type 2 diabetes, non-alcoholic fatty liver disease, and even some cancers often have something in common, a precursor called - metabolic syndrome. Metabolic syndrome was first named a medical condition in 1998. It is a series of risk factors that often show up as precursors to other diseases. Symptoms of metabolic syndrome include a large waistline (over 40 inches for men and 35 inches for women), low HDL cholesterol, high triglycerides, high blood pressure, and high fasting glucose levels.

People with the risk factors for metabolic syndrome have double the risk of cardiovascular disease than people who don't, and five times the risk of developing type 2 diabetes. They often become insulin resistant, meaning that their bodies don't respond correctly to insulin, which helps the liver turn food into fuel. This disruption in metabolism is a core to many of the problems that comprise metabolic syndrome, and can also lead to the development of non-alcoholic fatty liver disease (NAFLD).

Maintaining a healthy weight is one way to keep metabolic syndrome (and all of the diseases it can lead to) at bay. And while the lower caloric intake that comes along with drinking black coffee definitely helps, coffee also has components that directly help aid in metabolic processes. There is evidence that drinking coffee can speed up your metabolism and help you lose weight. "Bioactive compounds in coffee reduce insulin resistance and systemic inflammation," says Ming Ding, Harvard T.H. Chan School of Public Health.[1]

Multiple studies verify an inverse relationship between coffee consumption and metabolic syndrome. A 2015 meta-analysis conducted at Qingdao University Medical College in China, which looked at 11 published reports, 13 studies, and over 150,000 participants, found an inverse relationship between coffee drinking and metabolic syndrome in both cross-sectional and cohort studies.[2] It appeared that how much coffee a subject drank played a major role in how low their risk was to metabolic syndrome. Also, the group that consumed the most coffee had the lowest rates of metabolic syndrome and obesity.

Is it the caffeine or other components in coffee that have an effect on metabolism? It's well known that many athletes use caffeine as a performance-enhancer. A study published in the *International Journal of Sport Nutrition and Exercise Metabolism*, said that athletes who used caffeine, pre-workout, burned 15% more calories for the ensuing three hours than others who used a placebo.[3] But, other scientists have used controlled scientific tests to determine which metabolism-boosting properties were due to caffeine and which were the results of other components that are present in coffee – specifically chlorogenic acids (CGAs).

A 2015 Italian meta-analysis determined that most of coffee's effects on metabolism had nothing to do with caffeine, saying instead that, "Chlorogenic acids have demonstrated insulin metabolism."[4] This means that the CGAs in coffee produce healthy blood pressure levels because they have an anti-inflammatory effect on the tiny cells that make up the walls of the blood vessels. Plus, they improve how quickly and efficiently the body turns food into fuel. Some estimate it to be 3–11% improvement in metabolic rate for regular coffee drinkers.

Also, a 2016 Spanish study tracked urinary metabolomes.[5] After a period of time when they "washed out" all caffeine and other substances from their systems, two groups of participants between age 25-44 were assigned either a daily coffee beverage or a daily beverage that only contained

the same amount of caffeine found in a cup of coffee and none of the other characteristic compounds. The study determined specific metabolites, unique to coffee, impact energy metabolism. It showed biomarkers of both short- and long-term intakes of coffee products were involved in energy metabolism (after acute intake) and microbiota metabolism (after sustained intake).

The Healthiest Coffee – Purity

You can be assured the coffee you drink is supporting healthy metabolism and weight – if you're drinking the healthiest coffee you can buy – Purity coffee. Purity has the maximum level of antioxidants in any coffee, as well as CGAs that will help stimulate insulin sensitivity. Purity coffee was found to be two to ten times higher in antioxidants than 49 other brands that were independently tested.[6]

Purity coffee yields the greatest potential health benefits due to the way it is grown, handled, and roasted, plus it is tested with strict standards every step of the way. Most conventional coffees test positive for pesticides and herbicides, and low-quality coffees may contain up to 50% mold or mycotoxins.

Under-roasting or over-roasting can also have a dramatic effect on the health benefits of coffee. Purity uses a proprietary roasting method that roasts the beans just enough to reduce the acrylamide to the lowest levels and prevents over roasting, which risks the development of harmful polycyclic aromatic hydrocarbons (PAHs).

Supplements for Metabolism and Weight Management to Take with Coffee

- **L-theanine** is an amino acid found almost exclusively in teas from the plant, *Camellia sinensis*, (containing green tea catechins and caffeine). It is used to promote relaxation, without sedation, and rejuvenation. It has been shown to be effective at reducing stress.
- **Teavigo** contains caffeine-free pure EGCG, a powerful antioxidant that supports metabolism and benefits almost every organ in the body. It is cardio-protective, neuroprotective, anti-obesity, anti-carcinogenic, anti-diabetic, anti-atherogenic, liver protective, and beneficial for blood vessel health.
- **Capsiate Gold**™ is a clinically proven weight management supplement that increases your metabolic rate and can aid in weight management goals. This bio-identical chili pepper supplement (which has no burning) is taken in the morning, and increases metabolism and energy expenditure, while pursuing sustainable, long-term weight management. There are no stimulating side effects, nor unpleasant aftertaste. It is also gentle-on-the-stomach.
- **NuLean** is a weight-loss program demonstrated by research and proven by doctors and their patients.

The NuLean program is based on nutritional science and biological research. Studies show NuLean 21+7 Slim-Down Program is a proven and effective weight-loss program.[7] Excess

➤

Coffee, Metabolism and Weight Management

➤

fat is a symptom – a red light, indicating that you are probably suffering from both a sluggish metabolism and a toxic body. To lose weight the healthy way, you must cleanse the body of harmful toxins and provide the exact nutrients needed to kick start your metabolism. With these elements properly combined, your appetite will automatically adjust to crave healthy foods thereby cutting down on eating foods that are not good for you. All of this is easily accomplished with NuLean's Slim Down Program.

The first 21 days of the 21+7 Slim-Down Program consist of two phases: weight loss and detoxification. The last seven days is the third phase and is designed to successfully maintain weight loss. If you want to lose more weight, start the 28-day program again until you've lost the weight you want and then continue to follow the maintenance part of the program to maintain your weight loss.

The program consists of the following:

- **NuLean Fiber-Rich Protein Shake**, a proprietary blend of proteins, fibers, and digestive aids to act as a nutritious meal replacement and assist in losing weight, maintaining muscle mass, and energizing the cells.
- **NuLean Complete Body Cleanse**
- **NuLean Quick Burn**
- **NuLean Body Balance**
- **NuLean Gentle Colon Cleanse.**

Conclusion

Coffee might be the world's richest superfood – full of powerful antioxidants. It has been proven to have multiple health benefits:

- Enhances brain function
- Reduces the risk of Alzheimer's, Parkinson's, and dementia
- Protects the heart and cardiovascular system
- Fights cancer
- Reduces the risk of type 2 diabetes
- Protects the liver
- Improves sports performance
- Helps fight depression and enhances mood
- Reduced risk of retinal damage
- Reduced risk of MS
- Pain suppressant
- Extends your life.

As studies show, coffee is also a healthy way to boost metabolism and manage weight. To do this, drink the purest coffee you can for the best health benefits – Purity coffee.

References

1. Ding M, et al. Association of coffee consumption with total and cause-specific mortality in three large prospective cohorts. *Circulation*. 2015; 132:2305-2315.
2. Shang F, Li X, Jiang X. Coffee consumption and risk of the metabolic syndrome: A meta-analysis Department of epidemiology and health statistics, *Diabetes and Metabolism.* 2016; 42: 80–87.
3. Higgins S, Straight C, Lewis R. The effects of pre-exercise caffeinated coffee ingestion on endurance performance: an evidence-based review. *International Journal of Sport Nutrition and Exercise Metabolism*. 2016; 26: 221-239.
4. Buscemi S, Marventano S, Antoci M. Coffee and metabolic impairment: An updated review of epidemiological studies. *NFS Journal*. 2016; 3: 1-7.
5. Madrid-Gambin F, et al. Impact of chlorogenic acids from coffee on urine metabolome in healthy human subjects. *Food Research International.* 2016; 89: 1064-1070.
6. Independent laboratory tests. Purity Coffee. Available at: https://puritycoffee.com/lab-results/. Accessed September 23, 2018.
7. NuLean research. NuLean. Available at: https://www.nulean.com/research/. Accessed September 22, 2018.

◆

Dr. Steven Helschien (a.k.a. Dr. Coffee) is a coffee aficionado and believes that coffee is a powerhouse superfood. He is the founder of Level 1 Diagnostics (a cardiovascular testing program that uses advanced, noninvasive technology to detect and prevent cardiovascular disease), and Level 1 Therapeutics (a health and wellness program dedicated to supporting optimal health). Dr. Helschien is passionate about progressive health issues and encouraging people toward greater health and wellbeing.

Happy Holidays!

Our February/March Issue focuses on Women's Health and will be mailed in early February.

(No Issue will be mailed in January)

The *Townsend Letter* office will be closed December 17th to January 2nd for the holidays.

We wish you happy holidays and look forward to your reading the *Townsend Letter* in 2019!

FCT® and Weight, its Loss, Gain, and Eternal Struggles

by Savely Yurkovsky, MD©

When I first saw, in my office, a middle-aged dentist with a puffy round face and body and recommended that he eliminate white flour from his diet, this is what he said: "Doctor, let me make it clear what you are expecting of me. When I am driving and see a pizza place, I don't just drive by it, but I start shaking and drooling and for the next mile I am driving with my head turned back, glued to that door and fighting myself, tooth and nail, to turn around to go in or not. This is even if I am already stuffed up to my ears. The next pizza joint re-kicks this cycle. With bagels and pasta, it's just as bad, I crave them as a heroin addict, and eat them day and night, too."

Yet, at his last visit, with quite a few FCT treatments in-between, and my never pushing him to go cold turkey on these dietary 'heroin's', he stated something different: "Doctor, I want you to know that as far as pizza goes, not only I've lost all taste for it, but I almost hate it. Bagels, I care less about and from eating them six days a week, I do it only once on Saturdays or Sundays and even, then, for psychological reasons. Pasta has become a non-entity that I don't even look at." In the process, the good dentist has shed some good 30 pounds of his bulging belly and other parts, without indulging in any exercise activities or counting calories. As for the additional health bonuses, his energy level has doubled and become normal, and lifetime anxiety gone. Indeed, he was so encouraged by his ongoing health progress with FCT that he became too impatient to wait to remove his mercury fillings, by one of his colleagues, and committed some dental hara-kiri by stuffing a drill in his mouth and scooping these out.

So, what has been addressed by the FCT treatment between his aforementioned opposite statements explains why so many weight-loss low calorie and carbs diets either stop working in the short run or fail in the long term to correct carbohydrate intolerance and food addictions. These never fail to re-cycle the binges and falling off the wagon. Millions of overweight citizens have gone through these cycles mainly because these diets are incapable of addressing the very causes of food addictions and low metabolism, where the latter is set on weight retention and poor burning mode. They also know that fat-burning pills work only in TV and internet commercials where all of the quoted alleged 'science' behind these pills 'proved' itself just on lab animals, who normally have little to do with people.

While to the credit of alternative medicine, it connected food allergies and cravings to some of their causes – gastrointestinal infections with candidiasis and parasites – yet the majority of these treatments have often produced their own pattern of re-cycling, as the benefits of these treatments and diets don't hold. The reason is that underneath these infections lay other problems, which sustain them and cause more damage on their own, too. Among these are environmental pollutants, such as mercury, lead and other toxic metals, pesticides, residues of antibiotics, and deficiency of the protective gut bacterial flora – all of which have allowed these infections to become easily implanted and sustained. They owe this to the broken local immune and cellular barriers, as well as poor systemic immunity whose organs too have been undermined by most of the same pathogens and problems.

In addition, these infections are fed with sugar, starches, and antibiotics with the latter readily prescribed by the doctors and added to our foods. All of these assure their everlasting feast and longevity where drug, herbal, oxygenative, electrocuting and any other treatment that attempts to just kill them only makes them stronger, in the long run, due to their uncanny ability to mutate into more aggressive and resistant forms.

FCT focuses far more on the total state of impaired gut and systemic immunity, instead of just rushing to kill these infections. A big part of it addresses restoration of their main competitors – indigenous bacterial microflora – and doing this on an individualized basis, by determining through a bioresonance testing specific missing organisms and replenishing these with specific probiotics. A big role, also, in the pulling the rug from under the feet of infections, lies in addressing a total state of all organs of the immune system as well as its main power source – the endocrine system. Many of these organs are, usually, just as poisoned with mercury and other toxic metals and EMFs as the GI tract, itself.

Interestingly one patient has noticed that driving a car, which is a pure metallic electromagnetic cage, would trigger a protrusion of his abdomen. This is quite logical, since mercury and toxic metals, which reside inside the gut and bound to large parasites and yeasts, act as an antenna for electromagnetic radiation, everywhere, in our daily life. All and all, weight problems and their related food addictions and allergies are not isolated gastrointestinal or caloric problems, but

➤

➤

one of a multisystemic chronic disease of the entire body.

What is the best way to diagnose and treat all of these morbid agents and their victims – the gut and the rest of internal organs? Through a skillful bioresonance testing, one can overcome the inability of lab tests to detect the primary causes of all chronic diseases, which reside inside of the internal organs themselves. Based on applicable energetic properties of all living and nonliving, as established by physics, bio-resonance testing is able to noninvasively penetrate, through email-like signaling, any part of gastrointestinal tract, metabolic, detoxifying, endocrine, immune, and other organs to apprehend the primary causes of their malfunctions.

Following this intelligence gathering, the detected pyramids of causes get dismantled through informed water, which is the essence of homeopathy, as established by physics too. The contained information in water stimulates the body to carry out specific work to rid the causes of its illness in order to heal. The information in water may, as needed, stimulate the immune system against any infection and stimulate organs and tissues to release mercury and other environmental pollutants, antibiotics and other morbid agents.

As the causes leave, so do the food cravings, addictions, allergies, and excessive weight, with most of the latter being comprised far more of retained toxic fluids than fat. The vicious cycle of junk food cravings, sustained by gut infections and consuming carbs and sweets that, in their turn, feed and grow these infections and lead to more gain in weight and cravings, falls apart. Speaking of sugar, commonly promoted 'healthy' substitutes represent only unhealthy commercial myths since the microbes care less which type of sugar feeds them.

The following cases highlight the main aspects and advantages of this approach to overweight health problems.

Case 1. Alicia is only 12 years old but her bio-resonance testing has suggested as many as eight layers of causes affecting her digestive tract and many other organs, which would explain her progressive allergies and declining health. The allergies started at the age of four to only a few foods, but over the years and in spite of conventional and alternative-integrative treatments, have been spreading to more foods and, then, chemicals. She started severely reacting to even ordinary items, such as toothpaste, shampoos and earrings. Her general health has been declining too, with daily frequent hypoglycemic spells and mood swings requiring frequent eating, in spite of a strict healthy rotation diet. She also complained of mental sluggishness, puffy face, and pizza cravings. Her body systemic inflammation has been in such a hyperactive state that even a routine skin allergy testing has quickly led to a bilateral ear infection, requiring antibiotics, where she badly reacted to some of these, also. All and all, she has been progressing on a familiar path where the safe world was getting progressively smaller and smaller for her. The bio-resonance testing has offered good reasons for this in the way of detecting several yeast infections, bacterial and a few worm infections, residues of antibiotics, as well as mercury from different sources in her small intestine.

One of the sources of mercury was an allegedly 'healthy' rich-in-minerals salt which, according to my bio-resonance testing experience, turned out to be even more rich in mercury. This was confirmed by the two independent reputable toxicological laboratories. To avoid projecting any possible bias in my testing, I refrained from asking her mom, beforehand, which salt she was using at home, yet when out of more than 20 samples tested, I showed her the one whose toxic residues of mercury I have found in her daughter's gut, all she said, "This is it." She also confirmed the other usual source of mercury by admitting to having mercury fillings, which she completed removing shortly before the pregnancy. Yet mercury, still, had to remain in her body and passed to Alicia in utero and through breast milk.

Besides the small intestine, which is the main site of digestion and absorption of the nutrients, 10 other organs, from head to toe, covering brain, immune and endocrine systems deemed to malfunction too, either due to some of the same detected causes or getting worn out by an ongoing systemic stress imposed by them. In spite of taking probiotics for years, the test also pinpointed a deficiency of a specific probiotic, which was dispensed along with informed water remedies, for all of the found problems. The case is very recent and at the time of this writing I do not know yet her clinical response but, based on long experience in treating the underlying causes of conditions like these, her long-term prognosis looks very promising.

Case 2. Sixty-year-old Mr. G had a swollen body and face and carried an extra 30 pounds in weight. He was also addicted to sweets and wine. Bio-resonance testing detected small and large parasites as well as candida infection and lead intoxication in his large intestine. Many other organs, including the immune, were energetically drained, too, and remedies with informed water were administered to address all of the findings. He was also advised to eliminate sweets and wine in order to stop feeding those infections.

Three months later he returned with a normal-looking face and reported that he lost 25 pounds ae well as a lifetime addiction to sweets and wine. He also shared that he was able to discontinue two drugs for his hypertension with his blood pressure becoming even low for his age. Likewise, even after he discontinued two drugs for his prostate condition, his urinary stream has improved, urinary frequency went down, and occasional prostate pains ceased. Following the second testing and its based treatment, his chronic toenail black fungus much reduced and he has decided to end his retirement and go back to work, due to a gained superb energy level. He said: "Since I started your treatment, I feel I have energy like I'm 40 again."

Case 3. A 100-pound-overweight 40-year-old man was first seen in April 2018. Besides sugar and carb cravings, his multisystemic chronic disease was evident by multiple other complaints and conditions from the brain down. Among many malfunctioned organs the bio-resonance testing found his gastrointestinal tract being infested with multiple parasitic and yeast infections, pesticides, mercury, residues of antibiotics, and toxic metals from a popular brand of carbonated water. Remedies of informed water were administered to inform his body of the

exact work that it needed to do in order to eliminate these causes and regain health. Over the period of ensuing months, and while gradually removing mercury fillings, he lost 40 pounds of weight along with his cravings for carbs and sweets.

Case 4. This case is interesting because, typically, when the gastrointestinal tract is sufficiently cleansed from infections and toxins the weight does not stick even when the forbidden foods are consumed. Besides shedding many pounds, said this 58-year-old woman: "It is amazing I eat carbs and sweets and I don't blow up at all, as I used to." Even though the cravings are gone, yet for emotional reasons she has to revisit these comfort foods.

When Gaining Weight Is Not a Vice

While being overweight is mistakenly perceived as an attitude problem instead of disease, being underweight is a disease also. More often than not, underweight people avoid junk food and alcohol because they know that they are sick. But, in this disease too, instead of conducting bookkeeping operations with calorie intake and increasing these, one attempts to find and correct its primary causes and allow the body to do the rest.

Case 1. In the case of a scrawny looking man in his 50s, Mr. R, gluten intolerance was not just a matter of food allergy but, going all the way back to his early childhood, one of survival. For years, until he finally, in his teens, saw a good doctor who recognized severe gluten intolerance, he was constantly battling bad digestion, severe fatigue, low weight, and recurrent infections. The latter commanded a slew of antibiotics, which is a disease of its own that is packaged and spread in a pill form. Among the many reasons for this is, using a military term, a collateral damage inflicted by antibiotics destroys friendly bacterial flora, mutates both aggressive and friendly bacteria in the body, and feeds yeast infections. Not surprisingly, quite a few patients noticed an onset of sugar and carbohydrate cravings following antibiotics administration. Even after adhering to a 100% gluten free diet and gaining some energy and weight, Mr. R still remained sick.

At the time of his first visit, his weight, muscle mass, energy, and stamina were poor. He required regular supplies of nutrients both orally and intravenously, from his integrative MD, and his weight would never budge, for decades, beyond a gain of a pound that would vanish mysteriously anyway. Integrative medical services allowed him to keep his meat grinder job on Wall Street, but good health or quality of life he didn't have. The case of genetic gluten intolerance seemed certain, given such an early onset and severity; however, this turned out not to be the case following his FCT treatment,

FCT® and Weight

and I doubt if such pure genetic cases even exist. Following multiple FCT cycles of bio-resonance testing and treatment with informed water, the many causes behind his gluten sensitivity and overall poor health were elicited and addressed. These were multiple parasitic and yeast infections, deficiency of indigenous gut flora, residues of antibiotics and mercury,

➤

➤

as well as toxic metals from a bottled spring water. All of these were also poisoning and wearing out his immune and endocrine organs.

Soon after undertaking FCT cycles, he stopped and later said that he was no longer missing his oral and intravenous nutrients. He subsequently has gained and kept 11 pounds in weight, mainly as muscle mass: "I do 240 pushups a day. I never had such a muscle in my life, never," and "This treatment has turned me into a superman." Interestingly and speaking of genetic diseases, he has been consuming gluten routinely in any shape or form, without knowing what gluten allergy is anymore.

Case 2. A 60-year-old MD in the course of his FCT treatment, unrelated to weight, reported that, to his surprise and in spite of not pumping any weights or consuming muscle building supplements, he noticed a weight gain due to a considerable increase in his muscle mass.

Case 3. A 72-year-old woman with colon cancer and suspected metastases to liver on the CT scan had colon surgery to remove the tumor but refused chemotherapy. She presented to my office looking pale, sick, and complaining of poor appetite, low energy, and weight loss. Following the first FCT treatment she gained four pounds, good appetite, and energy and quoted her coworkers saying, "You look remarkable." Her oncologist and surgeon told her, too, that they've never seen 72-year-old people recovering that fast. After two FCT treatments, her total weight gain reached 14 pounds, and she continues doing well, working fulltime in spite of the serious disease.

Case 4. This young woman represents a typical case that shows how one chronic disease, frequent bronchitis, was replaced by another chronic disease caused by antibiotics. Initially, her frequent antibiotics prescribed for recurrent bronchitis seemed bringing these back sooner. Then, following one of their courses, she developed pneumonia which was treated with antibiotics. Shortly after, another bout of pneumonia set in that was treated with antibiotics, again, following which total hell broke loose. She developed up to 10 daily bouts of diarrhea, severe exhaustion, brain fog, food allergies, and 25-pound weight loss. Extensive GI work up by gastroenterologists have only issued a common label, irritable bowel syndrome, but not its causes. Her diet was perfectly healthy for her condition and allergen free.

Bio-resonance testing has elicited a number of candida infections, residues of several antibiotics, and *Clostridium difficile* bacterial infection in her gastrointestinal tract. Her bronchi tested as being still infected with *Mycoplasma pneumonia* bacteria, despite all of the antibiotics, and the immune organs poisoned with mercury, thanks to her mercury filling.

She was prescribed informed water to address all of these findings. Upon her return, seven weeks later, she stated that her diarrhea and fatigue were gone, and she regained all of her lost weight and even more, 30 pounds in weight. A pleasant side bonus, her sex drive was regained also.

Case 5. A woman in her mid-sixties with two primary cancers, breast and colon, with metastases to lymph nodes, lung, and bone was first seen in March 2016. Shortly after she underwent colon surgery to remove a substantial part of her colon and tumor, she lost 25 pounds and felt fatigued. She refused chemotherapy due to its unlikely benefit in her condition. The oncologist projected her survival to be less than a year. Her bio-resonance testing detected mercury (silver amalgam fillings removed in the past), multiple chemicals/carcinogens in her breast, colon and immune organs, as well as gastrointestinal and systemic infections. Informed water was prescribed to address these problems and stimulate her immune system against cancerous cells. She quickly gained some 10 pounds and full energy level and soon reported that her breast tumor felt smaller and softer.

At this time her weight remains stable, where loss would be an ominous sign, and she leads a normal lifestyle. Her oncologist has changed her tune from "do chemotherapy" to "keep doing what you are doing."

Conclusion

We train in this system those who wish to learn it for the sake of their own, their family's, and patients' health.

◆

Savely Yurkovsky, MD, is internationally known as an author and teacher with an extensive background in the thorough study of scientific principles behind the numerous alternative and conventional approaches. Having realized that the primary source of health and disease, according to physics, stems from the corresponding cellular energy fields, he adopted a revolutionary new medical model, one that interfaces the theories of biology and physics established by his mentor, Professor Emeritus William A. Tiller, PhD, of Stanford University.

Having evolved a unique bio-energetic medical system that integrates a great deal of pertinent but, until now, underused knowledge from medical and non-medical sciences, Dr. Yurkovsky's system has been able to transform the often vague nature of medical specialties from "hit and miss" paradigms into a far more effective, exact and predictable science. Dr. Yurkovsky has founded a teaching organization, *SYY Integrated Health Systems, Ltd.*, which is dedicated to sharing his medical system under the concept of FCT – Field Control Therapy® or Guided Digital Medicine™. Since 1999, he has taught this curriculum to medical doctors and licensed health care professionals with special emphasis on energy-based diagnostic and therapeutic modalities aimed particularly at toxicological, biological or nuclear agents. These, as a rule, elude conventional and most of the alternative diagnostic methods yet represent the primary source of all chronic diseases. His book, *Biological, Chemical, and Nuclear Warfare – Protecting Yourself and Your Loved Ones: The Power of Digital Medicine*, is an excellent illustration of both the scientific basis and effective practical means to combat the ravages of acute and chronic diseases in our toxic world. His system is the only alternative medical modality that has drawn attention from one of the departments of the Homeland Security Office. This year, along with several other doctors from premier medical schools in the US, he has been nominated for the prestigious Bravewell Leadership Award for "*significant contributions to the field of medicine*" and "*compelling vision for the future of medicine*."

Dr. Yurkovsky offers training to capable health care professionals. For enrollment, contact SYY Integrated Health Systems, Ltd.; www.yurkovsky.com; e-mail: info@yurkovsky.com; phone: 914-861-9161; fax: 914-861-9160

Mood and the Microbiome

by Jeremy Appleton, ND

The axis connecting the gut microbiome with the brain and central nervous system means that gut microbes can profoundly affect brain development, behavior, and mood. Gut bacteria composition may be determinative of normal neurologic development in utero and in the neonatal period. Moreover, intestinal permeability defects are thought to underlie the chronic low-grade inflammation observed in stress-related psychiatric disorders. Those with symptoms of depression frequently exhibit increased expression of pro-inflammatory cytokines, such as IL-1β, IL-6, TNF-α, as well as interferon gamma (IFN-γ), and C-reactive protein (CRP). And thus, anti-inflammatory drugs, like COX-2 inhibitors, have previously demonstrated efficacy in treating major depression.[1] Gut microbiota influence transcription of these same cytokines, with dysbiosis triggering the so-called inflammasome pathway, while beneficial metabolites (short-chain fatty acids in particular) reduce production of pro-inflammatory cytokines, such as NF-κB.

These converging observations have led to increased recognition that stress and mood disorders, such as depression and anxiety, are influenced by the health of the gut and the microbiome's ability to modulate systemic inflammation. Research has demonstrated that an inflammatory phenotype alters neurotransmitter metabolism by reducing the availability of neurotransmitter precursors and activating the hypothalamic-pituitary-adrenal (HPA) axis, all of which contribute to the pathogenesis of clinical depression. Although introduced as early as 1910, it has taken over a century to establish the so-called gut-brain axis as a critical pathway for the prevention and treatment of clinical depression.

The Gut-Brain Axis

The enteric and central nervous systems are connected by a bi-directional communication network now commonly referred to as the gut-brain axis. Its components are anatomical, endocrine, humoral, metabolic, and immune, with well-documented pathways throughout the autonomic nervous system and the HPA axis. Through this communication network, the brain influences intestinal activities, and the gut influences mood and cognition, a relationship that is guided by the microbiome.

The mechanisms of action by which this influence is directed continue to be clarified by many and varied teams of researchers working in overlapping fields of microbiology, medicine, genomics and other related disciplines. Alterations of the gut microbiota, seen in various scenarios of dysbiosis, have such a profound capacity to influence brain structure and function, that many consider it a paradigm shift in medicine and neuroscience.

Depression, anxiety, and autism spectrum disorders now have well-documented correlations with functional GI disturbances. Conversely, GI diseases, such as irritable bowel syndrome (IBS) and inflammatory bowel diseases such as Crohn's and ulcerative colitis, have psychological features. Research has demonstrated that both scenarios are under the influence of intestinal bacteria.

Stress is known to cause intestinal epithelial permeability alterations, allowing bacterial antigens and lipopolysaccharides (LPS) to enter into the circulation and become humoral influencers, with wide-reaching effects. In laboratory experiments, acute stress has been shown to act on the GI tract by inducing changes in colonocyte differentiation and decreased expression of mRNA encoding tight junction proteins. Also well-known is the relationship between intestinal permeability defects and various GI disorders, such as IBD, necrotizing enterocolitis, and the low-level inflammation commonly seen in metabolic syndrome, obesity and diabetes, as well as in some forms of allergy. Dysbiosis and associated increases in intestinal permeability are now recognized features of rheumatoid arthritis, Alzheimer's disease, asthma, autism spectrum disorders, and other systemic conditions. Research has demonstrated that probiotic supplementation can improve intestinal permeability defects, and thus support resolution of conditions caused or exacerbated by gut barrier dysfunction.

The gut microbiota is well known to support tight junction integrity between enterocytes. Although few clinical trials have directly investigated the influence of probiotic supplementation on epithelial barrier function in humans, evidence suggests lactobacilli are efficacious in this respect. One study showed that a multi-strain combination of lactobacilli, lactococci, and bifidobacteria (Ecologic® BARRIER, Winclove, Amsterdam) improved epithelial barrier function after

➤

➤

pathogenic bacterial and inflammatory stressors, inhibited mast-cell activation, stimulated Il-10, and decreased LPS circulation in vitro.[2] This same combination was later shown to be active in a clinical psychiatric setting.

Clinical Research in Humans

Today, a new class of probiotics, known as psychobiotics, are being embraced by many physicians as a nontoxic intervention for various psychiatric conditions. Preclinical research laid the groundwork to investigate the use of probiotics for the treatment of mood disorders in humans, and several clinical trials have examined the role that probiotic supplementation plays in the treatment of depression and anxiety.

In 2002, researchers conducted a pre- and post-intervention assessment of adults suffering from stress or exhaustion (n=34). They found that a combination of *L. acidophilus*, *B. bifidum* and *B. longum* improved subjects' general condition by 40.7% after six months.[3]

Two years later, a prospective, randomized, controlled, parallel study of healthy students (n= 136) was conducted. Researchers found no significant effects of *L. casei* supplementation on anxiety levels, although beneficial alterations of lymphocyte and CD56 cell counts were observed.[4]

In a randomized, double-blind trial from 2007, consumption of probiotic-containing yogurt had no effect on Profile of Mood States in 124 subjects, although there was improved self-reported mood of those whose mood was initially poor.[5]

In a 2009 double-blind pilot study, two months' supplementation with *L. casei* significantly improved Beck Anxiety Inventory scores in 35 subjects with chronic fatigue syndrome. There was no effect on Beck Depression Inventory scores.[6]

Two studies in 2011 were noteworthy. In the first, subjects with reduced urinary free cortisol had reduced anxiety and depression scores after consumption of probiotics.[7] In the second – a double-blind, randomized, controlled, parallel study – consumption of *L. helveticus* and *B. longum* reduced somatization, depression, and anger-hostility as well as Hospital Anxiety and Depression Scale global scores.[8]

A randomized, double-blind study in 2014 found no significant effects of *L. helveticus* supplementation on perceived stress or geriatric depression; improvements were noted, however, on the digit span test, story recall test, verbal learning test, rapid visual information-processing, and Stroop Tasks scores.[9]

In 2015, a study of young adults with anxiety (N=710) showed that consumption of fermented foods containing probiotic bacteria was inversely associated with social anxiety and neurosis.[10] The most important study of that year, however, was a randomized, triple-blind, placebo-controlled trial (n= 40 non-smoking healthy young adults, mean age 20 years).[11] Researchers investigated the effects of a multi-strain probiotic formula (Ecologic BARRIER, Winclove, Amsterdam). The formula contained specific strains of *B. bifidum, B. lactis, L. acidophilus, L. brevis, L. casei, L. salivarius*, and *Lactococcus lactis* at a dose of 5 billion CFU per day. Consumption of this multispecies probiotic significantly reduced overall cognitive reactivity to depression; specifically, aggressive and ruminative thoughts, as assessed by the Leiden index of depression sensitivity (LEIDS-R). This study is noteworthy because many patients, especially young people with no prior history of depression, would prefer non-pharmaceutical interventions as a first-line treatment.[12]

In a 2016 randomized, double-blind trial (n=40), administration of a combination of *Lactobacillus acidophilus*, *L. casei*, and *Bifidobacterium bifidum* for eight weeks improved scores on the Beck Depression Inventory.[13]

In 2017, Wallace and Milev conducted a systematic review of ten clinical trials, including some of those just discussed.[14] Most of the studies found positive results on measures of depressive symptoms.

To date, clinical trials on probiotics for depression and anxiety have been heterogeneous in terms of dosing, probiotic strain selection, and length of treatment, further randomized controlled clinical trials are warranted to validate the efficacy of this promising intervention.

Jeremy Appleton, ND, is a naturopathic physician and dietary supplement industry professional. An alumnus and former nutrition department chair of the National University of Naturopathic Medicine (Portland, Oregon), Dr Appleton is an author, educator, and Vice President of Science and Education for SFI USA, which manufactures dietary supplements under the Klaire Labs brand. Further clinical references available upon request.

References

1. Müller N, et al. The cyclooxygenase-2 inhibitor celecoxib has therapeutic effects in major depression: results of a double-blind, randomized, placebo controlled, add-on pilot study to reboxetine. *Molecular Psych*. 2006;11:680–684.
2. Van Hemert S, Ormel G. Influence of the Multispecies Probiotic Ecologic® BARRIER on Parameters of Intestinal Barrier Function. *Food Nutr Sci*. 2014;5:1739-45.
3. Gruenwald J, Graubaum HJ, Harde A. Effect of a probiotic multivitamin compound on stress and exhaustion. *Adv Ther*. 2002;19(3):141–150
4. Marcos A, et al. The effect of milk fermented by yogurt cultures plus Lactobacillus casei DN-114001 on the immune response of subjects under academic examination stress. *Eur J Nutr*. 2004;43(6):381–389.
5. Benton D, Williams C, Brown A. Impact of consuming a milk drink containing a probiotic on mood and cognition. *Eur J Clin Nutr*. 2007;61(3):355–361.
6. Rao AV, et al. A randomized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome. *Gut Pathogens*. 2009;1(1):1
7. Messaoudi M, et al. Assessment of psychotropic-like properties of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in rats and human subjects. *Br J Nutr*. 2011;105(05):755–764
8. Messaoudi M, et al. Beneficial psychological effects of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in healthy human volunteers. *Gut Microbes*. 2011;2(4):256–261.
9. Chung YC, et al. Fermented milk of Lactobacillus helveticus IDCC3801 improves cognitive functioning during cognitive fatigue tests in healthy older adults. *J Funct Foods*. 2014;10:465–474.
10. Hilimire MR, DeVylder JE, Forestell CA. Fermented foods, neuroticism, and social anxiety: an interaction model. *Psychiatry Res*. 2015;228(2):203–208.
11. Steenbergen L, et al. A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. *Brain Behav Immun*. 2015 Aug;48:258-64.
12. Hughes-Morley A, et al. Factors affecting recruitment into depression trials: Systematic review, meta-synthesis and conceptual framework. *J Affect Disorders* 2015;172:274–90.
13. Akkasheh G, et al. Clinical and metabolic response to probiotic administration in patients with major depressive disorder: a randomized, double-blind, placebo-controlled trial. *Nutrition*. 2016;32(3):315–320.
14. Wallace CJK, Milev R. The effects of probiotics on depressive symptoms in humans: a systematic review. *Ann Gen Psychiatry*. 2017;16:14. doi 10.1186/s12991-017-0138-2.

◆

KLAIRE LABS®

Target gb-X™

Clinically shown to support positive mood†

Klaire Labs' Target gb-X is the first probiotic clinically demonstrated to support positive mood by influencing the gut-brain axis through the microbiome.†

Powered by Ecologic BARRIER

Ecologic BARRIER is a proprietary blend of 9 probiotic strains shown to positively affect mood by decreasing overall cognitive reactivity to sad mood, rumination, negative and aggressive thoughts.†[1]

Ecologic® inside

PLACE YOUR GBX ORDER TODAY

klaire.com | 888 488 2488

1. Steenbergen L, Sellaro R, van Hemert S, Bosch JA, Colzato LS. A randomized, controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. *Brain Behav Immun.* 2015 Aug;48:258-64.

†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.

Psychiatry Redefined
The Evolution of Psychiatry: From the Measureless Medicine to Precision Healing

by James Greenblatt, MD

Measuring the Mind

Measurement is the basis of all scientific medicine. Clinical diagnoses, treatments, and success rates all rely on definitive, quantifiable data that can be accurately assessed, evaluated, and monitored. Numbers allow physicians to create comparable references and scales that identify and characterize a condition and its severity. Discrete data are vital for effective medical care in every category of health and allows researchers and clinicians to communicate with each other, to patients, and to the public. Technology has generated an era of precision medicine with tremendous potential for early detection and targeted treatment strategies. There currently appears to be no end in sight for advanced technology and the development of tests, devices, and, yes, even medications that improve healthcare practices for the growing and aging global population.

While modern information and innovation has driven the progress of diagnostic and treatment methods for physical health, the same cannot be stated for mental health practice. Traditional psychiatry has taken the role of the "measureless medicine" due to a lack of consistent, objective markers utilized. It is difficult to measure and quantify thoughts, feelings, and moods because each patient's perspective and experience is unique. Clinical diagnosis of a specific mental health condition relies on subjective symptom scales that attempt to categorize by the most commonly reported symptoms. The continually poor outcomes demonstrate that efforts to improve psychiatric treatment have been slow and resulting in more prescription medications but not always improvement in clinical outcomes, rates of recovery and, most important, remission of symptoms. Attempts to refine mental health diagnoses have only led to a thicker, heavier DSM volume and more turns of the revolving door representing failed prescriptions.

A set of objective markers for mental health is elusive because mental illness is not one disease. Even within conditions such as depression or schizophrenia, symptoms and severity often vary significantly in nature and degree. Consequently, there is not one test that can diagnose every case, nor is there one treatment protocol that applies to every patient under a diagnostic label. Furthermore, the typical approach to psychiatric treatment fails because traditional methods ignore the clear connection between the body and the brain. Indeed, many mental health sufferers first mention their symptoms to their primary care physician because of physical complaints that accompany their psychological struggles. Standard psychiatric evaluations neglect to assess or consider physical symptoms, diet, or other lifestyle behaviors that are linked to brain function. Mental illness is complex and multi-factorial, requiring a comprehensive analysis of the biochemical, physical, genetic, social, and environmental influences that induce and differentiate each patient's condition. This perspective describes the framework of integrative psychiatry, which takes into account the whole person as a function of a unique biochemical makeup and nutritional needs that must be balanced to restore and maintain physical and mental wellness.[1]

A Unique Set of Stripes

Biochemical individuality is a core concept of integrative and orthomolecular psychiatry. A comprehensive evaluation of the physical, genetic, biochemical, psychological, and environmental variables unique to each patient highlight specific imbalances throughout the brain and body that can be targeted with nutrition and dietary supplements in virtually all psychiatric conditions. Plenty of evidence supports the conclusion that psychiatric illness involves structural, biochemical, and metabolic abnormalities that influence mood and behavior. New imaging technology confirms that the anatomy of the brain and the integrity and connectivity of neurons is different in individuals with all types of mental illnesses, suggesting that specific and measurable biomarkers exist. Single or combinations of nutrient deficiencies manifest in varying forms and degrees of brain dysfunction based on their direct

and indirect effects on neurotransmitter concentrations and ratios.[1]

The zebra is a beautiful and highly recognizable creature with its distinctive and striking alternation of white and black stripes. One hardly stops to consider the number or direction of its stripes, immediately assigning the name 'zebra' at first glance by its stereotypical hide. It turns out that the pattern is unique to each animal, like its own identifying fingerprint. When I learned about this fact, it inspired me to coin the acronym THE ZEEBRA to describe my integrative, individualized approach to treating the mind, body, and spirit of patients struggling with mental illness:

T is for Take care of yourself (Healthy Diet and Lifestyle)
H is for Hormones and Herbs
E is for Exclude (Allergens and Food Sensitivities)

Z is for Zinc and Other Minerals
E is for Essential Fatty Acids and Cholesterol
E is for Exercise and Energy
B is for B-vitamins
R is for Restore (Intestinal Microbiome)
A is for Amino Acids and Protein.

THE ZEEBRA model encompasses a set of the most frequently encountered problems I have seen in my clinical practice as well as those topics supported by significant research evidence. With growing scientific and medical knowledge and advanced tools at our fingertips, this approach provides specific treatment targets that can be measured, compared, and monitored. Individual patients may have one or multiple components out of balance, but reversing nutrient deficiencies and restoring neurotransmitter balance can resolve multiple symptoms and improve the efficacy of other treatment modalities.[1] In this way, the methodology of THE ZEEBRA approach provides an entirely new and objective way of treating patients with the goal of long-term recovery.

The nutrients we obtain from food go far beyond fueling our daily movements and activities. Vitamins, minerals, amino acids, and essential fatty acids are critical building blocks for the hormones and neurotransmitters that direct the function of our brains and drive mood and emotion. Impediments to the digestion, absorption, transportation, and utilization of nutrients from food all have implications for mental health. Innate errors of metabolism, allergies and food sensitivities, and poor lifestyle habits all contribute to an individual's biochemistry. The steps of THE ZEEBRA model applied to each patient reflect a comprehensive biological snapshot of what needs to be reinforced, balanced, or compensated for due to genetic polymorphisms.[1] This article focuses on the "R" in THE ZEEBRA, describing an integrative approach to restoring harmony to the brain by way of the gut. This model offers help to clinicians on their journey to *redefine* the outdated model of contemporary psychiatry.

The Gut-Brain Connection

Regardless of whether we know or understand the science, we are all familiar with the connection between the gut and the brain. Everyone has experienced the powerful influences that hunger or an upset stomach can have on mood and focus. Our intestines are home to trillions of bacteria, forming a diverse and fluctuating community of beneficial and potentially harmful species that we call the microbiome. Despite a common wariness of bacteria, the presence and composition of the microbiome is essential in both the brain and body. As research on our gut bacteria continues to accumulate, there seems to be endless links between the nature and activity of these hardworking microbes and human health. While a majority effort has focused on the effects of the microbiome on gastrointestinal function and immunity, emerging evidence suggests many aspects of our psychology are also driven by these mysterious cohabitants.[2]

The gut-brain axis is a compact term that represents a dynamic, bidirectional superhighway of information communicated between the intestines and the nervous system. Messages travel to the brain directly via the vagus nerve, and more indirectly by immune cells, hormones, and neurotransmitters. Neurotransmitters serve as the boldest chemical messengers of information ➤

➤

that regulate emotion and behavior. Specific concentrations and ratios of neurotransmitters are required for optimal mental function; and imbalances between stimulatory and inhibitory signals exert powerful effects on mood, attention, and impulse control. Stable mental well-being is highly dependent on the balance of hundreds of neurotransmitters and the signals they provide to neurons in the brain.[3]

Throwing Off the Balance

A balance of bacterial populations in the gut is key to unhindered communication along the gut-brain axis. Intestinal dysbiosis occurs when the microbiome population contains a greater proportion of hostile bacteria that can wreak widespread damage and manifest as part of many chronic diseases outside the gastrointestinal system, including allergies, diabetes, and cardiovascular disease.[4] The *Clostridia* genus encompasses approximately 100 species of bacteria of both beneficial and potentially harmful strains, including *C. difficile*, the notorious originator of *C. diff* infections commonly acquired at hospitals. *Clostridia* are well-publicized for becoming antibiotic-resistant due to overuse of high-dose and long-term antibiotics. Overpopulations of *Clostridia* bacteria are often found in young children incessantly treated with antibiotics for ear infections and other childhood illnesses.[2]

Metabolic byproducts of the microbiome can also pass from the intestine into the bloodstream and deliver messages to the brain. Like their microbial source, these chemical signals can be both positive and negative. Beneficial bacteria linked to antidepressant and anxiolytic effects, often called psychobiotics, produce neurotransmitters such as serotonin and *gamma*-amino butyric acid (GABA) that stabilize mood and promote calm.[5] Unfriendly bacteria, including some strains of *Clostridia*, generate substances that can alter normal neurotransmitter signals and disrupt mood and focus. Though symptoms of autism, attention deficit hyperactivity disorder (ADHD), major depression, and schizophrenia appear widely distinct and variable, discovery of a novel biomarker may explain a shared antagonist in psychiatric patients characterized by aggressive and compulsive behaviors. *C. difficile*, along with seven other *Clostridia* species, promote the synthesis of 3-(3-hydroxyphenyl)-3-hydroxyproprionic acid (HPHPA) in combination with human metabolism of the amino acid phenylalanine. Clinically used as a biomarker of dysbiosis, HPHPA may also represent an important diagnostic indicator to guide the treatment of many mental health conditions.[2,6]

Associations between urinary levels of HPHPA and mental illness were first reported by Armstrong, et al., in 1957, who provided chemical evidence of the role of dietary factors in the etiology of many psychiatric disorders.[7] More recently, Dr. William Shaw brought HPHPA back into the spotlight after investigating its role in two young boys with autism and discovering its underlying mechanisms.[2,8] The potent influence of HPHPA has been demonstrated through the reversal of symptoms with targeted antibiotics in patients with various mental health conditions. Detected through an assay of organic acids in urine, the highest recorded HPHPA level was measured in a young female patient with first-episode schizophrenia.[9] Eradication of harmful *Clostridia* in this patient eliminated her auditory hallucinations. In addition to Shaw's initial cases with autism, other autistic children with gastrointestinal distress and irritable, aggressive behavior have shown remarkable improvement with treatment for *Clostridia*.[6]

HPHPA's primary mode of action involves upsetting the balance of neurotransmitters in the brain by directly targeting a critical enzyme in the metabolic breakdown of dopamine. Dopamine beta-hydroxylase (DBH) facilitates the conversion of dopamine to norepinephrine, regulating the concentrations of dopamine that are created from its precursor phenylalanine. As the population of intestinal *Clostridia* grows, more HPHPA travels the gut-brain axis to inhibit DBH, increasing brain concentrations of dopamine and reducing norepinephrine. A neurotransmitter imbalance favoring dopamine creates a hyper-stimulating, oxidative milieu that is toxic to neurons. In addition to damaging brain receptors with potential effects on motor control, excess dopamine drives abnormal risk-taking and reward-seeking behaviors. Substance abuse disorders, obsessive-compulsive disorder, ADHD, and psychosis have all been associated with elevated dopamine levels. Even at milder degrees, dopamine excess contributes to irritability, agitation, and anxiety. DBH inhibition by HPHPA also interferes with normal synthesis of norepinephrine, significantly impacting decision-making, attention, and memory.[2,3]

Happy Gut: Happy Brain

Beyond improving mental health, resolving *Clostridia* overgrowth is essential to restoring gastrointestinal health. Dysbiosis leads to severe damage of intestinal tissue leading to poor dietary absorption and digestion, reduced immunity, and greater risk of allergy. Furthermore, suppression of favorable bacteria contributes to intestinal dysfunction by inhibiting their synthesis of beneficial byproducts. The presence of elevated HPHPA does not rule out additional perpetrators of intestinal dysfunction; food allergies are frequent contributors in virtually every psychiatric condition, requiring minimal to drastic dietary changes.[3]

My thirty years of clinical experience suggests a significant number of children and adults with ADHD, anxiety, autism, and schizophrenia, particularly those with gastrointestinal symptoms will test high for urinary HPHPA. A number of clinical reports and published data corroborate the importance of assessing elevated HPHPA across the spectrum of psychiatric illness, warranting its routine inclusion in lab assays for patients

continued on page 32 ➤

The Great Plains Laboratory, Inc

GPL Academy

Practitioner Workshops

The Great Plains Laboratory, Inc. is pleased to bring you GPL Academy, a series of workshops designed to help practitioners learn how to integrate our comprehensive testing into their practices. When you attend a GPL Academy workshop, you will find out why our tests may be incredibly valuable to your practice, what particular markers may be the most meaningful to specific patients, and you will learn how to use our tests in tandem to provide your patients with the most personalized treatment plans possible. **CME available!**

DAY 1 WORKSHOP: ORGANIC ACIDS TESTING

You will learn:

- How to use this comprehensive test (74 markers) in your practice to help your patients
- How the OAT helps you discover underlying causes of many chronic conditions
- What kinds of treatments have been most effective

PRACTITIONERS ATTENDING ALL DAYS RECEIVE A FREE ORGANIC ACIDS TEST, WORTH $299!

DAY 2 & 3 WORKSHOP: ENVIRONMENTAL TOXIN TESTING

You will learn:

- About the epidemic of environmental toxin exposure
- About common environmental pollutants tested by our GPL-TOX Profile (172 markers)
- How these chemicals affect our health and what steps can be taken to help detoxify the body
- About multiple types of mold mycotoxins tested for in our new MycoTOX Profile
- About the chronic health conditions mycotoxin exposure can cause and treatment options

For all workshop details and to register, please visit: www.GPLWorkshops.com

The Great Plains Laboratory, Inc.

913.341.8949
www.GreatPlainsLaboratory.com
marketing@gpl4u.com

➤ *continued from page 30*

displaying these risk factors. When urinary HPHPA concentrations exceed 180 mmol/ml of creatine, my first line strategy is always a multi-strain, high-dose probiotic in doses of at least 200 billion CFUs per day; often 600 CFUs per day is required.[3]

In many cases, reintroducing commensal bacteria with a multi-strain, high-dose probiotic over a period of two to three months is enough to overcome the bacterial imbalance and realign the gut-brain axis. Individuals who do not respond to probiotics in the expected time may require a *Clostridia*-specific antibiotic to create an optimal environment for probiotics to take effect. In most patients requiring adjunct antibiotics, vancomycin in a 30-day pulsing protocol (1 day on; 2 days off) is sufficient to eliminate *Clostridia* and jumpstart recovery with probiotic treatment. In addition to restoring homeostasis of the microbiome, resolving *Clostridia* overgrowth often increases the efficacy of other necessary supplementations or medications.[3]

The Power of the Organic Acids Test and Probiotics

A 25-year-old adult male with a history of atopy, including multiple food allergies and a diagnosis of celiac disease, dry eye, and asthma arrived at my office after a referral for generalized anxiety and major depression. This patient had been in therapy and psychiatric treatment for over a decade and responded poorly to multiple prescription medications. His struggles with mental health began in high school and college, which seemed to align with severe gastrointestinal symptoms and disordered eating behaviors and, which the patient said, correlated with a highly stressful, demanding period of time. In recent years, the patient's symptoms had escalated to more significant issues with anger, rage attacks, panic, and self-harm. An organic acids test confirmed elevated HPHPA as the primary culprit. A prescription for a multi-strain, high-dose probiotic liberated this patient from years of suffering and removed barriers to success in his young life. This case emphasizes the array of debilitating physical and mental effects that HPHPA can inflict.

I regularly find elevated HPHPA in children with ADHD and autism, and frequently begin immediately with the organic acids test, especially in patients disposed to aggression, angry outbursts, and impulsivity. One patient, a four-year-old boy, was brought into my office by his mother with stereotypical ADHD symptoms that were characterized by many incidences of anger and violence towards others and pets. He often experienced "sensory overload" that triggered tantrums and impulsive, abnormal behaviors, followed by feelings of remorse. Not surprisingly, these episodes resulted in significant problems at home and school. Stimulant medications were ineffective and brought adverse side effects. His urinary HPHPA level, along with several other indicators from the organic acids test, was markedly elevated. A prescription of a multi-strain, high-dose probiotic and restriction of dairy from his diet resolved much of his symptoms and aggression and supported the return to a normal developmental track.

These are two cases that show the profound effect of elevated HPHPA on psychiatric symptoms and the astonishing transformation that can occur in response to simple and straightforward treatments. The HPHPA levels in the organic acids test represents one of the most highly valuable diagnostic tools available to mental health practitioners. Its utility for confirming intestinal dysbiosis has implications for many psychiatric conditions.[2,6] Restoring balance to the microbiome can lay the foundation for psychological healing. Psychiatry can no longer be called the measureless medicine. As psychiatrists and mental health clinicians, we understand how to utilize concepts of functional medicine and orthomolecular medicine. We can provide objective personalized treatment to alleviate the pain and anguish of mental illness. I believe testing for HPHPA has the potential to alleviate an inconspicuous source of mental health symptoms and support patients on a road to recovery.

Dr. James M. Greenblatt, MD, is chief medical officer and vice president of medical services at Walden. He provides medical management, leadership and oversight of Walden's eating disorder and psychiatric programs in Massachusetts and Connecticut. Dr. Greenblatt is board-certified in child and adult psychiatry.

He received his medical degree and completed his adult psychiatry residency at George Washington University in Washington, DC. He completed a fellowship in child and adolescent psychiatry at Johns Hopkins Medical School. In addition, Dr. Greenblatt is a clinical faculty member in the psychiatry department at Tufts Medical School as well as the Geisel School of Medicine at Dartmouth College in New Hampshire.

He lectures extensively throughout the United States and Canada on integrative therapies for mental health. . Dr. Greenblatt is the author of six books including one textbook and books on depression, eating disorders and ADHD. His latest book is on Integrative Therapies for Alzheimer's disease, exploring the research on nutritional lithium. Dr. Greenblatt is the founder of **Psychiatry Redefined**, a healthcare education training program for integrative psychiatry.

He can be reached at: Walden Behavioral Care, 9 Hope Avenue, Suite 500, Waltham, Massachusetts, 02453; 781-647-2901. For more information on Dr. Greenblatt please visit www.jamesgreenblattmd.com.

References

1. Greenblatt J, To W. *Breakthrough Depression Solution: Mastering Your Mood with Nutrition, Diet & Supplementation*. Sunrise River Press; 2016.
2. Shaw W. Clostridia Bacteria in the GI Tract Affecting Dopamine and Norepinephrine Metabolism. In Greenblatt, JM and Brogan, K. (Ed.), *Integrative Therapies for Depression: Redefining Models for Assessment, Treatment and Prevention.* Boca Raton, FL: CRC Press; 2015; pp.31-48.
3. Greenblatt J, Gottlieb B. *Finally Focused: The Breakthrough Natural Treatment Plan for ADHD That Restores Attention, Minimizes Hyperactivity, and Helps Eliminate Drug Side Effects*. Harmony; 2017.
4. Carding S, et al. Dysbiosis of the gut microbiota in disease. *Microbial Ecology in Health and Disease*. 2015; *26*(1), 26191.
5. Sarkar A, et al. Psychobiotics and the Manipulation of Bacteria–Gut–Brain Signals. *Trends in Neurosciences*. 2016; 39(11), 763–781.
6. Shaw W. Usefulness of HPHPA marker in a wide range of neurological, gastrointestinal, and psychiatric disorders. 2015. Great Plains Laboratory website. www.greatplainslaboratory.com/articles-1/2015/11/13/usefulness-of-hphpa-marker-in-a-wide-range-of-neurologicalgastrointestinal-and-psychiatric-disorders. Accessed 30 June 2018.
7. Armstrong M, Shaw K. The occurrence of (–)-β-m-hydroxyphenylhydracrylic acid in human urine. *J Biol Chem.* 1957; 225: 269–278.
8. Shaw W, Kassen E, Chaves E. Increased urinary excretion of analogs of Krebs cycle metabolites and arabinose in two brothers with autistic features. *Clinical Chemistry*. 1995; 41(8): 1094-1104.
9. Shaw W. Increased urinary excretion of a 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA), an abnormal phenylalanine metabolite of Clostridia spp. in the gastrointestinal tract, in urine samples from patients with autism and schizophrenia. *Nutritional Neuroscience*, 2010; 13(3): 135-143.

◆

Aging happens. Aging-related MEMORY decline doesn't have to!*

■ Brain function vastly improved by common ingredient in Indian food!

An Increasingly Common Aging-Related Problem

Jane began to notice some changes after menopause, "I clearly noticed a decline in my memory. Then I missed two payroll deadlines which were clearly marked in my calendar. Another time I suddenly forgot the code to enter my own office.

These few examples left me both worried and terrified. After taking Interceuticals **Better Memory™** for six months, my memory is much clearer and I feel more efficient and organized. Pretty amazing!"

We've all read the statistics; as we age, our brain function tends to decrease, leaving us with gradually failing memories. We struggle to recall words, struggle to focus, and even forget our friend's names! It's a frustrating problem, but one that we have been told "just comes with age." But the makers of Better Memory disagree that you need to "just accept" declined memory and brain function as you age. That's because they've developed a product that contains an incredible ingredient *scientifically shown* to improve memory and brain function.

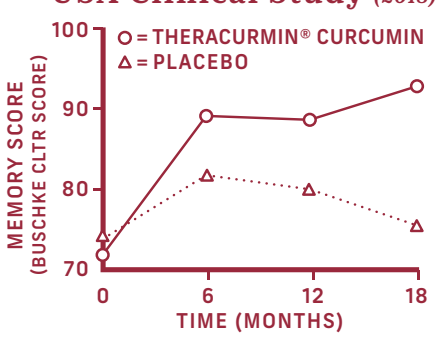
"Senior Moments" Be Gone!

A few years ago scientists began to notice that people in certain areas of the world didn't seem to have memory decline as quickly as most people as they aged. The secret, they discovered, was hidden in turmeric, a key ingredient in yellow curry dishes. Turmeric is a powerful anti-inflammatory herb that seems to have a significant positive effect on individuals who consume enough of it. And people in this northern region of India didn't just notice *slightly* better memory as they aged, they noticed **75% less** incidence of memory issues than American participants in the study. They had almost completely erased the "senior moment."

The Magic of Turmeric

Further studies showed that the ingredient contained in turmeric that helped with brain function is called "**curcumin**." Curcumin is a natural powerhouse in the fight against aging-related memory decline, but it must be delivered in a *very specific way in order for the body to use it effectively.* Thanks to a process called "nanotechnology," the curcumin in Better Memory Theracumin® Curcumin is absorbed into the blood at a concentration **27X** higher than competing products! That means **faster absorption** and a **significantly better effect** on memory and brain function as shown in USA Study. (See website.)

USA Clinical Study *(2018)*



Don't Just Live Longer. Live Better.

Better Memory can give you:

- Better Short-Term Memory*
- Better Long-Term Memory*
- Better Recall and Retrieval*
- Better Attention and Focus*
- Better Mood Balance*
- Only 2 Small Capsules Daily

Don't accept less with memory. Call now and demand better with Better Memory.

1-888-686-2698

Call NOW and ask how to get a **FREE** Bottle. Or order online at **BeBetterNow.com**.

For faster results, add **Better Memory PM** to your order to boost mitochondrial health!*

*These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease. Use as directed. Individual results may vary. ©2019 Interceuticals, Inc.

Diabetes Is Optional!

by Jacob Teitelbaum, MD

Diabetes is an increasingly common problem worldwide – especially for anyone eating a Western-style diet. It bears noting that in countries with non-Westernized diets, diabetes is essentially unheard of—until the diet changes to high sugar and low fiber. Processed foods and refined carbohydrates have essentially caused a condition that, shockingly, could affect one-third of adults.

However, the very fact that type 2 diabetes was once rare also provides a reason for hope. It shows that diabetes is optional, and that we have a choice as practitioners to help decide whether it continues unabated or becomes an unpleasant memory. In fact, there is compelling research on a little-known botanical that may be an effective answer to diabetes. But first, let's better understand the problem.

What Is Diabetes?

Though as health practitioners we have a fair understanding of diabetes' mechanism, sometimes it helps to take a quick look at the basics again, using simple language that the people we treat can understand.

Our bodies make sugar as a fuel for our cells' energy furnaces. For most of human history, we have had a high-fiber diet. Carbohydrates and sugars in our diets were released very slowly and steadily into the bloodstream over many hours. But these days, our diet includes almost 140 pounds of sugar per person, per year. That's 18 percent of our overall calories, and not surprisingly, it causes massive spikes in blood sugar. The effect is that it forces our bodies to prevent this sugar from entering the cells too quickly. This change is called "insulin resistance."

Insulin is an important key that opens our cell furnaces so the sugar can get in to be burned for energy. But when the body's cells become deaf to the insulin, the sugar builds up in the bloodstream instead. Meanwhile, the sugar can't get into the cell to be burned for fuel and the cells are, as unlikely as it seems, starving.

As a result, cells send out the message that they are energy starved, causing the body to make more sugar and more insulin. These high insulin levels then proceeded to turn the sugar into fat, causing people to pack on the pounds and become even more insulin resistant (thus the abdominal 'spare tire'). The cycle continues until the body can no longer compensate and the blood sugar goes up. At that point, most physicians will usually offer patients whatever the newest, most profitable, and sadly, most often toxic medication the drug companies are marketing to them.

Why the Diabetes Epidemic?

Several factors have created the perfect storm of diabetes. They include the following:

- Excess sugar, white flour, and low-fiber in the diet
- Vitamin D deficiency, especially from the misguided advice to avoid sunshine. Low vitamin D is associated with not only diabetes, but also markedly increased risk for autoimmune illness, pain, hypertension, and other problems.
- High rates of obesity
- Decreased exercise and sedentary lifestyles
- Magnesium deficiency is also associated with a significantly increased risk of developing type 2 diabetes. Over half of the magnesium that would otherwise be present in our diets is often lost in food processing.
- Numerous chemicals in the environment that block testosterone in men and increase testosterone in women.

Inadequate testosterone levels in men (in my opinion, anything under 500 ng/dL – research shows the "normal range" to be an absurdity) have been shown to cause metabolic syndrome, a combination of high blood pressure, high cholesterol, and either diabetes or prediabetes. When you see a 'spare tire' developing on a gentleman's abdomen, this is often the culprit.

In women, the opposite occurs. An *elevated* testosterone is often associated increased risk of diabetes, with polycystic ovarian syndrome (PCOS), acne, facial hair growth, and even infertility. Because of this, although testosterone can be helpful in women as well as men, it is important not to over-treat women because it can increase diabetes risk.

Testing

To screen for prediabetes, I will check a fasting insulin level. Ignore the normal range. If the fasting insulin is over 100 mmol/L, I take measures now for prevention. The same applies if the glycosylated hemoglobin (HbA1C) is over 5.8 percent.

Diabetes Is Optional

When I say "diabetes is optional," that's because it is true. It also happens to be the title of my newest book (now available on Amazon; see Sidebar). I

examine, in detail, recommendations and treatments, including the following:

- Direct your patients to take a readily-utilized multivitamin high in magnesium and vitamin D, and B vitamins. My favorites are the Daily Energy Enfusion vitamin powder or Bio Active Essentials.
- Remind them to cut back on sugar intake. This doesn't mean the person can't indulge their sweet tooth occasionally. In fact, dark chocolate in moderation is a health food. But cutting out sodas and fruit juices is a great start. Both have ¾ teaspoon of sugar per ounce, or 36 spoonfuls of sugar in a typical 48-ounce "Big Burp" soda. Encourage patients to enjoy whole fruit instead. Meanwhile, look at the nutritional label, and divide grams of sugar by four to see how many teaspoons of sugar are in a serving.
- Recommend walks in the sunshine. Or find other exercise, preferably outside, that they love.
- Encourage patients to maintain a healthy weight. This will be easier once their insulin sensitivity improves with an improvement in diet and a guided supplement regimen. With adequate weight loss, diabetes disappears in 86 percent of patients.
- Optimize your patients' testosterone levels. For men, I recommend bioidentical testosterone to bring the total testosterone up to about 900 ng/dL. In women, I recommend the treatments discussed in this article, along with the medications metformin and aldactone to lower elevated testosterone.

To receive one complimentary copy of the "Diabetes is Optional" book while supplies last, please email info@EuroMedicaUSA.com.

Treating Diabetes

For childhood diabetes, which is a totally different autoimmune illness, insulin is a lifesaving and necessary treatment. For adult diabetics, it is a loan shark which initially lowers blood sugar. But because it often causes massive weight gain, it can worsen the diabetes in the long-term. So, it may provide short-term effects, but it is a horrible overall solution for type 2 diabetes.

In my 40 years as a physician, I have found that most diabetes medications turn out to cause more harm and deaths than benefit. But routinely, physicians are not taught about the research on the drug's toxicities until after the patent runs out and it is no longer profitable. Then the drug companies are off teaching them about the newest, most profitable, diabetes medication.

I don't fault the drug companies for this. They are actually very nice people doing their job – which is to make money. It is the physician's job to be able to distinguish between what is real and truthful as opposed to slick advertising masquerading as science. But sadly, though even exhorted to do so by two past editors of the *New England Journal of Medicine*, most physicians don't realize the difference. Except for holistic physicians like you!

There is one medication that is an exception – metformin. It is a low-cost option that is effective, well-tolerated, and has stood the test of time. However, it *can* cause nausea or diarrhea (at which point I'd recommend lowering the dose) and will routinely cause vitamin B12 deficiency, so recommending a multivitamin is a good idea, too.

***Hintonia latiflora* to the Rescue**

Hintonia is an extract of the bark of a shrubby tree that grows in the Sonoran desert. It has been used in folk medicine in Mexico and Central America to treat and even reverse high blood sugar, insulin resistance, type 2 diabetes, and metabolic syndrome for over a century. It's been studied in detail for its ability to reverse high blood sugars for the past 60 years.

After a number of case reports showing efficacy, ten studies have been published examining this herb's effectiveness in treating diabetes.[1-10] Research has shown that it was so effective that many patients with type 2 diabetes could reduce or eliminate their need for insulin, especially those needing 25 units a day or less.[1] They were also routinely able to lower the dose or eliminate their oral hypoglycemic agents [2-10]

➤

Book Notice

Diabetes Is Optional! by Jacob Teitelbaum, MD
Paperback; 68 pp; 2018; $5.45 (US at Amazon)

Diabetes is an increasingly common problem. It bears noting that in countries with non-Westernized diets, diabetes is essentially unheard of – until the diet changes to high sugar and low fiber. Because of this, diabetes is largely a disease caused by our "modern" diet and lifestyle. Shockingly, it is now estimated that one-third of adults will get adult-onset diabetes. That it used to be exceedingly rare tells us that diabetes is optional.

Although this short book is written for the public, it also gives an excellent overview for physicians. It also includes over a dozen studies discussing the remarkable effectiveness of the herb *Hintonia latiflora* (available as Sucontral D).

Diabetes Is Optional reviews a comprehensive natural approach for treating diabetes. It also discusses the research on *Hintonia latiflora* (Sucontral D), which reduces glycosylated hemoglobin an average of about 10% (e.g. – from 7.5 to 6.5 percent). This results in many people no longer being diabetic.

This book, available on Amazon, is an excellent and simple tool for teaching the people you treat about diabetes. Health practitioners can receive one complimentary copy of *Diabetes Is Optional* while supplies last. To get your free copy, email info@EuroMedicaUSA.com.

➤

Both animal and in vitro studies also confirm this effect while demonstrating multiple underlying mechanisms of action.[11-13] To give an idea of its effectiveness, one *Hintonia latiflora* study followed 177 patients with prediabetes or mild type 2 diabetes for eight months.[2] Patients consumed capsules that included hintonia as the primary ingredient. During the study, patients were evaluated every two months on various parameters of diabetes, including A1C, fasting glucose, and postprandial blood sugar, as well as common symptoms associated with diabetes, such as neuropathy. At the end of eight months, researchers noted the following significant improvements:

- HbA1C improved by a significant average of 10.4 percent
- Fasting glucose improved an average of 23.3 percent
- Postprandial glucose decreased by an average of 24.9 percent

Improvements were also found in diabetic symptoms, as well as blood pressure, cholesterol, and liver enzyme values.

Hintonia latiflora is an incredibly safe herbal medicine. Researchers followed up with study participants for almost three years, and there were no side effects or any problems taking it in combination with blood sugar control medications.

Mechanisms of Action

Hintonia inhibits glucosidases, slowing the breakdown and absorption of sugar in the gut.[12] This delays the release of sugar into the bloodstream and keeps glucose levels low, instead of allowing them to spike, a main cause of excessive insulin release.

Coutareagenin, a polyphenol nutrient found in the bark extracts unique to hintonia, appears to be responsible for other blood-sugar controlling benefits of the botanical. This unique flavonoid has been shown to reduce insulin resistance and inflammation.[13-14]

One of hintonia's greatest benefits is that it maintains steady blood glucose throughout the day and night, contributing to long-term improvements in glucose control.

The president of the International Diabetes Foundation was the lead author on another study that strongly recommended the use of hintonia in treating and preventing type 2 diabetes, largely because of improved blood glucose control, but also because of its effectiveness in lowering cholesterol and triglycerides and increasing vasodilation [11]

What to Look for

The *Hintonia latiflora* you recommend should be standardized to contain 20 mg of polyphenols associated with coutareagenin and taken two to three times a day. Hintonia has only recently become available to the North American public in a product called Sucontral® D. No side effects or contraindications have been discovered in more than 60 years of research, and it has been used along with conventional medications.

You can help guide your patients toward a healthy path and away from diabetes. The bottom line? Diabetes truly is optional.

References

1. Kuhr R. Orale diabetestherapie mit einem Eupharbiazeenextrakt. *Landarzt*. 1953;29(23):542-549
2. Schmidt M, Hladikova M. Hintonia concentrate - for the dietary treatment of increased blood sugar values: Results of a multicentric, prospective, non-interventional study with a defined dry concentrate of hintonia latiflora. *Naturheilpraxis*. Feb. 2014. (Translated article).
3. Korecova M, Hladikova M. Treatment of mild and moderate type-2 diabetes: open prospective trial with *Hintonia latiflora* extract. *European Journal of Medical Research*. 2014;19(1):16
4. Korecova M, Hladicova M, Korec R. *Hintonia latiflora* bei Typ-2-Diabetes. Zeitschrift für Phytotherapie. 2006;27:272-278
5. Machens R. Therapieversuch mit Copalchi-Rinde bei pathologischer Glucosetoleranz. *Erfahrungsheilkunde*. 1996;45(9):605-608
6. Pellegrini A. Klinisches Gutachten über das Hintonia latiflora Produkt. Sonderdruck Fa. Sippel, Konstanz. 1951:1-7
7. Schmid P. Bericht über die Behandlung mit dem peroralen Antidiabetikum Hintonia latiflora. Sonderdruck Fa. Sippel, Konstanz. 1951: 1-4.
8. Vida F. Erfahrungsbericht mit dem peroralen Antidiabetikum Hintonia latiflora. *Med Welt*. 1951;20:1623-1624
9. Ritzmann H. Beitrag zur DiabetesBehandlung. Hippokrates. 1950;21(6):161-168
10. Cristians S, et al. Hypoglycemic activity of extracts and compounds from the leaves of *Hintonia standleyana* and H. Latiflora: potential alternatives to the use of stem bark of these species. *Journal of Natural Products*, 2009 Mr 27:72(3);4-08-13
11. Vierling, C, et al. The vasodilating effect of a *Hintonia latiflora* extract with anti-diabetic action. *Phytomedicine* 2014 Oct 12:21(12):1582-6.
12. Mata R, et al. Mexican antidiabetic herbs: valuable sources of inhibitors of α-glucosidases. *J Nat Prod*. 2013 Mar 22;76(3):468-83.
13. Korec R, et al. Effects of the neoflavonoid coutareagenin, one of the antidiabetic active substances of *Hintonia latiflora*, on streptozotocin-indicted diabetes mellitus in rats. *Arzneimittelforschung.* 2000 Feb;50(2):122-8.
14. Chen J, Mangelinckx S, Adams A, Wang ZT, Li WL, De Kimpe N. Natural flavonoids as potential herbal medication for the treatment of diabetes mellitus and its complications. *Nat Prod Commun*. 2015 Jan;10(1):187-200.

◆

Jacob Teitelbaum, MD, is one of the most frequently quoted integrative medical authorities in the world. He is the author of 10 books, including the best-selling *From Fatigued to Fantastic!, The Complete Guide to Beating Sugar Addiction*, *Diabetes Is Optional* and the popular free Smart Phone app *Cures A-Z*. Dr. Teitelbaum appears often as a guest on news and talk shows nationwide including Good Morning America, The Dr. Oz Show, Oprah & Friends, CNN, and FoxNewsHealth. Learn more at Vitality101.com.

SUPPORTS HEALTHY A1C LEVELS*†

Sucontral® D with clinically studied *Hintonia latiflora* from Germany
Proven blood sugar support throughout the day*†

EuroMedica®

Available Exclusively At: emersonwellevate™

www.emersonecologics.com | 800.654.4432

† Supports healthy blood sugar levels already within normal range

*THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT DISEASE.

The Incredible Gastrointestinal Barrier System and Permeability: Laboratory Assessment and Insights for Intervention

by David Quig, PhD

The multilayered gastrointestinal (GI) barrier system is very complex and too often underappreciated. The integrity of the barrier system is essential for prevention of unregulated assimilation of highly antigenic and pro-inflammatory macromolecules from the lumen of the gut. This article will highlight the components of the highly integrated multi-layered system, and the incredible symbiotic interactions between the GI metabolome and its encompassing and supportive barrier terrain. Important information regarding the integrity of the barrier systems can be gleaned from a truly comprehensive stool analysis report. Indirect and direct assessment of the terrain, and clinical intervention to support the barriers will be addressed.

Like any ecosystem, the GI ecosystem entails a complex network of interactions among and between organisms, and their environment (the barrier system/terrain). The barriers prevent uptake of highly antigenic and pro-inflammatory macromolecules from the lumen of the gut and are also integral to surveillance, protection, and modulation of the GI microbiome. In turn the commensal bacteria facilitate functional integrity of their encompassing terrain. A major component of the GI ecosystem is the GI glycobiome that has been sorely underappreciated. For example, mucins (highly glycosylated proteins) comprise the mucus barrier gradient that provides not only a protective barrier but also regulation of host-pathogen interactions.[1]

Breaches in the GI barrier systems that potentiate paracellular systemic uptake of macromolecules may be associated with insufficiency dysbiosis, chronic stress, caloric deprivation and low fiber diets, direct adhesion of *any* bacteria to GI endothelial cells, alcohol/pharmaceuticals/NSAIDS, environmental xenobiotics, inflammation, gluten, an energy dense "Western style diet, and excessive exercise with heat stress.[2,3] Such breaches may result in systemic inflammation (including neuroinflammation), autoimmunity, food sensitivities, asthma, insulin resistance and behavioral abnormalities.[2] The multifactorial, layered, and highly integrated barrier system is crucial for optimal health and entails far more than the well-appreciated endothelial cell tight junction protein complexes.

The Multi-Layered Barrier Systems

There are three primary components of the barrier system including the essential commensal bacteria and their metabolites (the GI metabolome).[4] Secondly there are the chemical/biochemical components that include cytokines, antimicrobial peptides digestive secretions, sIgA and lysozyme (antimicrobial enzyme); the latter three can be evaluated with comprehensive stool analysis. The final components are the external *physical* barriers, which include the viscous mucus gradient, the glycocalyx, the endothelial cells (EC) with their tight junctions, and the underlying lamina propria that is enriched with immune cells.

Commensal Bacteria

Insufficiency dysbiosis is often overlooked. Very often clinicians anticipate the presence of dysbiotic microbes in symptomatic patients; the traditional goal is to simply eradicate the "bad dudes" using botanical or pharmaceutical anti-microbial agents. Clinicians are often disappointed when undesirable microbes are not detected and sometimes challenge the competency of the laboratories. Many years ago, Dr. Leo Galand emphasized the fact that insufficient colonization by "beneficial"/commensal bacteria can be associated with GI symptoms and increased permeability that may adversely affect both GI and systemic health. A primary consequence associated with poor status of the beneficial bacterial guilds is diminished production of the short chain fatty acid butyrate that is the master mediator of microbial-host cross talk. Binding to G-protein coupled receptors on specialized cells on/in the GI mucosa,[5] butyrate mediates the release of anti-inflammatory cytokines, mucins, hydrogen peroxide, antimicrobial peptides, and lysozyme.[6] Butyrate also regulates expression of tight junction proteins between the endothelial cells.[7] Therefore adequate *constant* production of butyrate is essential for maintaining the integrity of the GI barrier system.

Simply providing probiotics is commonly insufficient for remediation of optimal barrier function and aberrant GI permeability. Fiber intake associated with the typical Western diet is dismally

low. Provision of adequate fermentable "food" for the bacteria in the form of soluble fiber is of utmost importance. Soluble fiber is not digestible in the upper bowel and is thereby provided to resident commensal bacteria lower in the bowel. There the bacteria saccharolytically ferment the soluble fiber to short-chain fatty acids; butyrate being quintessential.[1] Good dietary sources of the soluble fiber include onions, asparagus, leeks, yams, chicory root, agave, bananas, chickpeas, lentils, beans, oatmeal, and vegetables and berries. Starvation (anorexia) and low fiber intake are associated with increased permeability and diminished mucus barrier thickness.

Since some patients do not tolerate dietary fiber well, it would be great to have an effective delivery system that enables supplemental butyrate to reach the lower bowel. It is noteworthy that butyrate is rapidly absorbed and readily crosses the blood brain barrier where it can suppress neuroinflammation.[8] The bottom line is that we absolutely must "feed" the commensal bacteria; simply providing high-quality probiotics is futile unless adequate soluble fiber/butyrate is concomitantly provided. When reviewing the results of a truly comprehensive stool analysis, it is very important to note the levels of key commensal bacteria and the *concentration* of fecal butyrate.

Clostridium Species – Unduly Unappreciated

"Clostridiaphobia" is widespread. The five toxigenic *Clostridium* species, such as *C. difficile*, have instilled undue concern about the normal presence of the approximately 100 non-toxigenic *Clostridium* species. Commensal *Clostridia* are major butyrate producers that facilitate microbial-host cross talk that is paramount to GI barrier integrity.[9] Decreased abundance of *Clostridium* species has been reported for patients with colorectal cancer and inflammatory bowel disease.[10] It should be noted that in addition to *Bifidobacterium*, commensal *Clostridium* species are vertically transferred from the maternal microbiome into mom's lymph and breast milk with colonization in the bowels of breastfed infants during the first month of life.[11] The mechanism for that transfer of maternal bacteria involves the long extended "feet" of dendritic cells that reach up through pores in specialized M cells in the mucosa. An increased abundance of commensal *Clostridium* species is associated with high fiber intake from fruit, vegetables, beans, and chickpeas (raffinose).[9]

A result of 3-4+ for *Clostridium* species (anaerobic cultivation) should not necessarily invoke clinical concern. Only when patients present with multiple daily bouts of profuse watery diarrhea should additional testing for potential toxin producing *C. difficile* be considered. Unnecessary antibiotic treatment of asymptomatic *C. difficile* carriers has resulted in near complete antibiotic resistance.[12] High-sensitivity molecular testing for toxin-producing *C. difficile* is available for use on anaerobically cultivated *C. difficile* or directly on a stool specimen.

Mucins and the Mucus "Blanket"

Mucins are highly glycosylated proteoglycans produced by goblet cells in the mucosa; the protective mucins are constantly reshaped and refreshed.[1] There are cell-bound and secretory mucins. The cell-tethered mucins, along with lipids, form a viscous protective gel layer (glycocalyx) atop the apical surface of the mucosa. They prevent direct binding of *any* bacteria, even commensals, to endothelial cells. Mucins are protective to endothelial cells as biofilm is to bacteria and yeast. Above the glycocalyx is an inner dense, loosely associated mucus blanket that is prime real estate that harbors sIgA, antimicrobial peptides, and reactive oxygen species.[4] Proteolytic activity of the mucins decreases the density of the mucus blanket as it extends up towards the lumen. The less dense upper mucus layer provides a "loose river" that facilitates passage of pathogens via normal peristalsis. GI goblet cells produce about 5 liters of mucus each day, and they also deliver antigens to associated dendritic cells in the lamina propria. Signaling from the associated detrocytes induces abrupt release of more mucus-forming mucins.[4] Mucus production is regulated by butyrate released from commensal bacteria.

The importance of the mucus barrier system is emphasized by the fact that patients with ulcerative colitis tend to have less commensal bacteria, thinner mucus barriers, increased colonization of pathogens, and increased GI permeability.[13] Obesity and high-saturated fat intakes are also associated with decreased mucus thickness and increased GI inflammation and permeability.[14] Juxtaposed, prebiotics (oligosaccharides/soluble fiber) increase mucin-stimulating bacteria and butyrate production. The importance of adequate dietary intake of soluble fiber cannot be over emphasized.

Secretory IgA (sIgA) – Constant Surveillance, Sampling, and Communication

Secretory IgA in the gut is the major first line of defense by the humoral immune system.[15] sIgA is a "brick" in the mucus barrier. It is anchored in the inner dense mucus layer and on the surface of endothelial cells where it provides immune exclusion of microbes (including specific viruses) and enterotoxins.[4] When sIgA binds to pathogenic microbes, it alters their membrane potential and decreases their ability to produce energy. That diminishes the pathogens motility and ability to produce self-protective biofilm. sIgA also facilitates antiparasitic activity of eosinophils and has anti-inflammatory activity in that it suppresses NF-κB-induced proinflammatory cytokines.

Increased fecal sIgA is an *appropriate* immune response to enteropathogens, and fecal levels may remain elevated up to six weeks after a specific GI virus. It is not normal to have non-detectable or very low levels of fecal sIgA. It regulates the composition of the microbiota by providing constant surveillance, sampling and communication with immune cells.[16] Major Candida overgrowth may be associated with low fecal sIgA because it has been reported that 38 species of Candida isolated from patients expressed sIgA -specific protease activity.[17] Chronic stress (high cortisol, low DHEA) is also associated with low levels fecal sIgA.[18] Intervention for low sIgA includes omega-3 fatty acids, zinc, vitamins D and A, *S. boulardii, L. rhamnosus GG, Bifidobacterium lactis Bb-12,* prebiotics (butyrate), and glutamine.[19,20] An appropriate level of sIgA in the gut is a critical barrier constituent in the maintenance of a healthy microbiome.

➤

Gastrointestinal Barrier System

➤

GI Epithelial Cells – The Final Barrier

When the supra endothelial barriers structure/function is compromised, dysbiotic microbes and antigenic/pro-inflammatory macromolecules have a much greater chance of breaching the GI endothelial cell (EC) barrier by means of unregulated paracellular influx. Zonulin, a protein produced and released from the EC, is currently the only known physiological reversible regulator of the EC tight junction protein complexes (TJP).[21,22] *Sustained* release of zonulin that result in elevations in serum zonulin (antigen) is causally associated with proteolytic breakdown of the TJP. Such occurs consequentially with autoimmune diseases (celiac, Crohn's, RA, T1DM), some cancers, neurological conditions (demyelinating polyneuropathy, MS), obesity, juvenile non-alcoholic fatty liver disease, asthma, metabolic syndrome, and even non-celiac gluten sensitivity.[7,23-29]

Some triggers for excessive release of zonulin include gliadin, inflammation, direct adherence of any bacteria to EC, excessive LPS, bacterial enterotoxins, excessive fructose, and possibly some industrial food additives.[30] Some of the suspect food additives include emulsifiers, microbial transglutaminase ("meat glue"), and nanoparticles. Elevated serum zonulin (antigen) levels are highly correlated with high urinary ratios of lactulose to mannitol (L:M); both are indicative of paracellular epithelial permeability. To date we have seen similar rates of positivity for high serum zonulin (14.5%) and high L:M (15%) in specimens from patients; that challenges the popular suggestion that "we all have intestinal permeability" to a sustained clinically significant extent. Based upon the results of lactulose:mannitol load testing in healthy adults (n=47), it has been suggested that the reliability of the "gold standard" test of intestinal permeability is improved when urine is collected between 2.5 and 4 hours as opposed to the traditional six-hour collection.[30]

Clinical intervention to restore the EC barrier entails *first* removing the trigger(s) for excessive zonulin release. Documented supports for then increasing the expression of the tight junction proteins include specific probiotics and prebiotics (11 grams inulin/day),[31] curcumin, quercetin, vitamin D and retinol, and γ-linoleic acid.[2,4] Chitosan and ethanol consequentially *decrease* the expression of the tight junction proteins.[32]

In summary, clinically important information can be gleaned from a truly comprehensive stool analysis regarding the highly integrated, multi-factorial GI barrier system. Do consider the aforementioned consequences of insufficiency dysbiosis for symptomatic patients even in the absence of dysbiotic microbes. Factor in low levels of butyrate (absolute), sIgA, high levels of inflammatory proteins (e.g. lysozyme, calprotectin, lactoferrin), and mucus (shedding) in stool specimens. GI permeability of the epithelial cell barrier is indicated by elevated levels of serum zonulin or urinary lactulose: mannitol. A broader appreciation of the entirety of the GI barrier system may improve clinical success and patient satisfaction.

David Quig, PhD, received his BS and MS degrees in human nutrition from Virginia Tech and a PhD in nutritional biochemistry from the University of Illinois. After a five-year stint as a research associate studying lipid biochemistry and cardiovascular disease at Cornell University, he worked as a senior cardiovascular pharmacologist for seven years with a major pharmaceutical company. For the past 22 years, David has served as the Vice President of Scientific Support for Doctor's Data, Inc. He has focused on toxic metals, methylation and amino acid metabolism, the clinical application of the biochemistry of endogenous detoxification, and the influence of the gastrointestinal metabolome on health and sustained adverse conditions. David regularly speaks at national and international medical conferences and has facilitated and co-authored an array of studies, spanning exposure and retention of environmental toxicants, nutritional status, and gastrointestinal dysbiosis.

References

1. Moran AP, et al. Sweet-talk: role of host glycosylation in bacterial pathogenesis of the gastrointestinal tract. *Gut*. 2011;60:1412-25.
2. Bischoff SC, et al. Intestinal permeability- a new target for disease prevention and therapy. *BMC Gastroenterl.* 2014;14:189.
3. Pendyala S. A high-fat diet is associated with endotoxemia that originates from the gut. *Gastroenterol.* 2012;142:1100-01.
4. Yu lch, et al. Host-microbial interactions and regulation of intestinal epithelial barrier function: from physiology to pathology. *World J Gastroint Physiol.* 2012;15:27-43.
5. Thangaraju M, et al. Coupled receptor for the bacterial fermentation product butyrate and functions as a tumor suppressor in colon. *Cancer Research.* 2009;69:7 DOI: 10.1158/008-5472.CAN-08-4466.
6. Ouwekerk J, et al. Glycobiome: bacteria and mucus epithelial interface. *Best Prac Res. Clin Gastroenterol*. 2013;27:25-38.
7. Ploger S, et al. Microbial butyrate and its role for barrier function in the gastrointestinal tract. *Ann NY Acad Sci.* 2012;1258:52-9.
8. Matt S, et al. Butyrate and dietary soluble fiber improve neuroinflammation associated with aging in mice. *Front Immunol*. 2018:19 DOI: 10.3389/fimmu.2018.01832.
9. Lopetuso LR, et al. Commensal clostridia: leading players in the maintenance of gut homeostasis. *Gut Pathogens* 2013;5:23
10. Chen HM, et al. Decreased dietary fiber intake and structural alterations of gut microbiota in patients with advanced colorectal adenoma. *Am J Clin Nutr*. 2013;97:1044-52.
11. Jost T, et al. Vertical mother-neonate transfer of maternal gut bacteria via breastfeeding. *Environ Microbiol.* 2013;8.
12. Tenover FC, et al. Antimicrobial resistant strains of Clostridium difficile in North America. *Antimicrob Agents Chemother*. 1012;56:2929-32.
13. Johansson ME, et al. Bacteria penetrate the normally impenetrable inner colon mucus layer in both murine colitis models and patients with ulcerative colitis. *Gut*. 2014;63:281-91.
14. Serino M, et al. Metabolic adaptation to a high-fat diet is associated with a change in the gut microbiota. G*ut.* 2012;61:543-53.
15. Corthesy B. Multi-faceted functions of secretory IgA at mucosal surfaces. *Front Immunol* 2013:4
16. Mathia A, et al. Role of secretory IgA in the mucosal sensing of commensal bacteria. *Gut Microbes* 2014;5:688-95.
17. Kaptustino OA, et al. Resistance of the fungi Candida to human innate immunity. *Gig Sanit.* 2012;4:27-9.
18. Compos-Rodriguez R, et al. Stress modulates immunoglobulin A. *Front Integrat Neurosci* 2013;7
19. Andrade ME, et al. The role of immunomodulators on intestinal barrier homeostasis. *Clin Nutr.* 2015;34:1080-7.
20. Ami-Romach E, et al. Bacterial population and innate immunity-related genes in rat gastrointestinal tract are altered by vitamin A-deficient diet. *J Nutr Biochem.* 2009;20:70-7.
21. Fasano A. Zonulin and its regulation of intestinal barrier function: the biological door to inflammation, autoimmunity, and cancer. *Physiol Rev.* 2011;91:151-75.
22. Lammers KM, et al. Gliadin induces an increase in intestinal permeability and zonulin release by binding to the chemokine receptor CXCR3. *Gastroenerol.* 2008;135:194-204e.
23. Fasano A. Zonulin, regulation of tight junctions, and autoimmune diseases. *Ann NY Acad Sci.* 2012;1258:25-33.
24. Sapone A, et al. Zonulin upregulation is associated with increased gut permeability in subjects with type I diabetes and their relatives. *Diabetes* 2006;55:1443-9.
25. Pacifico L, et al. Increased circulating zonulin in children with biopsy-proven nonalcoholic fatty liver disease. *World J Gastroenterol.* 2014;20:17107-114.
26. Asmar RE, et al. Host-dependent zonulin secretion causes the impairment of small intestine barrier function after bacterial exposure. *Gastroenterol.* 2002;123:1607-15.
27. Fasano A, et al. Nonceliac gluten sensitivity. *Gastroenerol.* 2015;148:1195-204.
28. Zak-Golab, et al. Gut microbiota, microinflammation, metabolic profile, and zonulin concentration in obese and normal weight subjects. *Int J Endocrinol.* 2013.
29. Moreno-Navarrete, JM et al. Circulating zonulin, a marker of intestinal permeability, is increased in association with obesity-associated insulin resistance. *Plos One.* 2012;7:e37160
30. Lerner A, Matthias T. Changes in intestinal tight junction permeability associated with industrial food additives explain the rising incidence of autoimmune disease. *Autoimmun Rev.* 2015;14:479-89.
31. Russo F, et al. Inulin-enriched pasta improves intestinal permeability and modifies the circulating levels of zonulin and glucagon-like peptide in healthy young volunteers. *Nutr Res.* 2012;32;940-46.
32. Elamin E, et al. Ethanol impairs intestinal barrier function in humans through mitogen activated protein kinase signaling: a combined *in vivo* and *in vitro* approach. *Plos One.* DOI: 10.1371/journal.pone.0107421.

◆

Comprehensive Stool Analysis with Parasitology

Functional Testing by Doctor's Data

Gastrointestinal complaints are among the most common in medical care. This comprehensive profile helps pinpoint the causes of gastrointestinal symptoms and chronic systemic conditions, and measures key markers of digestion, absorption and inflammation.

DOCTOR'S DATA INC.

SCIENCE + INSIGHT

doctorsdata.com

The New Paradigm for Cognitive Health

by Albert H. Mensah, MD, BCIP

Psychiatric disorders have long been challenging arenas in the field of medicine. In the early days, they were often considered a form of celestial punishment for familial wrong-doings, or individual curses in the form of demonic possession. Thereafter, the idea of generalized internal dis-regulation due to unknown causes (often believed to be due to parasitic infection or poisoning) came into being. Barbaric practices for treatment often included corporal punishment (to "beat" the affliction out of someone) with pain as the catalyst for healing. Leaching at one point was considered almost a panacea for all illness both mental and physical.

Thankfully, we have moved on from the "dark ages" of psychiatric treatment. Since that time, emotional instability was thought to be due to trauma of some type stemming from either parental or societal influences. Relationship challenges produced depression or anxiety. Long periods of sleep deprivation could induce schizophrenic changes.

Understanding "cause" was one issue, "treatment" was another. We sought assistance from our understanding of neurotransmitter imbalance and delved deeper into the realm of serotonin, dopamine, and norepinephrine manipulation to achieve symptomatic improvement. Tremendous research has yielded a quantifiably impressive armamentarium of psychiatric tools to battle mental health challenges and at least help keep patients stable if not functional. Categories of medications evolved from antidepressants to anxiolytics to antipsychotics and on to atypical antipsychotics. Without question, many of these medications have proven functional for many people. Yet, for many others, the side effect profile proved to be too much to continue, or tolerances developed over time that necessitated dosage adjustment and often increase.

Despite all our efforts, little progress had been made in the realm of true cause and effect until pioneers like Abram Hoffer, MD, PhD, and Carl Pfeiffer MD, PhD, began to delve deeper into the world of molecular interaction and dysregulation. They began to re-evaluate the role of co-factors in biochemical reactions. What they discovered was truly amazing. Absolute concentration of co-factors such as vitamin C, zinc, vitamin B6 bore relevance to cognitive dysfunction. By evaluating chemical reactions in bio-synthetic pathways, these early pioneers developed treatment regimens that not only stabilized patients, but brought them back to thriving status, many without the use of pharmaceutical assistance. Patients with bipolar disorder and catatonic schizophrenia were normalized by correcting underlying imbalances that made these individuals susceptible to the triggers that produced these conditions. In other words, we now had insight into the areas of weakness in the biochemical "armor" that we all possess. The strength and capacity of an individual's armor is not always predictable, but we now know how that armor can be made vulnerable due to biochemical imbalances.

In order to move forward, we actually had to re-evaluate certain foundational dictums of traditional medical training. We are taught early in medical school that vitamins bear little relevance outside of corporal health and that only minor concentrations are necessary to achieve systemic homeostasis. We now understand quite the opposite to be true. William Walsh, PhD, joined Carl Pfeiffer in his research and further elucidated the true capacity of *Nutrient Power* (which is the title of Dr. Walsh's highly recommended book). He and Dr. Pfeiffer studied over 1 million chemical assays in over 30,000 patients with "mental illness." Consistently, the same categories of chemical imbalances manifested that when corrected yielded positive, if not life changing, results for those treated.

I will never forget when Dr. Walsh once said to me, "Albert, a true scientist must be willing to throw away his or her most cherished belief when presented with truth to the contrary." I was a particularly unflinching skeptic until, working with Dr. Walsh, I saw consistent healing with patients that traditional medical approaches could not begin to help.

Interestingly, this is NOT what I would call alternative medicine. This is a more comprehensive approach, looking deeper at molecular interactions that should be relevant to almost any sub-specialty of medicine, but especially psychiatry, family medicine, internal medicine, and OB/GYN.

Let's examine some case histories.

Case 1: Jeffrey, a 49-year-old man struggled with a great deal of inner

tension, stress intolerance, rage, and a propensity for alcohol "overuse." He relates that he has always been this way and that it has taken its toll on his family. His wife told him that if he did not seek help, this would be the end of their marriage and she would take their two children and leave. We performed biochemical testing and discovered kryptopyrrole (KP) levels of 35 (N=10) and zinc level at 60 (N=90). We began a corrective nutrient protocol to treat the pyrrole disorder and zinc deficiency. Within three months, his symptoms had improved dramatically.

Let's discuss the science. KPs are molecules derived from RBC destruction that under conditions of oxidative stress form strong molecular bonds with two key elements necessary for balanced neurotransmitter production i.e. zinc and vitamin B6. Without these two nutrients in the correct concentrations, serotonin, dopamine, and GABA synthesis is challenged. As a result, erratic mood swings, anxiety, depression, rages and a vicious cycling of these mood states occurs. Many individuals with this condition have been misdiagnosed as being ''rapidly cycling bipolar" and placed on medication when simple blood and urine tests are available that elucidate the true underlying cause and direct corrective and restorative treatment via more appropriate means.

Case 2: Carol, a 60-year-old female, presents with a 40-year history of severe depression, fatigue, anxiety, and fibromyalgia. She had been placed on several medications over time and was told at one point that her conditions were caused by her hormones earlier in life combined with emotional trauma and that little could be done to address said conditions. Upon testing, we found that Carol was an estrogen dominant female who had copper dysmetabolism. She had inherited the inability of her system to regulate copper. With treatment, she has not only normalized, but now shares how she is not sure that she ever really knew what the emotion of "joy" felt like. She thought everyone experienced the world as she had in the past.

The science: copper inhibits three enzymes in the glycolytic pathway in the first phases of carbohydrate metabolism resulting in decreased ATP production and therefore decreased electron transmission in oxidative phosphorylation and the electron transport system-end result...fatigue. With regard to anxiety and depression, copper pushes dopamine into the norepinephrine pathway (fight or flight with nowhere to go and no discernible cause).

Case 3: Eddie (name changed to assure anonymity), a seven-year-old male, has a history of behavior disorder. Birth history was significant for prematurity at 28 weeks, secondary to maternal preeclampsia. His parents related a history of Tourette's, dysgraphia, anxiety and impulsivity ➤

The New Paradigm for Cognitive Health

➤

that resulted in a special education placement in school. His initial biochemical profile revealed high copper levels, pyrrole disorder, low zinc, and over-methylation. One year after biochemical treatment, his father sent the following email to our office:

> Just wanted to pass along some feedback I got during my son's IEP meeting on Monday. He is doing really, really well. No anger/aggression. He communicates when he's frustrated and stays focused and on task. They are still working on some impulsivity but said it's mostly because he's always very excited, especially when he knows the answers. They even talked to him about putting him back in regular school because he is thriving! I'm so glad I took a chance on Mensah Medical; the protocol really works!

These are just a few examples of the clinical ramifications of biochemical imbalances. I would posit that, in time, we will come to see that many "psychiatric" disorders are actually medical in nature – i.e. there is a testable, discernible cause that when addressed, symptom resolution and condition resolution occurs. The lines between quite a few of our subspecialties is becoming blurred in reciprocal directions, all to the great benefit of our patients.

While we are eternally indebted to the rebellious Carl Pfeiffer for challenging the previous paradigms surrounding mental illness evaluation and treatment, I am personally grateful to my mentors, the great Robert Devito, MD, (neuropsychiatry) and the amazing William Walsh, PhD. Together they have changed and continue to change the world of science and medicine around psychiatric and cognitive health. Much credit also needs to be given to the ever-discerning Judith Bowman, MD, whose research and ongoing evaluations in the field of nutrient imbalances in women's health is unparalleled while her expertise in autism is similarly inspiring.

◆

Dr. Albert Mensah received his undergraduate degree from Northwestern University (Evanston, Illinois) and his medical degree from Finch University of Health Sciences-Chicago Medical School. Following residency in family medicine, he completed additional fellowship training in academic development at John H. Stroger Cook County Hospital (Chicago). He is board certified in integrative pediatrics by the American Association of Integrative Medicine (AAIM). From 2005 to 2008, Dr. Mensah treated patients at the former Pfeiffer Treatment Center. Dr. Mensah co-founded Mensah Medical in Warrenville, Illinois, with Dr. Judith Bowman in 2008. The clinic specializes in the treatment of biochemical imbalances, and the cognitive (and physical) disorders caused by those imbalances. As a physician in this specialized field since 2005, Dr. Mensah has treated over 30,000 patients using all-natural, non-pharmaceutical, advanced targeted nutrient therapy. Dr. Mensah currently serves on the board of the Walsh Research Institute, and as a faculty member of the Walsh Research Institute's International Medical Practitioner Education Program, training doctors around the world in the use of advanced nutrient therapy to treat biological and biochemical imbalances.

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
www.TheTownsendLetter.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

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

British Columbia Naturopathic Conference

by Jacob Schor, ND, FABNO

I'm sprawled out on our Ikea couch watching Netflix and chilling after flying home from Vancouver, British Columbia, and the BC naturopathic association's conference. My wife starts shouting from the laundry room; "It's a miracle. It's a miracle!" Her exclamations outcompete *Disenchantment*, and I hit pause. Entertainment must wait.

Years ago, I shared a hotel room with Torrey Smith, ND, from Alaska at an AANP conference in Oakland. He brought an empty suitcase along just to have enough space to bring home the vendor samples he collected. Free stuff is always hard to resist, and the eminent Dr. Smith managed to easily fill his suitcase.

I try to limit how many samples I carry home as they often just sit around for years; yet, I can never resist bringing home a few pens. Those pens vendors give away are often nicer than the ones we purchase from Office Depot. We have yet to switch over to EMR. I still take patient notes using a clipboard, pad of paper, and pen. So, when free pens are offered, I can't resist.

Before turning on the TV that evening, I had tossed the three white dress shirts that I wore in Vancouver into our washing machine along with the white blouses that my dear wife wears when volunteering to usher at the theatre downtown. She grabbed a handful of white things from the laundry hamper and turned on the machine. Neither of us checked my shirt pockets. So, neither of us found the pen I'd brought home. The pen that leaked out in the wash.

"It's only shirts" she is saying as she began her inventory of the damage. "It could be worse: our house has not been blown away by a hurricane." Moments later she abandons this calm rationalizing. "It's a miracle, Baruch H'Shem," (as in 'Blessed is the Name', an expression usually employed by my very religious sister-in-law but not by my usually agnostic wife).

The ink has leaked out of the pen for certain, but it was entirely contained on a single pair of her underwear and one of my 'wife beater' undershirts. Our white dress shirts and blouses were spared. "This must be a sign" she starts saying. But of what I wonder?

If all of our shirts had been ruined, I would have taken it as a sign to quit my day job; no more going to the office. I would wear flannel shirts and live in the woods where ink splotches don't matter. Miracles, if they are anything, are exclamation points in life that suggest one pay attention. But to what?

Was there something at the conference, some imparted wisdom or an epiphany that I missed that I'm supposed to heed? I actually open and relook at the conference PowerPoints. Glen Cassie, the executive director of the BC naturopathic association, put on a solid conference, no question about that. It was tightly and smoothly run, without any noticeable hiccups and, thank goodness, he supplied thumb drives of all the lectures. On top of that, we lucked out with sun all weekend, something that I'm told is rare.

I like Canadian conferences. I've written that before. With the current exchange rate as it is, as soon as we Americans cross the border, it is as if everything is on sale. How can you not love that? Between the accents, the European styles, my impression is that our Canadian colleagues are smarter, healthier, and better looking than we Americans are. They always seem so earnest about everything. Plus, that was the week pot was going to be legalized nationwide. There was a buzz of excitement in the air.

This conference's topics were kind of cerebral. Let me explain that. Most of the lectures had something to do with the brain and how it functions. Doni Wilson lectured on Alzheimer's disease, Bill Code, MD, on neurovascular connections to the brain, Pamela Hutchison on dissociative disorders, David Musnick, MD, on healing brain injuries, Laurie Mischley on Parkinson's, Nalini Chilkov, LAc, on treating cancer chemo-brain, and so on. See what I mean? The lecture topics were focused on cerebral function.

This made for an interesting overall effect as many of the speakers covered similar terrain, each adding a slightly different perspective to the same territory. I found that approach novel. The same basic ideas related to brain health showed up again and again, and perhaps even started to sink in. Though there is a limit on how much you want to hear about stress and glycemic control before it gets old.

As many nice things as I have to say about Canadians, I confess that I wonder if they aren't too nice, or sometimes naïve to the point of being gullible. They may bring less skepticism to the table, and perhaps are more willing to take a speaker's word on things than I am. In my (oft repeated) view, there is a standard for referencing and citations that should be expected in all professional communications these days that was lacking in some of the presentations. If a speaker states

➤

➤

a novel idea or makes an unusual claim, I expect a citation backing it up. I don't think speakers are making things up or are delusional. I just need a citation if I share their idea with another doctor, especially a medical practitioner who may not share our casual approach to science.

For example, one speaker stated that patients recovering from traumatic brain injury (TBI) must absolutely be on diets free of gluten and dairy. There is little debate anymore that celiac disease may have neurological complications.[1] This is accepted fact. Yet to suggest that gluten avoidance may benefit a non-celiac TBI patients in my opinion deserves a reference. I've failed at finding one.

When it comes to milk and TBI, there is an August 2018 paper by YY Gao et al that suggests the opposite of this idea to avoid milk to heal brain trauma. Gao suggests that a factor in milk, "… milk fat globule-EGF factor-8 (MFG-E8) provides neuroprotection through modulation of inflammation, oxidative stress, and especially apoptosis…" after traumatic brain injury.[2] This is exactly why I want speakers to use citations. I want to know how they arrived at their ideas, and I want to be able to believe what they tell me.

I was half joking that much of the conference was cerebral because it was about brain dysfunction and related morbidities. These lectures were also cerebral in the regular sense; they were very brainy, in a functional medicine kind of way; they were the kind of lectures MDs give when they think they are practicing naturopathy. The lectures were heavy on chemical pathways, Venn diagrams and charts with arrows and pathways that all fit together and left me with lists of exotic lab tests to run and supplements to sell.

There was one notable exception to this cerebral line up. Alan Logan gave a keynote lecture that inspired me to think far outside the box of my normal clinical practice model. He reviewed highlights from the scientific literature supporting the benefits exposure to nature has on health. As heavily cited and intellectual as his lecture was, he touched my heart. To

Twenty Things About Nature I Noted

Alan Logan, ND, gave the keynote at the British Columbia Naturopathic Association's conference in October 2018. His content resonated deeply with me. Let me summarize the points that struck home as I listened:

1. Depressive symptoms are associated with inflammatory markers.[4] Exposure to nature reduces both.
2. Levels of psychological distress are increasing over time[5] and people are shifting away from empathy toward more narcissistic patterns of thinking.[6]
3. It's time to put nature back in naturopathy.
4. Excellent book: *The Oxford Textbook of Nature as Medicine* is available.
5. Various schemes have been developed to measure how connected people are with nature. Assessments of nature relatedness, nature connectivity, and nature connectedness, all attempt to measure the degree the Vis flows from nature into us (my words).[7,8] This connection is increased by exposure to nature. The greater the connection, the happier people appear to be.[9]
6. Daniel Baxter in a 2018 review: "It is our overall conclusion that the literature supports the claims that human beings have a basic psychological need to feel a secure and pleasant experiential connection in a cognitive, emotional and physical sense."[10]
7. Higher scores on nature relatedness correlate with overall psychological well-being, vitality, and meaningfulness in life. They also associate with lower anxiety and greater empathy.[11,12]
8. No surprise: the more tree canopy in a neighborhood, the higher people score on nature relatedness.[13]
9. Scientific understanding of what factors affect nature connectedness is still very weak. Logan proposed a list of questions that need to be investigated.[14]
10. People in MRI functional scanners shown photos of rural scenes have increased activity in areas of the brain associated with emotional stability and empathy.[15]
11. Viewing nature scenes lowers biomarkers of stress.[16]
12. For patients in hospital having a window view of trees leads to shorter hospital stays, fewer post-surgical complaints and reduced need for analgesics.[17]
13. "Shinrin-Yoku" – Forest Bathing: studies have involved over 1000 subjects, and two dozen different forest settings: Spending time in forest (vs. built) setting equals less stress and depressive symptoms; increased vigor.
14. Urban nature walking reduces depression.[18]
15. Views of nature outside classrooms produced measurable cognitive benefit in Michigan high school students in 101 schools.[19] Proximity to green space was associated with improved academic performance in Massachusetts.[20] Nature exposure reduces aggressive behavior.[21]
16. People sleep better the closer they live to parks.[22]
17. "[D]ose-response analysis for depression suggests that visits to outdoor green spaces of 30 minutes or more during the course of a week could reduce the population prevalence by up to 7%."[23]
18. Exercise improves mental attitude and exercising outside has 50% more positive effect on attitude than exercising in a gym.[24]
19. The closer a woman lives to green space the lower her risk for an adverse pregnancy outcome,[25] lower her risk to be depressed during pregnancy,[26] and the lower the risk for her kids to develop asthma.[27]
20. For children, lack of access to green space increases chances of having emotional problems.[28]

Treefarm Communications recorded the entire conference and Logan's lecture can be purchased from them: www.TreeFarmTapes.com

this he added a review of the evidence of how nature exposure affects the body's biome and even suggested that this may in part be the mechanism of action of how nature exposure improves health. This combination of viewing the health-imparting effects of nature on both a macro and microscopic level was fascinating. He suggested that we should be actively accessing the degree of nature exposure our patients get and then actively promoting increases in their exposure. Dr. Logan presented a solid argument that this growing field of medicine, the Medicine in Nature, is a niche that the naturopathic profession should claim ownership of. While I try to keep up with this research, I have not actively incorporated these ideas into my practice as rigorously as I might. I now intend to. I might add that our naturopathic schools do not appear to offer adequate classes for students to even learn the techniques to employ nature in clinical practice.

Logan started his lecture with a quote from a 1914 *British Medical Journal* article and then reminded us all of how urbanized our world has become in the intervening years since JA Thompson wrote these words:

> It is, I submit, a condition of sanity to know the country and the seasons, the hills and the sunrise, the birds and the flowers; to know – not merely to read about – the changeful music of the sea. There would be less psychopathology of everyday life if we kept up our acquaintance with the bonnie briar and the cry of the moorland"[3]

Logan's lecture resonated deeply and reminded me why I felt called to become a naturopath in the first place. I've never taken well to selling supplements. I became a naturopath because it seemed like a way to celebrate our natural world and preserve it. Personally, I have always taken pleasure and solace in being outside but have not prescribed the same to patients.

Logan did a great job of reviewing the science that supports our belief that exposure to nature has healing effects. In that respect he was perhaps the most cerebral of the presenters. We're all vaguely familiar with these ideas as they are often covered in the popular media, and some of our colleagues have made efforts to bring these studies to our attention over the years. (I'm thinking of Kurt Beil's writing in the *Natural Medicine Journal*.) Logan questioned why nature and what the researchers call nature connectedness are not a fundamental part of naturopathic education and why all of us aren't assessing the level of nature exposure in each of our patients and working hard to increase it.

The explanation I've heard from some is that there is no money in nature. I queried a conference planner recently about organizing a nature-focused conference. The response, "I don't think we could make any money, or really even break even because there isn't really a sponsor opportunity…." Our current conference financial model is dependent on vendor sponsors who have something to sell. We may need a new model of funding our conferences so that we can break even. At the same time our professional associations and individual doctors who set up conferences depend on and are highly desirous of making profits. Nature has nothing to sell, will not buy booths in the vendor hall, and will not sponsor meals.

If the other conference lectures were cerebral, Logan's lecture was the opposite: his ideas resonated in my heart of hearts and echoed loud in my core. I do not often say that about a conference speaker.

If I'm going to consider our ink episode a minor miracle, (it's not in the Red Sea-parting league obviously), the message was delivered in Dr. Logan's lecture. It's time to focus naturopathy back on nature.

➤

➤

References

1. Briani C, et al. Neurological complications of celiac disease and autoimmune mechanisms: a prospective study. *J Neuroimmunol.* March 2008;195(1-2):171-5.
2. Gao YY, et al. Recombinant milk fat globule-EGF factor-8 reduces apoptosis via integrin β3/FAK/PI3K/AKT signaling pathway in rats after traumatic brain injury. *Cell Death Dis*. 2018 Aug 28;9(9):845.
3. Thomson JA. The popular lecture: Vis Medicatrix Naturae. *BMJ*. 1914;2:277-79
4. Marteinsdottir I, et al. Psychological Resources Are Independently Associated with Markers of Inflammation in a Middle-Aged Community Sample. *Int J Behav Med*. 2016

Grand Rounds Sessions

Glen Cassie did something unique at the naturopathic conference held in Vancouver in October, or at least new to me. He organized what he called a "Grand Rounds" session. A room was set up with large round tables and at each table was either a lecturer or expert on a particular topic. Conference attendees picked a table and talked with the presenter for a 'session' before moving on to another table. I had the opportunity to sit in a small group with Neil McKiney, who always has something interesting to talk about in regard to treating cancer. Then after we switched tables, I had the pleasure of hearing from Jody Stanislaw, a ND and diabetes educator from Seattle who is a hoot.

When queried, Neil admitted that his next book is scheduled to come out in late Spring of 2019. While I have copies of his early books on my shelf, it's time for me to get a copy of his next one. Neil is quite excited with the results he is seeing with a new protocol he's developed for advanced prostate cancer. It centers around using *Polygonatum cyrtonema* (aka Solomon's seal) in an herbal formula:

> I prescribe 60% Solomon's seal tincture with 20% each yew and periwinkle, take ½ tsp twice daily in juice or water – eg. shake well, put 1 tsp in liquid, drink half in the am and half in the pm…. It has been very well tolerated and almost every cancer patient so far has responded immediately and strongly. Some cases take a month or two to improve. The yew and periwinkle are restricted herbs. Yew (*Taxus brevifolia*) is the source of the taxane family chemo drugs such as Docetaxol and Paclitaxel. It can cause nausea. Periwinkle flower (*Catharanthus rosea* or *Vinca rosea*) is added as an anti-inflammatory. It can lower blood sugar. It is not suitable for brain cancers.

Jody Stanislaw, ND, was diagnosed with juvenile diabetes when she was seven and brings a lifetime of experience to her practice along with an enthusiastic personality that made listening to her fun. Her practice is all telemedicine, and her website links to useful videos that will prove useful to the right patients. (She only works with autoimmune diabetics, that is type 1 diabetics.) Her Vancouver lecture was about how to preserve beta-cell function in these patients, an admirable, highly useful, but at this point still unproven goal. Her website is DrJodyND.com.

5. Twenge JM. Time Period and Birth Cohort Differences in Depressive Symptoms in the U.S., 1982–2013. *Soc Indic Res*. 2015;121: 437.
6. Twenge JM. Overwhelming evidence for generation me. *Emerg Adulthood*. 2013;1:21–6.
7. Nisbet E, et al. The nature relatedness scale. *Environ Behav*. 2009;41:715-40.
8. Nisbet EK, Zelenski JM. The NR-6: a new brief measure of nature relatedness. *Front Psychol*. 2013;4:813.
9. Capaldi CA, Dopko RL, Zelenski JM. . The relationship between nature connectedness and happiness: a meta-analysis. *Front Psychol*. 2014 Sep 8;5:976.
10. Baxter DE, Pelletier L. G.I.'s nature relatedness: a basic human psychological need? A critical examination of the extant literature. *Canadian Psychology/ Psychologie canadienne*, Apr 16, 2018.
11. Martyn P, Brymer E. The relationship between nature relatedness and anxiety. *J Health Psychol*. 2016 Jul;21(7):1436-45.
12. Capaldi CA, et al. The relationship between nature connectedness and happiness: a meta-analysis. *Front Psychol*. 2014 Sep 8;5:976.
13. Shanahan DF, et al. Variation in experiences of nature across gradients of tree cover in compact and sprawling cities. *Landscape Urban Plan*. 2017;157:231-8.
14. Craig Logan. Prescott Journal of Physiological Anthropology. 2016.
15. Kim TH, et al. Human brain activation in response to visual stimulation and rural urban scenery pictures: a functional magnetic resonance imaging study. *Sci Total Environ*. 2010;408:2600-7.
16. Berto. The role of nature in coping with psycho-physiological stress: a literature review on restorativeness. *Behav Sci*. 2014 Oct 21;4(4):394-409.
17. Ulrich R. View through a window may influence recovery from surgery. *Science*. 1984;224:420-1.
18. Berman, et al. Interacting with nature improves cognition and affect for individuals with depression. *J Affect Disord*. 2012 Nov;140(3):300-5.
19. Matsuoka R. Student performance and high school landscapes: examining the links. *Landscape and Urban Plan*. 2010;97:273-82.
20. Wu CD, et al. Linking student performance in Massachusetts elementary schools with the "greenness" of school surroundings using remote sensing. *PLoS One*. 2014;9:e108548.
21. Younan D, Environmental Determinants of Aggression in Adolescents: Role of Urban Neighborhood Greenspace. *J Am Acad Child Adolesc Psychiatry*. 2016 Jul;55(7):591-601.
22. Johnson BS, et al. Exposure to neighborhood green space and sleep: evidene from the Survey of the Health of Wisconsin. *Sleep Health*. 2018 Oct;4(5):413-419.
23. Shanahan DF, et al. Health Benefits from Nature Experiences Depend on Dose. *Sci Rep*. 2016 Jun 23;6:28551.
24. Gladwell, et al. A Lunchtime Walk in Nature Enhances Restoration of Autonomic Control during Night-Time Sleep: Results from a Preliminary Study. *Int J Environ Res Public Health*. 2016 Mar 3;13(3). pii: E280
25. Casey JA, et al. Greenness and Birth Outcomes in a Range of Pennsylvania Communities. *Int J Environ Res Public Health*. 2016 Mar 11;13(3). pii: E311.
26. McEachan RR, et al. The association between green space and depressive symptoms in pregnant women: moderating roles of socioeconomic status and physical activity. *J Epidemiol Community Health*. 2016 Mar;70(3):253-9.
27. Sbihi H, et al. Greenness and Incident Childhood Asthma: A 10-Year Follow-up in a Population-based Birth Cohort. *Am J Respir Crit Care Med*. 2015 Nov 1;192(9):1131-3.
28. Snell, et al. Contact with Nature in Childhood and Adult Depression. *Child Youth Environ*. 2016;26:111-124.

◆

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

Shorts

briefed by Jule Klotter
jule@townsendletter.com

Cochrane Collaboration Crisis

In 1993, Ian Chalmers and a group of 70 other international colleagues, including Danish physician-scientist Peter Gøtzsche, founded the Cochrane Collaboration to provide evidence-based reports on medical procedures. To produce these systematic reviews, Cochrane aimed to lessen bias by investigating published studies, unpublished data, and negative results as well as by evaluating the reliability of the information, giving more weight to randomized clinical trials. Cochrane Systematic Reviews have become a trusted source for health practitioners.

Peter Gøtzsche, who heads the Nordic Cochrane Centre and was voted onto the Cochrane Governing Board in 2017, was expelled from the Cochrane Collaboration in September 2018, ostensibly due to his violation of the Cochrane Spokesperson Policy and bad behavior that threatened Cochrane's reputation. An outside law firm hired by the Board of Trustees found no evidence to support this or other charges made by CEO Mark Wilson. Wilson, whose background is in business management and journalism, came to Cochrane in 2012. The Governing Board, headed by CEO Mark Wilson, has 13 members. In addition to the five who opposed Gøtzsche's expulsion and Gøtzsche (who was not allowed to vote), one member abstained; a "majority" of six voted for his removal from the organization. Four of the five governing board members who opposed Gøtzsche's expulsion resigned the next day because they could not publicly defend the action, as would be expected of Governing Board members.

Gøtzsche has been a long-time advocate for transparency and scientific debate. He has authored several books and over 70 articles published in major medical journals including Cochrane reviews such as the one that reported the dangers of over-diagnosis with mammography. He has also been very critical of the pharmaceutical industry, targeting the harms and overuse of psychiatric drugs and, more recently, the serious adverse effects of the HPV vaccine. In 2016, Gøtzsche criticized the European Medicine Agency for its incomplete and inaccurate report on the safety and efficacy of the human papillomavirus (HPV) vaccine.

Throughout 2018, Gøtzsche, along with Lars Jørgensen of Nordic Cochrane Centre and Tom Jefferson at the Centre for Evidence Based Medicine in the UK, has engaged in a running debate about the quality of Cochrane's review on the HPV vaccine that was published in May 2018. The Cochrane review by M. Arbyn et al downplayed the risk of adverse effects; its authors reported that they "did not find an increased risk of serious adverse effects" and the Cochrane press release, written by six UK experts, reported "'...the HPV vaccine is the most effect way for young girls to protect themselves against cervical cancer' and that 'the vaccine causes no serious side-effect.'"

In response Jørgensen et al have published critiques and responses to the review authors and Cochrane editors in the *British Medical Journal* and on the *BMJ* blog. They report that the M. Arbyn et al review "should have included at least 35% (25,550/73,428) additional eligible females in its meta-analyses." Moreover, the reviewers relied solely on published reports. As Jørgensen et al explain in *BMJ Evidence-Based Medicine,* "harms cannot be assessed reliably in published trial documents – especially in journal publications of industry-funded trials where even serious harms often are missing.... As an example, the journal publication for the PATRICIA trial is 14 pages long while its publicly available corresponding clinical study report is over 7000 pages long....Clinical study reports are usually confidential documents, but they can be requested from the European Medicines Agency (EMA) and ClinicalStudyDataRequest.com (CSDR)."

In addition, Jørgensen et al point out that, throughout the review, Arbyn and colleagues use the term "placebo" when, in actuality, none of the 26 studies used a true, inert placebo (e.g. saline). All trials in their meta-analyses used active comparators: aluminum-based adjuvants or hepatitis vaccines that contain aluminum adjuvants. These adjuvants are known to have harmful effects, according to vaccine manufacturer GlaxoSmithKline. "The use of active comparators probably increased the occurrence of harms in the comparator groups and thereby masked harms caused by the HPV vaccines," say Jørgensen et al. Moreover, the review authors did not mention

that several of the studies they used only counted adverse events that occurred within 14 days of vaccination, nor did they investigate reports of postural orthostatic tachycardia syndrome (POTS) or complex regional pain syndrome. Instead, they relied on the European Medicine Agency's conclusion that was based on "manufacturers' own unverified assessments," which claim no association between the vaccines and these conditions.

Jørgensen et al also point out that three of the review's four authors had major conflicts of interest related to HPV vaccine manufacturers. Gøtzsche had been pushing for changes to Cochrane conflict-of-interest policy for over a year before his expulsion. At present, Cochrane allows up to half of a review's authors to have financial conflicts of interest. In the case of the May 2018 HPV review, more than half of the authors had ties to vaccine manufacturers. Apparently, this very public criticism of a Cochrane review, along with previous altercations with the Cochrane CEO, led to the vote for expulsion.

In response to Gøtzsche's removal, Cochrane Iberoamerica, consisting of 31 signatories, sent a letter to all Cochrane members requesting an ad-hoc commission to independently review the conflict as well as immediate elections to fill the vacant governing board positions. In response to this letter, David Hammerstein, one of the Governing Board members who resigned after Gøtzsche's expulsion, responded: "The crisis in Cochrane is about the credibility of Cochrane and not a question concerning the 'behaviour' by one individual."

Hammerstein views the crisis as a conflict of competing paradigms: CEO Mark Wilson and allies, who are primarily interested in financial growth and stability rather than public health, vs. people like Peter Gøtzsche, who want "much stronger policies to avoid biases and conflicts of interest in Cochrane reviews, much greater visibility of Cochrane in policy debates on health technology evaluation, open access publishing, shared structured data and open models of biomedical innovation. What is essential for this group is where the 'evidence' comes from, who pays for it and if all the clinical evidence is publicly available or not.

As I write this in November, the outcome is uncertain. Dr. Gøtzsche continues to post relevant documents and letters concerning the conflict at his website www.deadlymedicine.dk. After the expulsion, Cochrane Collaboration reportedly took control of the Nordic Cochrane Centre website and declared that Gøtzsche was no longer the center's director. Dr. Gøtzsche declares this to be false. He continues to be the director of Nordic Cochrane Centre, which has withdrawn from the Cochrane Collaboration: "We are now an independent centre, no longer subjected to the scientific censorship that the current Cochrane leadership favours, and we continue our work as usual." Other centers may follow his lead.

Demasi M. Cochrane – A sinking ship? September 16, 2018. https://blogs.bmj.com.

Hammerstein D. Regenerate Cochrane to strengthen the production of trusted evidence for the common good of public health. October 8, 2018.

Jørgensen L, Gøtzsche PC, Jefferson T. The Cochrane HPV vaccine review was incomplete and ignored important evidence of bias. *BMJ Evidence-Based Medicine.* October 2018;23(5):165-168.

Jørgensen L, Gøtzsche PC, Jefferson T. Response to Cochrane editors: Jørgensen, Gøtzsche Jefferson. September 23, 2018. Available at https://blogs.bmj.com.

Shah HM, Chung KC. Archie Cochrane and his vision for evidence-based medicine. *Plast Reconstr Surg.* September 2009;124(3):982-988.

Aluminum and Autism

In 2018, a team of British researchers reported "extraordinarily high" levels of aluminum, a known neurotoxin, in tissue from the brains of five people (4 male; 1 female) with confirmed autism diagnosis. The UK study, led by Matthew Mold and funded by the non-profit Children's Medical Safety Research Institute, said the results showed "some of the highest values for brain aluminium content ever measured in healthy or diseased tissues in these male ASD [autism spectrum disorder] donors...." Tissue from a 15-year-old boy had a mean level of 6.02 µg/g.

In addition, the UK researchers used fluorescence microscopy to examine brain sections from 10 other donors with ASD. They found more aluminum deposits in males (129 in 7 individuals) than in females (21 in 3 individuals). The deposits were extracellular and intracellular, affecting neurons and non-neuronal cells, including microglia. Aluminum compounds (aluminium) were also found in mononuclear white blood cells in the meninges, indicating that the metal might be entering the brain via the lymphatic system. The authors conclude: "The presence of aluminium in inflammatory cells in the meninges, vasculature, grey and white matter is a standout observation and could implicate aluminium in the aetiology of ASD." This was the first study to measure aluminum content in the brains of people with autism.

In a Letter to the Editor regarding this study, Ivan Ivanovski et al state that consumption is unlikely to be the source of the high aluminum levels, despite its widespread presence in processed foods, cooking utensils, and drinking water. They point out that only about 0.25% of ingested aluminum (Al) is absorbed into the circulation, although it may be more if the intestinal mucosa is damaged. In contrast, nearly 100% of aluminum hydroxide, commonly used as an adjuvant in vaccines, enters circulation when injected intramuscularly. Moreover, the injected Al adjuvant binds with transferrin, which ➤

➤

allows it to cross the blood-brain and blood-cerebrospinal fluid barriers. It is unlikely to be excreted once it enters the brain.

The US vaccine schedule delivers about 4925 µg of aluminum parenterally by the age of 18 months, according to Ivanovski et al. The authors suggest postponing aluminum-containing vaccines until children lose their last primitive reflex, indicating physiological maturation, which is usually about six to seven months old. They also suggest replacing aluminum adjuvants with compounds that may be less toxic, such as squalene, calcium phosphate, or a zinc compound.

Ivanovski I, et al. Aluminium in brain tissue in autism. *J Trace Elements in Medicine and Biology.* 2019;51:138-140.
Mold M, et al. Aluminium in brain tissue in autism. *J Trace Elements in Medicine and Biology.* 2018;46:76-82.

Nanorobots in Medicine

Micro/nanorobots, measuring a few micrometers or less, offer new possibilities for medical diagnosis and treatment, according to a 2017 review from the department of nanoengineering at University of Southern California-San Diego. Nanoengineers have developed a variety of ways to power the tiny machines, many of which are made from biocompatible components that can degrade when their task ends. Some are chemically powered, using locally supplied components to fuel their activity. Others depend upon externally applied ultrasound or magnetic energies for power. Some tiny robots have also been integrated with living organisms that are capable of moving.

At this point, most research has been in vitro, with a few in vivo animal studies. Nanoengineers have shown that micro/nanorobots can make their way through complex biological media and narrow capillaries. Some have carried therapeutic compounds directly to tumors or other diseased areas. Tiny robots with microgrippers can retrieve tissues and cells from hard-to-reach locations. Eventually, the microgrippers may evolve into a tool for microsurgery, according to the authors. Micro/nanorobots can also perform ablation. Detoxification is another use; the authors envision a cohort of micro/nanorobots working together to capture and remove toxins from a body.

Of course, several hurdles need to be overcome before nanorobotics becomes part of medical practice. The authors say, "…nanorobotic scientists should work more closely with medical researchers for thorough investigations of the behavior and functionality of the robots, including studies on their biocompatibility, retention, toxicity, biodistribution, and therapeutic efficacy."

Li J, et al. Micro/nanorobots for biomedicine: Delivery, surgery, sensing, and detoxification. *Sci Robot.* March 1, 2017.

Glyphosate Food Contamination

In September 2018, the Environmental Working Group (EWG), along with Stonyfield Farm, Nature's Path, National Co-op Grocers and others, petitioned the Environmental Protection Agency (EPA) to prohibit the use of glyphosate-based herbicides as a pre-drying agent and to limit residues on oats. About three-fourths of oat-based foods, commonly eaten by children, had higher glyphosate levels (according to independent testing conducted the previous month) than EWG scientists consider advisable. Because of glyphosate's use as a pre-drying agent immediately before harvest, even non-GMO crops (i.e., oats, wheat, and beans) may be contaminated with high levels of the herbicide – unless they are certified organic.

John Peterson Myers and a group of US colleagues published a review of the concerns and risks associated with glyphosate-based herbicides, such as Roundup, in 2016. About 240 million pounds of glyphosate was used on US farms and ranches in the year 2014, a huge increase from the 180-185 million pounds used in 2007. When it was registered for use in 1974, scientists assumed that glyphosate would have few negative effects on mammals because it targets an enzyme found only in plants. In reality, the herbicide produces multiple negative effects on mammals (and other animals).

Glyphosate disturbs mitochondrial metabolism and produces oxidative damage to the liver and kidneys in animals and humans. Glyphosate also disrupts endocrine-signaling systems, according to in vitro and animal studies. Animal studies indicate the possibilities of neurotoxicity and cancer. Severe birth defects have increased in Argentina and Paraguay where Roundup Ready crops are grown. Birth defects have also been observed among pigs and poultry that eat glyphosate-contaminated feed. Being a chelating agent, glyphosate binds to nutrient metals, including manganese, cobalt, and zinc, making these nutrients inaccessible to plants and the animals that use them for food. Myers et al say, "These micronutrient metals are enzymatic cofactors, so their loss has the potential to contribute to a number of deleterious effects, especially on kidney and liver function." Finally, glyphosate's antibiotic properties can have adverse effects on the GI microbiome.

Myers et al mention that US EPA was scheduled to release its risk assessment and re-registration on glyphosate-based herbicides in 2015-2016. This did not happen. A proposed interim registration review decision is expected in 2019, according to EPA's website. The decision "will outline any proposed mitigation measures."

The Great Plains Laboratory can test a person's glyphosate exposure. William Shaw, PhD, and Matthew Pratt-Hyatt, PhD, wrote an article about testing for glyphosate, which appears in the January 2017 issue of *Townsend Letter*. Their article is also available online. In addition to testing individuals' contamination, GlyphoCheck™ Strip Test, available at www.detoxproject.org, can detect glyphosate in food and water samples. Avoiding glyphosate as much as possible is the first step in avoiding risks.

Myers JP, et al. Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. *Environmental Health.* 2016:15-19.
US Food Brands Petition EPA to Ban Pre-Harvest Glyphosate Spraying. Sustainable Pulse. September 28, 2018.

◆

Literature Review & Commentary

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

Iron Deficiency Anemia and Hemoglobin A1c

In a study of Asian Indians with iron-deficiency anemia (IDA; n = 62) and age- and sex-matched healthy controls without IDA (n = 60), the mean hemoglobin A1c (HbA1c) level was significantly higher in those with IDA than in controls (5.51% vs. 4.85%; $p < 0.001$). In subjects with IDA, there was a significant negative correlation between the HbA1c concentration and the hemoglobin level, hematocrit, and serum ferritin concentration. In subjects with IDA, the mean HbA1c level fell from 5.51% at baseline to 5.04% after iron supplementation ($p < 0.001$). Fourteen of 20 subjects (70%) with an HbA1c level in the prediabetes range at baseline had a normal HbA1c level after iron supplementation. Of six patients with a pretreatment HbA1c level in the diabetes range, five reverted to the prediabetes range and one had a normal HbA1c level after iron supplementation.

Comment: One possible interpretation of these findings is that IDA leads to impaired glycemic control and that correction of IDA improves glycemic control. However, that conclusion would contradict previous research indicating that iron deficiency has a positive effect and iron excess has an adverse effect on blood glucose regulation. A more plausible explanation for the findings in this study is that IDA leads to erroneous (i.e., false-high) measurements of HbA1c. In IDA, the quaternary structure of hemoglobin is altered, resulting in increased susceptibility to glycation. In addition, patients with IDA may have a lower proportion of young erythrocytes, because new erythrocytes are not being formed at an adequate rate. The concentration of HbA1c in erythrocytes increases linearly with the cell's age; therefore, the low proportion of young erythrocytes could result in a higher HbA1c value. After iron supplementation, rapid erythropoiesis results in a lower average erythrocyte age and, consequently, a lower HbA1c level. The results of this study suggest that HbA1c measurements should be interpreted with caution in patients with IDA.

Madhu SV, et al. Effect of iron deficiency anemia and iron supplementation on HbA1c levels - Implications for diagnosis of prediabetes and diabetes mellitus in Asian Indians. *Clin Chim Acta*. 2017;468:225-229.

Blue Light-Blocking Lenses to Treat Insomnia

Fourteen individuals (aged 18-65 years; mean age, 46.6 years) with insomnia were randomly assigned to wear blue light-blocking amber lenses or clear placebo lenses for two hours before bedtime for seven days. After a four-week washout period, each person wore the alternate lenses for an additional seven days. The blue light-blocking lenses blocked about 65% of the blue light, whereas the clear lenses blocked about 10% of the blue light. Compared with the clear lenses, the blue light-blocking lenses significantly improved the mean Pittsburgh Insomnia Rating Scale score by 18.3% ($p = 0.023$), significantly increased mean total sleep time (399 vs. 347 minutes; $p < 0.01$), and significantly improved sleep quality ($p < 0.04$) and sleep soundness ($p = 0.004$).

Comment: Exposure in the evening or at night to normal room lighting or to light-emitting diode (LED) computer screens reduces melatonin secretion and also increases arousal independently of melatonin secretion. Each of these effects can interfere with normal sleep patterns. The blue-light portion of the visible spectrum (450-480 nm) appears to be the most efficient wavelength range for suppressing melatonin secretion and increasing arousal. Most computers, televisions, and smart phones, and many light bulbs are lit by LEDs, which have a peak wavelength of around 460 nm. As many as 90%

➤

➤

of Americans use some type of LED device within an hour of bedtime. The results of the present study suggest that wearing blue light-blocking lenses for two hours before bedtime can improve sleep in people with insomnia.

Shechter A, et al. Blocking nocturnal blue light for insomnia: a randomized controlled trial. *J Psychiatr Res*. 2018;96:196-202.

Cherry Juice for Insomnia

Eleven healthy subjects (mean age, 68 years) with insomnia were randomly assigned to receive, in double-blind fashion, 240 ml of tart cherry juice or placebo twice a day, in the morning and one hour before bedtime, for 14 days. After a two-week washout period, each person received the alternate treatment for an additional 14 days. The placebo contained fructose, glucose, and lemon powder, and looked and tasted like cherry juice. An overnight polysomnographic sleep study was conducted at the end of each treatment period. Three subjects were found on polysomnography to have sleep apnea and were excluded from the analysis. Among the remaining eight subjects, mean total sleep time according to polysomnography was 84 minutes longer with cherry juice than with placebo ($p < 0.02$). Sleep efficiency as determined by questionnaire was significantly better with cherry juice than with placebo ($p = 0.03$), but sleep efficiency as determined by polysomnography was only nonsignificantly better with cherry juice than placebo ($p = 0.19$). The mean serum kynurenine-to-tryptophan ratio was significantly lower with cherry juice than with placebo ($p < 0.05$), indicating less metabolism of tryptophan to kynurenine.

Comment: Tryptophan is metabolized to serotonin and melatonin, both of which play a role in sleep. Tryptophan is also metabolized by a separate pathway to kynurenine by the enzyme, indoleamine 2,3-dioxygenase (IDO). This enzyme is inhibited by inflammation, and cherry juice has been reported to have an anti-inflammatory effect. *In vitro*, procyanidin B-2 (a flavonoid present in cherries and apples) inhibited IDO in a dose-dependent manner. Inhibiting the metabolism of tryptophan to kynurenine would make more tryptophan available to be converted to serotonin and melatonin.

The results of the present study suggest that consumption of cherry juice can increase sleep time and improve sleep efficiency in elderly people with insomnia, possibly by increasing the availability of tryptophan for serotonin and melatonin synthesis. However, a larger study is needed to confirm these findings. Of note, only one of the seven variables assessed on the questionnaire (i.e., sleep efficiency) showed a statistically significant advantage of cherry juice over placebo. The fact that no adjustment was made for multiple comparisons increases the probability that the significant improvement in sleep efficiency was due to chance.

Losso JN, et al. Pilot study of the tart cherry juice for the treatment of insomnia and investigation of mechanisms. *Am J Ther*. 2018;25:e194-e201.

Do Cooking Methods Affect Diabetes Risk?

A prospective study was conducted among 52,752 women from the Nurses' Health Study (NHS) (followed from 1996 to 2012), 60,809 women from NHS II (followed from 2001 to 2013), and 24,679 men from the Health Professionals Follow-Up Study (followed from 1996 to 2012) who were free of diabetes, cardiovascular disease, and cancer at baseline. During 1.74 million person-years of follow-up, 7,895 new cases of type 2 diabetes were documented. After adjustment for baseline body mass index and total consumption of red meat, chicken, and fish, higher frequency of open-flame and/or high-temperature cooking was independently associated with an increased risk of type 2 diabetes. When comparing open-flame and/or high-temperature cooking more than 15 times per month with less than four times per month, the pooled hazard ratio for type 2 diabetes was 1.28 (i.e., a 28% increase in risk; p for trend < 0.001). The association remained significant when red meat and chicken were examined separately.

Comment: In this study, open-flame and/or high-temperature cooking of red meat and chicken was associated with an increased risk of developing type 2 diabetes, independently of the amounts of these foods consumed. High-temperature cooking of meats and of various other foods results in the formation of advanced glycation end products (AGEs). AGEs have been reported to promote insulin resistance and to damage pancreatic islet cells in mice[1] and to accelerate the progression of nephropathy in mouse models of type 1 and type 2 diabetes.[2] Consumption of a high-AGE diet has also been shown to promote insulin resistance in humans with type 2 diabetes[3] and in overweight nondiabetic individuals.[4]

The AGE content of the diet can be decreased by cooking at lower temperatures and in the presence of water or other liquids. Thus, boiling, steaming, or poaching of foods results in less AGE formation than does grilling, frying, roasting, or baking. Of course, raw foods have a very low AGE content.

Liu G, et al. Meat cooking methods and risk of type 2 diabetes: results from three prospective cohort studies. *Diabetes Care*. 2018;41:1049-1060.

How Much Vitamin D for Infants?

Nine hundred seventy-five healthy term infants in Finland (all of Northern European ethnicity) were randomly assigned to receive 400 or 1,200 IU per day of vitamin D from age two weeks to 24 months. The primary outcome measures were bone strength of the left tibia (as determined by bone mineral content, bone mineral density, cross-sectional area, and polar moment of inertia [an indicator of resistance to torsion]) and incidence of parent-reported infections at 24 months. There was no significant difference between groups with respect to any of the four measures of bone strength or in the incidence of infections.

Comment: Guidelines for vitamin D supplementation for children are mostly based on studies focusing on prevention of rickets. The optimal dose for bone strength and infection prevention in healthy infants remains unclear. In this study

of Northern European infants, 400 IU per day of vitamin D appeared to be adequate for children younger than 2 years of age, and increasing the dose to 1,200 IU per day had no effect on bone strength or incidence of infections. An earlier double-blind study of healthy, term breastfed infants in Montreal, Canada, found that gross motor development was significantly better in those receiving 400 IU per day of vitamin D than in those receiving 800 or 1,200 IU per day.[5] Thus, the available data suggest that healthy infants should not be given more than 400 IU per day of vitamin D unless there is evidence that the benefits of using a higher dose would outweigh the risks for a particular child.

Rosendahl J, et al. Effect of higher vs standard dosage of vitamin D_3 supplementation on bone strength and infection in healthy infants: a randomized clinical trial. *JAMA Pediatr*. 2018;172:646-654.

High-Dose Vitamin D May Adversely Affect Muscle Strength and Physical Performance

Eighty-one postmenopausal Danish women (aged 60-80 years) with a serum 25-hydroxyvitamin D level below 20 ng/ml (mean, 13.2 ng/ml) and secondary hyperparathyroidism were randomly assigned to receive, in double-blind fashion, 2,800 IU per day of vitamin D3 or placebo for three months during the winter. Vitamin D supplementation increased the mean 25-hydroxyvitamin D level by 230% and decreased the mean parathyroid hormone level by 17% ($p < 0.001$). Compared with placebo, vitamin D reduced maximal handgrip strength by 9% ($p < 0.01$) and knee flexion strength by 13% ($p = 0.02$), and increased the time required to complete the Timed Up and Go test by 4.4%; ($p < 0.05$). Levels of physical activity, postural stability, well-being, and quality of life did not change.

Comment: Vitamin D deficiency has been associated with reduced muscle strength, physical performance, postural stability, well-being, and quality of life. When vitamin D deficiency is the cause of or contributes to impaired physical functioning, vitamin D supplementation would be expected to lead to improvement. However, a growing number of studies in people with various clinical conditions suggest that high doses of vitamin D are not more effective, and may even be less effective, than moderate doses of the vitamin (such as 800-1,200 IU per day). In the present study, supplementation with 2,800 IU per day of vitamin D for three months had an adverse effect on certain parameters of physical performance in postmenopausal women with low baseline levels of 25-hydroxyvitamin D.

Studies on vitamin D supplementation to prevent falls in elderly people have produced conflicting results. However,

➤

➤

the trend in those studies appeared to suggest that moderate doses prevent falls, higher doses are less effective, and periodic administration of large bolus doses actually increases the risk of falls.

Short-term administration of large doses of vitamin D may be appropriate for correcting a deficiency. However, the present study, when combined with other research, suggests that large doses should not, in most cases, be given for long periods of time. As I have pointed out elsewhere, serum 25-hydroxyvitamin D appears to be an unreliable indicator of vitamin D status.[6] A case can be made that practitioners should not use that test as a guide for vitamin D dosing. At present there is no convincing evidence that routinely basing dosage recommendations on 25-hydroxyvitamin D levels is safe or improves outcomes. For adult patients who are likely to benefit from vitamin D supplementation, my usual practice has been to recommend 800-1,200 IU per day and not to measure the 25-hydroxyvitamin D level. The final word on proper vitamin D dosing is not yet in.

Bislev LS, et al. Effects of vitamin D3 supplementation on muscle strength, mass, and physical performance in women with vitamin D insufficiency: a randomized placebo-controlled trial. *Calcif Tissue Int*. 2018 Jun 21 [Epub ahead of print].

Pancreatic Enzyme Therapy for Pancreatic Cancer

Eighty-eight patients with inoperable pancreatic cancer were randomly assigned to receive, in open-label fashion, pancreatic enzymes (pancrelipase; 48,000 lipase units per meal) or no pancreatic enzymes (control group). Ninety percent of the patients had exocrine pancreatic insufficiency at baseline, as determined by the N-benzoyl-tyrosyl para-aminobenzoic acid (NBT-PABA) test. The primary outcome measure was the change in body mass index at eight weeks. Secondary outcomes included other measures of nutritional status, such as hemoglobin, albumin, total cholesterol, and triglycerides. There was no significant effect of pancreatic enzymes on any of the outcome measures. Median survival time was higher in the group receiving pancreatic enzymes than in the control group (19 vs 12 months; $p = 0.07$).

Comment: Pancreatic cancer is frequently associated with exocrine pancreatic insufficiency, which may lead to decreased nutritional status. However, the role of pancreatic enzyme replacement therapy has not been well studied. In the present trial, administration of pancreatic enzymes did not improve nutritional status in patients with inoperable pancreatic cancer. However, it did increase median survival time by seven months, an effect that was of borderline statistical significance.

In 1999, Gonzalez and Isaacs reported the results of 11 patients with pancreatic cancer who were treated with a program that included large doses of pancreatic enzymes, dietary modifications, and coffee enemas. Median survival time in those patients was 17 months, which was substantially higher than the median survival time of six months that was reported in the then-current literature for similar patients.[7]

Both of these studies suggest that pancreatic enzyme supplementation can prolong survival in patients with pancreatic cancer, even if it does not improve nutritional status.

Saito T, et al. A multicenter open-label randomized controlled trial of pancreatic enzyme replacement therapy in unresectable pancreatic cancer. *Pancreas*. 2018;47:800-806.

Thyroid Hormone Improves Fatty Liver

Twenty men (mean age, 48 years; mean body mass index, 30.9 kg/m^2) with type 2 diabetes and nonalcoholic fatty liver disease, who were considered euthyroid by laboratory criteria (a normal free-T4 level and a TSH level between 1 and 10 mIU/L) were treated with levothyroxine, with the dose titrated to maintain a low-normal TSH level (0.34-1.70 mIU/L). The treatment was continued for 16 weeks after the maintenance dose was achieved. Patients were advised to maintain their usual diet and exercise patterns. At baseline, the mean TSH level was 1.86 mIU/L, which decreased to a mean of 1.41 mIU/L during the titration phase. The median maintenance dose of levothyroxine was 18.75 µg per day (range, 12.5 µg every 2 days to 87.5 µg per day). Compared with baseline, the mean fat content of the liver decreased by 12% ($p < 0.05$). Mean body weight decreased by 1 kg during the study ($p < 0.05$).

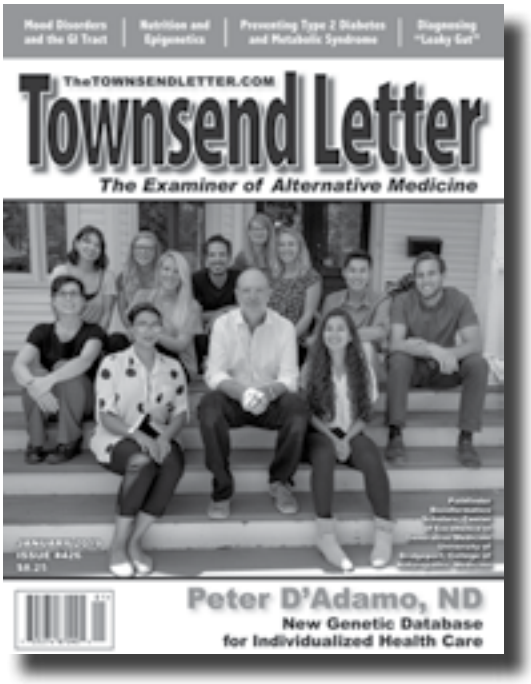
Comment: These results suggest that low-dose levothyroxine can decrease intrahepatic lipid content in patients with type 2 diabetes and nonalcoholic fatty liver disease. The mechanism of action of thyroid hormone is not clear. It is unlikely that the beneficial effect was due to the small amount of weight the patients lost during the study.

Bruinstroop E, et al. Low-dose levothyroxine reduces intrahepatic lipid content in patients with type 2 diabetes mellitus and NAFLD. *J Clin Endocrinol Metab*. 2018;103:2698-2706.

References

1. Hofmann SM, et al. Improved insulin sensitivity is associated with restricted intake of dietary glycoxidation products in the db/db mouse. *Diabetes*. 2002;51:2082-2089.
2. Zheng F, et al. Prevention of diabetic nephropathy in mice by a diet low in glycoxidation products. *Diabetes Metab Res Rev*. 2002;18:224-237.
3. Uribarri J, et al. Restriction of advanced glycation end products improves insulin resistance in human type 2 diabetes: potential role of AGER1 and SIRT1. *Diabetes Care*. 2011;34:1610-1616.
4. Mark AB, et al. Consumption of a diet low in advanced glycation end products for 4 weeks improves insulin sensitivity in overweight women. *Diabetes Care*. 2014;37:88-95.
5. Wicklow B, et al. Impact of vitamin D supplementation on gross motor development of healthy term infants: a randomized dose-response trial. *Phys Occup Ther Pediatr*. 2016;36:300-342.
6. Gaby AR. Vitamin D. In Gaby AR. *Nutritional Medicine, Second Edition*. Concord, NH, 2017. www.doctorgaby.com. Chapter 23.
7. Gonzalez NJ, Isaacs LL. Evaluation of pancreatic proteolytic enzyme treatment of adenocarcinoma of the pancreas, with nutrition and detoxification support. *Nutr Cancer*. 1999;33:117-124.

◆



On the cover

Datapunk Circuits: A Multi-Dimensional, Open-Source, Genomic Database for Clinical Investigation

by Peter D'Adamo, ND

The Center of Excellence in Generative Medicine (COEGM) at the University of Bridgeport College of Naturopathic Medicine is rapidly becoming the leading research and industry leader in naturopathic clinical bioinformatics. Much of the utility and pertinence of the software solutions produced by the COE lies in its recognition that today's physicians cannot easily parse increasingly available large datasets (such as produced by genome or microbiome reporting services) in any sort of real-time efficient manner. This is indeed a dilemma, as 'big data' approaches (in particular those employing machine learning algorithms) are increasingly pointing the way to the possibilities of more precise treatment based on high-value considerations.

One possible approach to the problem was a more 'generative' approach, as advanced by William Wimsatt: That we are limited beings and the world we try to understand is complex.[1] For Wimsatt, robustness (believing that a particular apple exists because we can see it, feel it, smell it, taste it, and hear it crunch when we eat it) is measured by the multidimensionality of the data models: The more we can detect things in multiple ways, the more we are inclined to believe they exist. Closely connected to robustness are the heuristics, rules of thumb that we use to think about the world and which are foundational to his epistemology.

Heuristics can be wrong or biased but tend to work well when applied to what is robust in the world. For example, a basic generative heuristic is derived from cybernetics and is known as 'law of requisite variety.' In essence, it mandates that the number of states of a control mechanism must be greater than or equal to the number of states in the system being controlled. This heuristic, along with personalized clinical data and robust molecular network data, permits the design of computationally generated, personalized, multi-axis polypharmacy, well-suited for natural products, where the therapeutic index of the agent combination rises significantly, but the overall safety profile remains essentially unaltered.

The generative paradigm works well in addressing the challenge of how to approach the onslaught of 'big data' into the clinical workspace. Person-specific genomic, metabolomic, and microbiome data files can easily reach into the hundreds of megabytes of information. Clearly, we need analytic tools capable of automating the basic handling, analysis, and integration of this wealth of information. The challenge is daunting, but the potential rewards are almost unfathomable: A more precise clinical impression, where (paradoxically) 'more data is better than better data,' and broadly applied evidence-based conclusions are only one part of the evaluation framework.

➤

Datapunk Circuits

➤

Over the past five years in partnership with Datapunk Bioinformatics LLC, the COEGM has developed a variety of computational tools for precision medicine using generative-based algorithms; some proprietary, such as the well-known and regarded *Opus23* genomic development platform, along with its two add-on analytic modules, Utopia (microbiome) and Icarus (metabolome). Other apps on the servers are open source and free-to-use.

On August 25, 2018, the COEGM announced the release of 'Circuits' a gene-based open source platform combining genomic data in a variety of robust dimensions. Circuits is web-based, has an imaginative and intuitive user interface, and is free to use. I'd like to use the rest of this article to introduce and describe the capabilities of Circuits and invite the readers of the *Townsend Letter* to explore its possibilities.

The Interface

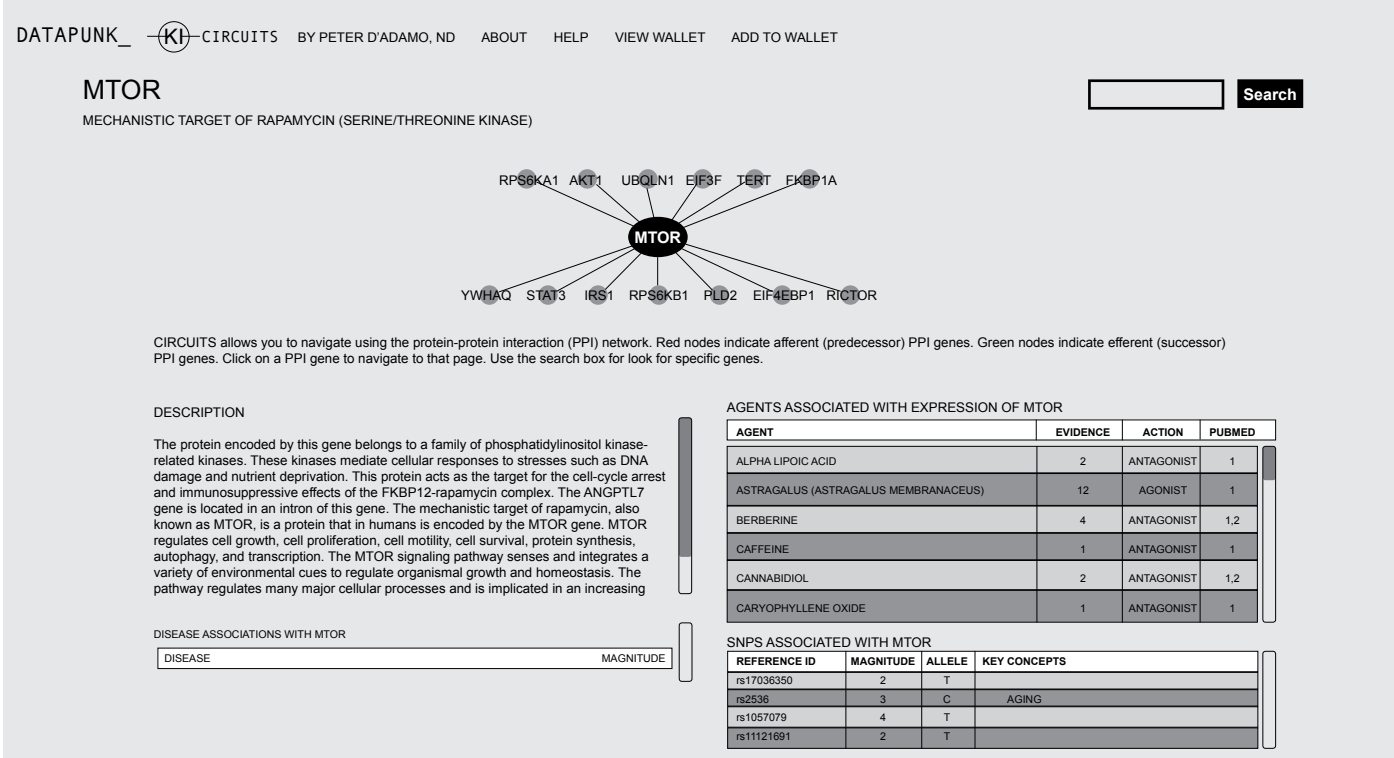
Circuits resides at the web address https://www.datapunk.net/circuits and can be accessed by any modern browser. Because of the data depiction density, it is not optimized for small handheld smart phones, and it is recommended that a desk or laptop machine be used to access the app.

Circuits' initial presentation appears as shown below. In its default state, Circuits displays the data for the gene MTOR (mammalian target of rapamycin) as a place-filler. Immediately below the title slug, Circuits displays the known PPI (protein-protein interactions) associated with the target gene (in this case MTOR) as a Cytoscape network. Afferent nodes are shaded red whilst efferent nodes are colored green. This network is an effective way to navigate Circuits as any node will bring up its related gene and load it into the main window. Users can also search for any gene/protein by using the traditional search input at the top right of the screen. To help users refine their query, the search feature will autocomplete over 30K currently recognized gene symbols.

Scrolling downwards, the user will see the six scrollable panes that contain the data mash-ups. From the top left we can see a detailed description of the gene, and across from that, a pane that depicts the available data on agents associated with the expression of the gene. This is a unique, human-curated database that was originally developed for use with the Opus23 platform.

Circuits employs a variety of modal popups to provide additional contextual data. Clicking on any agent will trigger a popup window that draws a unique radar plot that

Circuits Main Window Graphic



we call the 'genomic logo' of the agent. This logo depicts the strength, action, and targets of the indicated agent, using a complex algorithm based on study design, scope, and subject type.

The next row of two panes further down show disease associations and clinically relevant SNPs (single nucleotide polymorphisms) associated with the target gene. Pathology data is derived from ClinVar, OMIM and GWAS, while SNP associations are from GWAS and the exclusive human-curated SNP database developed for use in the Opus23 program. Clicking on a hyperlinked disease or SNP will also launch informational popups.

The next row of panes highlights, on the left, any adverse drug reactions linked to specific polymorphisms of the target gene and known tissue and organ distributions of the target gene. As with all internal hyperlinks, clicking on any link in these panes will trigger a popup containing additional data.

The next row of informational panes shows, on the left, pathway regulations associated with the target gene pathway and its effect (either up-regulation or down-regulation). The bottom right pane shows etiological links associated with the target gene that are inferred via the target gene's disease associations.

The final single pane displays HMDB (Human Metabolome Database) linkages to the target gene. Clicking on the metabolite common name will trigger a popup display detailing the metabolite.

The Data

Most of the data used by Circuits was developed initially for use by the *Opus23* application from publicly available repositories. Exceptions include the SNP and agent expression datasets, which were developed entirely by Datapunk human curators. The PPI, etiome, and diseaseome datasets were enriched by combining multiple source data, in some cases programmatically through structured machine earning. A few of the larger sources are listed as references.[2-8] It should be noted that the publication date of several of the references may be over several years old; however, these articles typically announce and describe the dataset, the actual databases they represent are almost all continuously updated; and through its network of application programming interfaces (APIs), so is Circuits.

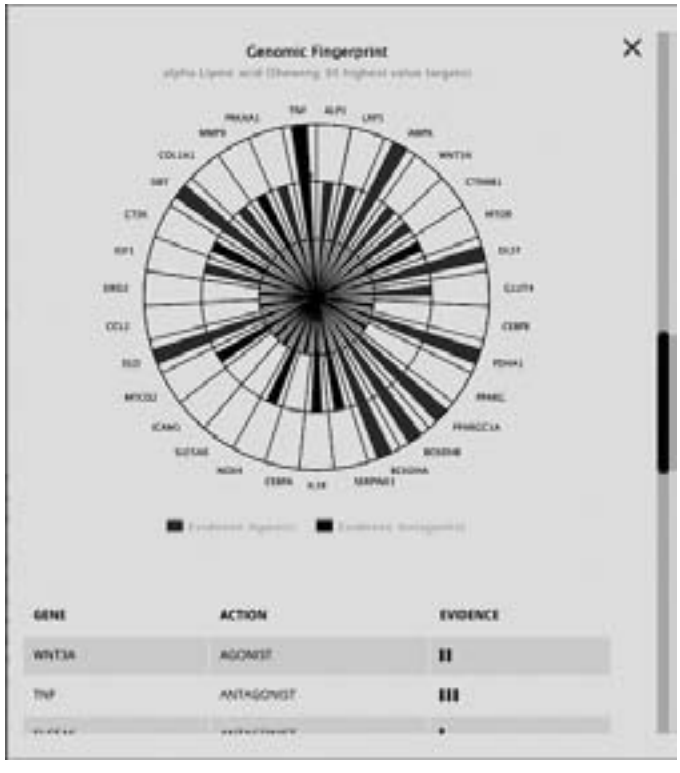
Test-Driving Circuits

Readers are encouraged to 'surf' Circuits and explore the target genes that seem more interesting. Click away! However here are a few hard links to help get you started.

- The ABO 'secretor' gene (FUT2)
  https://www.datapunk.net/circuits/index.pl?FUT2
- Mitochondrial enzymes that catalyze the oxidative deamination of amines, such as dopamine, norepinephrine, and serotonin (MAOA and MAOB)
  https://www.datapunk.net/circuits/index.pl?MAOA
  https://www.datapunk.net/circuits/index.pl?MAOB
- Catechol-O-methyltransferase (COMT) catalyzes the transfer of a methyl group from S-adenosylmethionine to catecholamines, including the neurotransmitters dopamine, epinephrine, and norepinephrine.
  https://www.datapunk.net/circuits/index.pl?COMT
- PPAR-gamma is a regulator of adipocyte differentiation. Additionally, PPAR-gamma has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis, and cancer.
  https://www.datapunk.net/circuits/index.pl?PPARG

➤

Model Popup Showing Data for Alpha-Lipoic Acid Graphic



➤

- MTHFR catalyzes the conversion of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, a co-substrate for homocysteine (HCy) remethylation to methionine.
  https://www.datapunk.net/circuits/index.pl?MTHFR

The Code

The server-side portion of Circuits was written in the Perl language, the 'Swiss Army Chainsaw' of bioinformatics. Client-side elements, such as network depictions and graphic displays of information, were coded in JavaScript using the Cytoscape JS and HighCharts JS frameworks. The PPI network was normalized using the Graphviz graphing package and the CPAN Graph module.

The Easter Egg

Users can store particularly interesting or important genes in a non-tracking cookie 'wallet,' for long-term use, thus allowing them to retrace prior investigations.

I hope the *Townsend Letter* readers have half as much fun exploring Circuits as I did envisioning and coding it. We at the Pathfinder Scholar Program at the COEGM are planning on expanding our open-source offerings to include a microbiota explorer that uses taxon interaction networks and Markov chains to produce a multigenerational approach to eubiosis; and a small metabolite (metabolome) explorer that employs machine learning classifiers to generate metabolic patterning characteristics. I'll make sure to alert the readers when these tools become available.

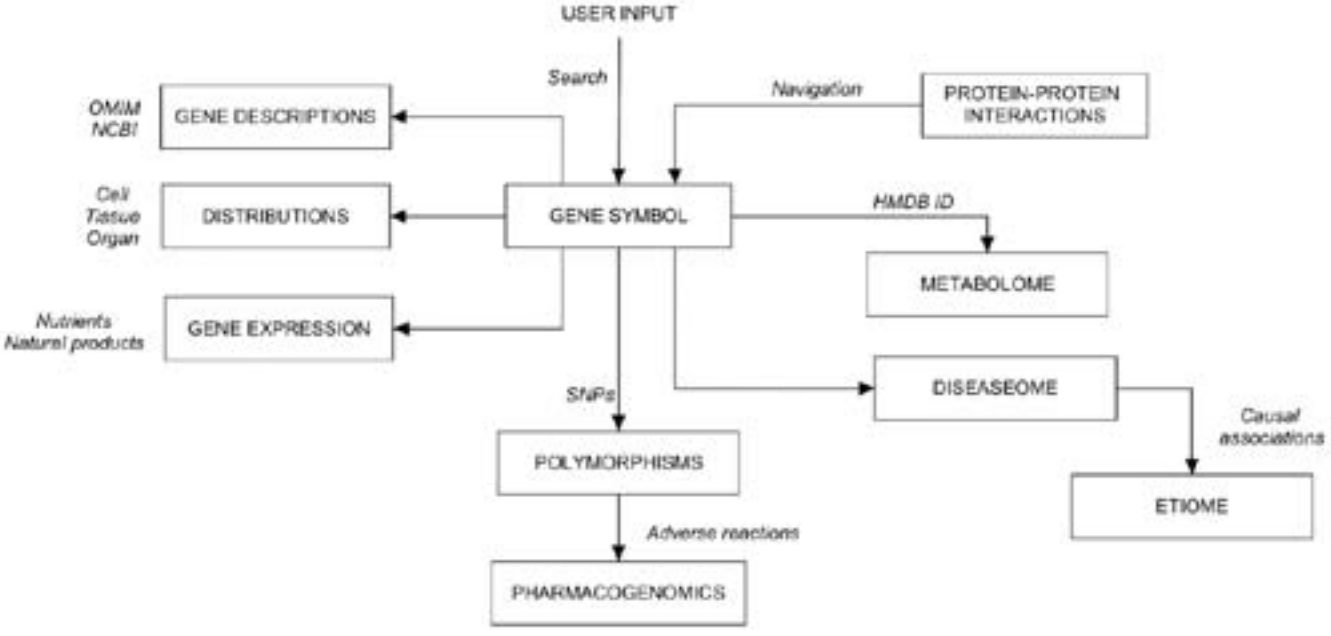
References

1. Wimsatt W. *Re-Engineering Philosophy for Limited Beings: Piecewise Approximations to Reality.* Cambridge: Harvard University Press. 2007
2. Landrum MJ, et al. ClinVar: improving access to variant interpretations and supporting evidence. *Nucleic Acids Res.* 2018 Jan 4. PubMed PMID: 29165669.
3. Prasad, TSK, et al. Human Protein Reference Database - 2009 Update. *Nucleic Acids Research*. 2009;37, D767-72.
4. Liu YI1, Wise PH, Butte AJ. The "etiome": identification and clustering of human disease etiological factors. *BMC Bioinformatics*. 2009 Feb 5;10 Suppl 2:S14.
5. Kaplun A, et al. PGMD: a comprehensive manually curated pharmacogenomic database. *The Pharmacogenomics Journal*. 2016;16:124–128.
6. Thul PJ, Lindskog C. The human protein atlas: A spatial map of the human proteome. *Protein Sci*. 2018 Jan;27(1):233-244.
7. Barabási A-L, Gulbahce N, Loscalzo J. Network Medicine: A Network-based Approach to Human Disease. *BMC Bioinformatics*. 2009; 10(Suppl 2): S14.
8. Wishart DS, et al., HMDB 4.0 — The Human Metabolome Database for 2018. *Nucleic Acids Res*. 2018. Jan 4;46(D1):D608-17. 29140435

Peter J. D'Adamo, ND
Distinguished Professor of Clinical Medicine and Bioinformatics
Center of Excellence in Generative Medicine
University of Bridgeport, College of Naturopathic Medicine
https://www.coegm.com/

◆

Circuits: Dataset Linkages Graphic



Xanthurenic Acid, Kynurenic Acid, Liver Function, and Blood Sugar Control

by Andrea Gruszecki, ND

The prevalence of metabolic syndrome (insulin resistance) and type II diabetes in the US population continues to increase and predisposes individuals to other diseases, including chronic inflammation, cardiovascular disease, kidney disease, depression, and dementia.[1,2] Early detection of insulin and blood sugar dysregulation is essential to prevent disease progression.[3] A better understanding of the liver's role in blood sugar balance and energy metabolism may allow clinicians to better interpret "early warning" laboratory results such as urinary xanthurenic and kynurenic acid.[4,5] The addition of both xanthurenic and kynurenic acid to a 24-hour urine or dried urine hormone profile may provide valuable clinical information about a patient's metabolic status.[6]

Disruption of the tryptophan-kynurenine pathway may result in elevations of xanthurenic acid (XANA) and kynurenic acid (KYNA), which may cause a decrease in liver nicotinamide adenine dinucleotide (NAD^+) synthesis.[5] High levels of XANA and/or low levels of NAD^+ may alter the function of the liver and pancreas and result in damage to these organs.[7-9] This damage, combined with a Western diet and sedentary lifestyle, may contribute to metabolic syndrome, non-alcoholic fatty liver disease, type II diabetes, and other inflammatory disorders. It is vitally important to confirm a disruption in NAD+ synthesis prior to supplementing with niacin (vitamin B3), as high levels of the nicotinamide metabolite *N*[1]-methylnicotinamide may also contribute to the development of insulin resistance. High levels of this metabolite may accumulate during the consumption of a Western diet (meats and fortified grain products) or the accumulation may be due to inherited variation or acquired inhibition of the enzyme aldehyde oxidase (AOX1; riboflavin, molybdenum).[10]

The Tryptophan-Kynurenine Pathway

The tryptophan-kynurenine pathway controls tryptophan availability for serotonin synthesis in the gastrointestinal tract and the central nervous system.[5,11,12] The pathway also controls hepatic heme synthesis and disposes of excess tryptophan absorbed from the gut. The kynurenine pathway metabolizes tryptophan and produces immunoregulatory and neuroactive metabolites. The pathway also supplies quinolinic acid for the synthesis of niacin (as nicotinic acid) and the co-factor nicotinamide adenine dinucleotide (NAD^+).

The rate of flux down the tryptophan-kynurenine pathway is determined first by the level of free circulating tryptophan and then by the activity of the enzymes tryptophan 2,3-dioxygenase (TDO2; heme) in the liver and indoleamine 2,3-dioxygenase 1 and 2 (IDO1, IDO2; heme) elsewhere in the body (Figure 1).[13-15] During homeostasis, the primary site of kynurenine pathway activity is the liver, where all of the enzymes to metabolize tryptophan into NAD^+ and $NADP^+$ are found. In a healthy state the liver accounts for about 90% of tryptophan metabolism. Systemic metabolism of tryptophan via IDO increases when the immune system is activated, or when pro-inflammatory cytokines are present. When tryptophan metabolism is shifted to IDO in the periphery, NAD^+ may not be produced because not all of the pathway enzymes are found outside the liver. It is possible that these incomplete IDO-induced pathways outside the liver contribute to higher circulating levels of XANA, KYNA, and neurotoxic quinolinic acid.

Xanthurenic Acid, Kynurenic Acid, and Blood Sugar Regulation

Early detection and laboratory testing are important to prevent or reverse the progression of non-alcoholic fatty liver disease (NAFLD), metabolic syndrome and type II diabetes.[16] Routine screening for blood sugar dysregulation includes fasting blood sugar and hemoglobin A1c. Additional testing, such as the post-prandial insulin (Kraft/Hayashi) assay may improve the detection of insulin resistance, and urinary xanthurenic and kynurenic acids may provide further clinical insight (see Figure 2).[17] XANA and KYNA provide information regarding nutritional status, blood sugar regulation, and the capacity of the tryptophan-kynurenine pathway to synthesize NAD^+.[5,18] Importantly, *both* XANA and KYNA must be evaluated for a complete analysis.[19] The comparison of XANA and KYNA values may provide

➤

➤

insight as to the nature of the pathway dysregulation and the application of corrective therapies.[6]

KYNA and/or XANA may be formed when tryptophan is metabolized down the kynurenine pathway. Briefly, through a series of enzymatic steps, tryptophan is normally converted into kynurenine, then to 3-hydroxykynurenine via kynurenine 3-monooxygenase (KMO; B2, $NADP^+$), then 3-hydroxyanthranilic acid is formed by kynureninase (KYNU; B6), and proceeds down the pathway to become either acetyl-coA, picolinic acid or quinolinic acid, which is further converted into NAD^+ through another series of enzymatic steps.[5,11,12,20,21] If the pathway is blocked at either the KMO or the KYNU enzyme step, then the metabolites are shunted through a different set of enzymes and are instead converted into XANA and/or KYNA. If XANA and KYNA are synthesized instead, there is little substrate for NAD+ synthesis further down the pathway.[7]

KMO is dependent upon two cofactors, one is synthesized from vitamin B2 (riboflavin); the other cofactor is niacin-derived NAD^+ itself, in the phosphorylated form $NADP^+$. If an individual is deficient in either riboflavin or niacin, KYNA will elevate and XANA will be low.[19] Obesity is a known risk factor for both metabolic syndrome and type II diabetes.[22] Early evidence from human white blood cells indicates that obesity and inflammation may dysregulate the kynurenine pathway and increase the activity of KMO, elevating KYNA levels and lowering XANA levels.[18]

KYNU is a vitamin B-6 dependent enzyme, and it is the enzyme most sensitive to low B-6 levels in the kynurenine pathway.[5] The inhibition of KYNU may occur due to either clinical or *sub-clinical* B-6 deficiency. Such a deficiency may occur due to the presence of diabetes, chronic inflammatory disease, celiac disease, smoking, or alcohol use.[23] Nutritional requirements for B-6 (pyridoxine or pyridoxal 5'-phosphate) may be increased by the use of certain medications (oral contraceptives, isoniazid, hydralazine, benserazide, penicillamine, phenelzine, cycloserine, thiamphenicol carbidopa, etc.).[11,23] KYNU may also be inhibited by high levels of exogenous estrogens (oral birth control, bioidentical or synthetic hormone replacement) and the endogenous high estrogens of pregnancy.[24-27] The inhibition of KYNU elevates *both* XANA and KYNA.[5]

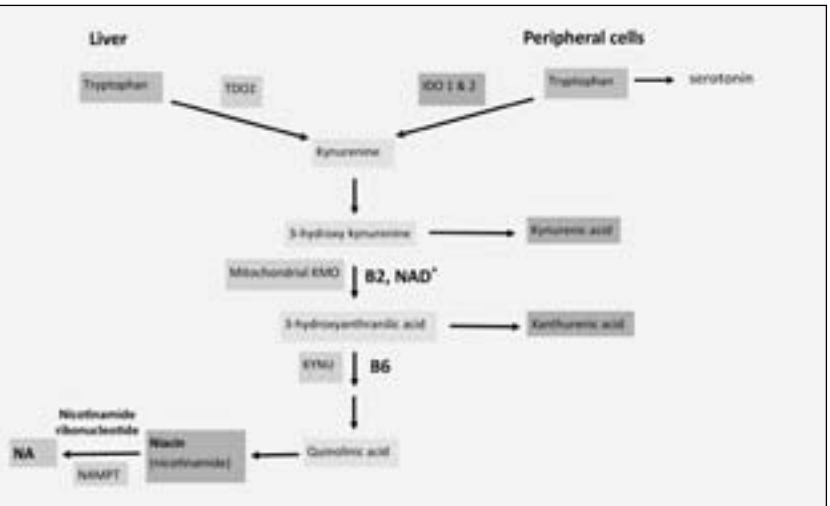


Figure 1. Tryptophan metabolism in the liver synthesizes NAD^+. In the periphery, increased circulating levels of tryptophan result in increased levels of kynurenic and xanthurenic acid.

Legend: 3-OH kynurenine, 3-hydroxykynurenine; IDO, indoleamine 2,3-dioxygenase 1; KMO, kynurenine 3-monooxygenase; KYNU, kynureninase; NAMPT, nicotinamide phosphoribosyltransferase; TDO, tryptophan 2,3-dioxygenase

High levels of XANA have toxic effects in pancreatic islets and can bind to insulin, decreasing its activity at insulin receptors. High urinary XANA levels have been associated with metabolic syndrome, gestational and type II diabetes in human studies.[5,25]

The primary signals regulating the kynurenine pathway are cortisol and inflammatory cytokines, although the other hormones also contribute to kynurenine pathway signaling. Elevated cortisol and inflammation are also common in metabolic syndrome, type II diabetes and NAFLD.[28-30] The effects of hormonal regulation become apparent during menopause, when estrogen levels decline, signaling pathways shift, inflammation increases, and more tryptophan is diverted down the peripheral kynurenine pathway.[5] Aging and menopause are associated with an increased incidence of insulin resistance. During menopause interferon gamma levels increase and induce peripheral IDO activity.[31] While the flux down the pathway increases, KYNU activity is partially inhibited, which may elevate both XANA and KYNA levels.

NAD^+, Liver Function, and Blood Sugar Regulation

The liver plays an important role in blood sugar regulation; it converts excess carbohydrate into glycogen for storage and metabolizes glycogen to glucose as needed for release into the circulation.[4,32] Excess dietary carbohydrates may also be converted into fatty acids and stored in the liver. The liver breaks down glucose for energy; NAD^+ is an essential cofactor for the synthesis of adenosine triphosphate (ATP) during cellular respiration. Low levels of NAD^+ affect blood sugar balance and regulation by preventing normal cellular respiration, which impairs liver functions.[7]

NAD^+ is an essential compound in the body; it is required for normal mitochondrial function, energy production from the tricarboxylic acid (TCA) cycle, and fatty acid oxidation. More recently, NAD^+ has been recognized as a signaling molecule in cells.[33] NAD^+ is a cofactor in DNA repair and a variety of biochemical

processes, including insulin secretion, which is regulated by four separate NAD^+-dependent signaling mechanisms. Evidence is accumulating that increasing age, combined with a sedentary lifestyle, high-fat diet and decreasing NAD^+ levels may play a role in the induction of non-alcoholic fatty liver disease. NAFLD, in humans, is strongly associated with the presence of metabolic syndrome and type II diabetes.[32]

The liver also regulates circulating tryptophan levels by synthesizing NAD^+ from dietary tryptophan; in the periphery, cells cannot synthesize NAD^+ but can recycle metabolized NAD^+ with the enzyme nicotinamide phosphoribosyltransferase (NAMPT; nicotinamide ribonucleotide).[7,34] NAMPT is the rate-limiting enzyme for cellular NAD^+ levels because it controls both NAD^+ recycling and the conversion of quinolinic acid (from the tryptophan-kynurenine pathway) into NAD^+. Increasing age decreases both NAMPT expression and levels of NAD^+ in animal and human studies. Lower levels of NAD^+ increase cellular oxidative stress, disrupt cellular signaling, and impair mitochondrial function because the mitochondria must synthesize or recycle most of their NAD^+ independently.[33,34] In a recent study, subjects over 60 years old had, on average, 30-35% less NAD^+ in surgical liver samples compared to 45-year-olds.[7] In concurrent mouse studies, the investigators also observed that lower NAMPT expression both induced NAFLD and worsened diet-induced fatty liver inflammation. Other animal studies have also shown that high-fat diets decrease NAMPT expression and NAD^+ levels. The pancreas is also NAD^+ dependent. Increasing NAD^+ levels have decreased inflammation in experimentally-induced pancreatitis (animal studies).[9] Other avenues of research are targeting NAMPT activity and NAD^+ recycling as factors in pancreatic cancer.[8]

Human and animal studies both demonstrate that supplementation of NAD^+ precursors may restore intracellular NAD+ levels.[35] Several precursors may enter the NAD^+ synthesis or recycling pathways at different points: nicotinamide, nicotinic acid, nicotinamide riboside, and nicotinic acid riboside are all referred to as "niacin" or vitamin B3.[34] Of these different forms, NAMPT has high affinity for nicotinamide, and it is the form used by cells during NAD^+ recycling. Tryptophan may also be converted into NAD^+ in the liver, but the rate of exchange is high: 60 milligrams of tryptophan are required to synthesize one milligram of niacin equivalent.[36] Some individuals may not be able to use nicotinamide or nicotinic acid due to inherited or acquired cell dysfunctions. Animal and early human studies indicate that, in such cases, nicotinamide riboside may improve cellular NAD^+ status.[37,38] It may be important to recall that a true niacin deficiency (inherited or acquired) will present with symptoms of the skin, digestive tract and nervous system: diarrhea, sun-sensitive dermatitis, and neurological symptoms (headache, apathy, fatigue, depression, disorientation, and memory loss).[36]

Niacin has long been recognized as an effective cholesterol therapy in cardiovascular disease but is not often considered in the treatment of other medical conditions.[39] It is, perhaps, time to routinely consider B vitamin and NAD+ status in patients with other chronic inflammatory disorders such as metabolic syndrome and type II diabetes. Laboratory analysis of xanthurenic and kynurenic acids is available and may be used to evaluate the activity of the tryptophan-kynurenine NAD+ synthesis pathway. Early detection of low NAD^+, metabolic syndrome, type II diabetes, and fatty liver disease may prevent the progression of these reversible metabolic disorders into irreversible disease.

References

1. Topic R, et al. Somatic comorbidity, metabolic syndrome, cardiovascular risk, and CRP in patients with recurrent depressive disorders. *Croatian Medical Journal.* 2013; 54(5): 453-9.
2. Jayaraman A, Pike C. Alzheimer's Disease and Type 2 Diabetes: Multiple Mechanisms Contribute to Interactions. *Current Diabetes Reports.* 2014; 14(4): 476.
3. Montori V. Changes in diet and physical activity prevented type 2 diabetes mellitus in people with impaired glucose tolerance. *Evidence-Based Medicine.* 2001; 6(6): 176-176.
4. Han H, et al. Regulation of glucose metabolism from a liver-centric perspective. *Experimental & Molecular Medicine.* 2016 vol; 48 (3): e218.
5. Oxenkrug G. Insulin resistance and dysregulation of tryptophan-kynurenine and kynurenine-nicotinamide adenine dinucleotide metabolic pathways. *Molecular Neurobiology.* 2013; 48 (2): 294-301.
6. Hattori M, Kotake Y, Kotake Y. Studies on the urinary excretion of xanthurenic acid in diabetics. *Acta Vitaminologica et Enzymologica.* 1984; 6(3): 221-8.

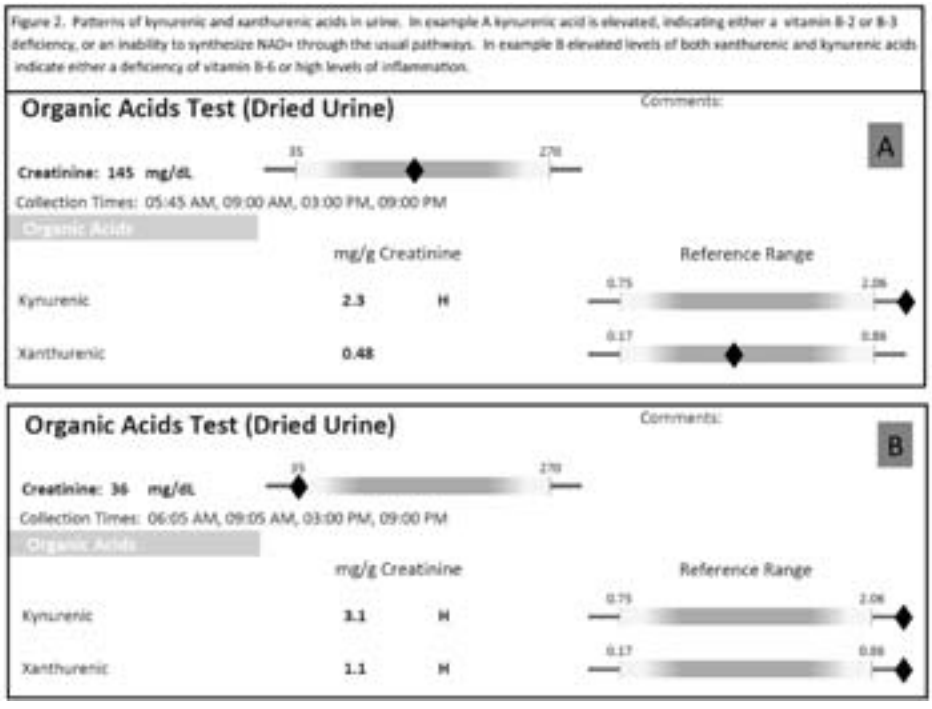


Figure 2. Patterns of kynurenic and xanthurenic acids in urine. In example A kynurenic acid is elevated, indicating either a vitamin B-2 or B-3 deficiency, or an inability to synthesize NAD+ through the usual pathways. In example B elevated levels of both xanthurenic and kynurenic acids indicate either a deficiency of vitamin B-6 or high levels of inflammation.

7. Zhou C, et al. Hepatic NAD+ deficiency as a therapeutic target for non-alcoholic fatty liver disease in ageing. *British Journal of Pharmacology.* 2016; 173 (15): 2352-68.
8. Chini C, et al. Targeting of NAD metabolism in pancreatic cancer cells: potential novel therapy for pancreatic tumors. *Clinical Cancer Research.* 2014; 20 (1): 120-30.
9. Shen A, et al. NAD+ augmentation ameliorates acute pancreatitis through regulation of inflammasome signaling. *Scientific Reports.* 2017; 7(1): 3006.
10. Zhou S, et al. Nicotinamide overload may play a role in the development of type 2 diabetes. *World Journal of Gastroenterology.* 2009; 15(45): 5674-84.
11. Badawy A. Kynurenine Pathway of Tryptophan Metabolism: Regulatory and Functional Aspects. *International Journal of Tryptophan Research: IJTR.* 2017; 10: 1178646917691938.
12. Lugo-Huitrón R, et al. Quinolinic Acid: An Endogenous Neurotoxin with Multiple Targets. *Oxidative Medicine and Cellular Longevity.* 2013; 2013: 104024.
13. Universal Protein Resource. Tryptophan 2,3-dioxygenase. https://www.uniprot.org/uniprot/P48775 Accessed 07 August 2018.
14. Universal Protein Resource. Indoleamine 2,3-dioxygenase 1. https://www.uniprot.org/uniprot/P14902 Accessed 07 August 2018.
15. Universal Protein Resource. Indoleamine 2,3-dioxygenase 2. https://www.uniprot.org/uniprot/Q6ZQW0 Accessed 07 August 2018.
16. Jialal I. The Role of the Laboratory in the Diagnosis of the Metabolic Syndrome. *American Journal of Clinical Pathology*. 2009; 132(2): 161-162.
17. DiNicolantonio J, et al. Postprandial insulin assay as the earliest biomarker for diagnosing pre-diabetes, type 2 diabetes and increased cardiovascular risk. *Open Heart.* 2017; (2): e000656.
18. Favennec M, et al. The kynurenine pathway is activated in human obesity and shifted toward kynurenine monooxygenase activation. *Obesity.* 2015; 23(10): 2066-2074.
19. Shibata K, Yamazaki M, Matsuyama Y. Urinary excretion ratio of xanthurenic acid/kynurenic acid as a functional biomarker of niacin nutritional status. *Bioscience, Biotechnology, and Biochemistry.* 2016; 80(11): 2208-2216.
20. Universal Protein Resource. Kynureninase https://www.uniprot.org/uniprot/Q16719 Accessed 26 July 2018.
21. Universal Protein Resource. Kynurenine 3-monooxygenase https://www.uniprot.org/uniprot/O15229 Accessed 26 July 2018.
22. Ginsberg H, MacCallum P. The Obesity, Metabolic Syndrome, and Type 2 Diabetes Mellitus Pandemic: Part I. Increased Cardiovascular Disease Risk and the Importance of Atherogenic Dyslipidemia in Persons with the Metabolic Syndrome and Type 2 Diabetes Mellitus. *Journal of the Cardiometabolic Syndrome.* 2009; 4(2): 113-9.
23. Ueland P, et al. Direct and Functional Biomarkers of Vitamin B6 Status. *Annual Review of Nutrition.* 2015; 35: 33-70.
24. Wilson S, et al. Oral contraceptive use: impact on folate, vitamin B_6, and vitamin B_{12} status. *Nutrition Reviews*. 2011; 69(10): 572-583.
25. Law K, Zhang H. The pathogenesis and pathophysiology of gestational diabetes mellitus: Deductions from a three-part longitudinal metabolomics study in China. *Clinica Chimica Acta.* 2017; 468: 60-70.
26. Fukuwatari T, Shibata K. Nutritional Aspect of Tryptophan Metabolism. *International Journal of Tryptophan Research.* 2013; 6 (Suppl 1): 3-8.
27. Rios-Avila L, et al. Metabolite Profile Analysis Reveals Association of Vitamin B-6 with Metabolites Related to One-Carbon Metabolism and Tryptophan Catabolism but Not with Biomarkers of Inflammation in Oral Contraceptive Users and Reveals the Effects of Oral Contraceptives on These Processes. *The Journal of Nutrition*. 2015; 145 (1): 87-95.
28. Badawy A. Modulation of Tryptophan and Serotonin Metabolism as a Biochemical Basis of the Behavioral Effects of Use and Withdrawal of Androgenic-Anabolic Steroids and Other Image- and Performance-Enhancing Agents. *International Journal of Tryptophan Research.* 2018; 11: 1178646917753422.
29. Jeong I. The Role of Cortisol in the Pathogenesis of the Metabolic Syndrome. *Diabetes & Metabolism Journal*. 2012; 36(3): 207-10.
30. Tarantino G, Finelli C. Pathogenesis of hepatic steatosis: The link between hypercortisolism and non-alcoholic fatty liver disease. *World Journal of Gastroenterology*. 2013; 19(40): 6735-43.
31. Ghosh M, Rodriguez-Garcia M, Wira C. The Immune System in Menopause: Pros and Cons of Hormone Therapy. *The Journal of Steroid Biochemistry and Molecular Biology.* 2014; 142: 171-5.
32. Paschos P, Paletas K. Non-alcoholic fatty liver disease and metabolic syndrome. *Hippokratia.* 2009; 13 (1): 9-19.
33. Cantó C, Menzies K, Auwerx J. NAD+ metabolism and the control of energy homeostasis - a balancing act between mitochondria and the nucleus. *Cell Metabolism.* 2015; 22(1): 31-53.
34. Nikiforov A, Kulikova V, Ziegler M. The human NAD metabolome: Functions, metabolism and compartmentalization. *Critical Reviews in Biochemistry and Molecular Biology*. 2015; 50(4): 284-97.
35. Elhassan Y, Philp A, Lavery G. Targeting NAD+ in Metabolic Disease: New Insights Into an Old Molecule. *Journal of the Endocrine Society.* 2017; 1(7): 816-835.
36. Linus Pauling Institute (2018) Niacin. Oregon State University http://lpi.oregonstate.edu/mic/vitamins/niacin accessed 20 July 2018.
37. Chi Y, Sauve A. Nicotinamide riboside, a trace nutrient in foods, is a vitamin B3 with effects on energy metabolism and neuroprotection. *Current Opinion in Clinical Nutrition and Metabolic Care.* 2013; 16(6): 657-661.
38. Trammell S, et al. Nicotinamide riboside is uniquely and orally bioavailable in mice and humans. *Nature Communications.* 2016; 7: 12948.
39. Ginsberg H, Maccallum P. The Obesity, Metabolic Syndrome, and Type 2 Diabetes Mellitus Pandemic: II. Therapeutic Management of Atherogenic Dyslipidemia. *Journal of Clinical Hypertension.* 2009; 11(9): 520-7.

◆

Andrea Gruszecki, ND, received her BA in ecology and evolutionary biology from the University of Connecticut, where she was exposed to a variety of research projects; her own research project examined the effects of diurnal cycles on *Poeciliopsis* species. Trained as a Radiologic Technologist and Army medic, she spent the years prior to graduation working in urgent care and hospital settings, gaining valuable clinical experience. She received her Doctorate in Naturopathy from Southwest College of Naturopathic Medicine. Upon her graduation from SWCNM, she worked with patients at the Wellness Center in Norwalk, Connecticut, before starting her own naturopathic practice.

Her experiences in private practice evolved into an inclusive model of medicine for use by conventional and CAM providers, designed to allow cross-specialty communication among health care providers ("Forward into the Past: Reclaiming Our Roots Through an Inclusive Model of Medicine." *NDNR eNewsletter*, June 2013). She has presented at a variety of venues, including the American Academy of Environmental Medicine, Integrative Medicine for Mental Health, International College of Integrative Medicine, and the California Naturopathic Doctors Association.

Dr. Gruszecki is a member of the consulting department at Meridian Valley Laboratory, where she may provide interpretive assistance with laboratory results, write interpretations, and create conference presentations.

Xanthurenic and Kynurenic acids now included!

CompletePlus Dried Urine Hormone Profile

Dried Urine Hormone testing combines the benefits of a 24-hour urine test with the time-specific advantages previously available only in a saliva test. Our CompletePlus dried urine hormone panel gives you hormone metabolites, previously only available in 24-hour urine tests, along with 4-point cortisol and cortisone. The CompletePlus profile* includes a full complement of estrogen, progesterone, and androgen metabolites, as well as the most comprehensive evaluation of adrenal function available on the market.

Estrogen Metabolites

The estrogen portion of the profile provides a detailed understanding of your patient's estrogen metabolism including:

- Detoxification pathways
- Indicators of risk for osteoporosis
- Indicators of risk for estrogen-related cancers

Androgen Metabolites

Accurate assessment of true, bioavailable androgen levels:

- DHEA
- Testosterone
- Androgen metabolites, including 5 α-DHT

COMPLETE Adrenal Profile

A complete picture of adrenal health including:

- Adrenal metabolites
- Mineralocorticoids
- Circadian cortisol/cortisone pattern
- Free and conjugated cortisol and cortisone for the best assessment of bioavailable hormone

Unlimited FREE Consults

Free physician to physician telephone consultations help you get the most out of your results.

Fast Turnaround

Turnaround times that are some of the fastest in the industry.

*Smaller profiles available

Meridian Valley LAB

6839 Fort Dent Way, Ste. 206 | Tukwila, WA 98188
tel **206.209.4200** | **Toll free 855.405.TEST (8378)**
fax 206.209.4211

info@meridianvalleylab.com
MeridianValleyLab.com

Exploring the Complexities and Caveats of Safe Internal Use of Essential Oils for Pain: Highlighting Intestinal Discomfort, Part 2

by Sarah A. LoBisco, ND, IFMCP

Editor note: Part 1 of this article, published in December 2018, discusses issues of safety, essential oil quality, metabolism, and synergy when using essential oils orally. Part 2 looks at the clinical application of ingested essential oils for intestinal discomfort.

Preliminary Considerations

Before selecting a therapeutic modality of any kind, it is important to address the underlying cause and use a naturopathic and functional medicine approach to address it. I would be amiss to not briefly review some preliminary considerations for using essential oils.

For intestinal discomfort and symptoms, an integrative doctor will want to take a full history, perform a physical exam, and run the appropriate tests. Examples of laboratory assessments include imaging for detecting pathology and functional issues, assimilation and absorption markers (e.g., pancreatic elastase, products of protein breakdown, fecal fats), excess inflammatory indicators (e.g., calprotectin, eosinophil protein X (EPX), lactoferrin), a Celiac panel, SIBO breath test, markers for bacterial, viral, fungal, and parasitic overgrowth, and microbiota panels.

A "Five R" program for restoring and healing a diseased gastrointestinal tract is the preferred protocol in functional medicine, but the aspects are likely be implemented by most integrative practitioners. These Five R's are the following:

1. Removing the cause and contributors (i.e., dietary, microbes, or environmental),
2. Replacing the nutrients that are needed for assimilation and digestion,
3. Repairing the damage to the gut,
4. Re-inoculating the good bacteria, and
5. Rebalancing lifestyle factors (sleep, stress, exercise) that can perpetuate a dysfunctional gut.[122-124]

Oral Use of Essential Oils for Intestinal Discomfort

Now, I will start the discussion on the "nuts and bolts" of internal administration of essential oils for gut discomfort. I will review the evidence in the research for the use of the most common essential oils for intestinal health and those that I personally use in my practice. I will also provide dosages, if available, that are recommended from scientific reviews and experts. Next, I will give a summary on essential oils' antimicrobial effects and their impact on the microbiome. Finally, I will give a synopsis of how I would incorporate these essential oils in my practice.

Despite the controversary surrounding oral application of essential oils, many practitioners are already currently administrating two essential oils for gut comfort without concern. Many practitioners who run the previously mentioned lab markers have witnessed that certain essential oils are deemed "sensitive" to dysbiosis markers on various functional gastrointestinal health panels. For this reason, many functional and naturopathic medicine practitioners have experience administering the essential oils of oregano for its antimicrobial properties[124-127] and enteric coated peppermint oil for irritable bowels.[128-132] Two additional essential oils I personally use in my practice are fennel and ginger. Please refer back to the previous section on "Internal Usage of Essential Oils: Controversy, Scare Tactics, and Bad Science" in which I highlighted the benefits of fennel oil for gut distress and its safe internal use. There is also one proprietary blend I have found to be very clinically effective.

Peppermint Oil

Peppermint is perhaps the most researched and clinically evaluated essential oil used for intestinal discomfort. It has even been validated in several trials for its efficacy in IBS subjects.[128-131]

Peppermint's mechanism of action on pain has been studied but is not conclusive. It may be related its impact on TRPM8, a transient receptor potential (TRP) cation channel. This receptor has been found to be activated by cold temperatures and menthol, a main constituent found in peppermint essential oil. It induces smooth muscle contractions inversely relational to stimulation (temperature) and initiation of Rho-kinase. This leads to smooth muscle contraction. Furthermore, there is some controversial evidence that menthol modulates

intracellular calcium stores. In summary, peppermint oil may relieve intestinal discomfort through activation of TRPM, modulating calcium stores, and stimulation of menthol.[129]

There is a safety precaution reported in the literature that peppermint may delay gallbladder emptying. The evidence cited for this is based on one study of 12 healthy volunteers that was assessing gastrointestinal motality.[128, 130-131]

In this experiment, the researchers compared the effects of a combination of 90 mg of peppermint oil in 50 mg of caraway oil to a proprietary formulation to two medications and a placebo that contained NaCl (salt). The participants were tested at baseline and after drinking apple juice at various time intervals. The authors simultaneously measured gastric and gall-bladder emptying ultrasonically and orocaecal transit time using the H2 breath test using lactulose.[128] The authors concluded the following:

> Further investigations need to be conducted to study the effect of peppermint oil and caraway oil on a maximal contraction stimulus on the gall-bladder (e.g.after a fatty meal), to investigate the effect of a combination of both oils (as found in a number of herbal drugs) and to examine whether the pharmaco-dynamic effects can also be shown in patients suffering from motility disorders.[128]

I take issue to making this safety flag for peppermint oil based on twelve healthy volunteers. Under normal conditions, fatty acids stimulate gallbladder contraction. The test drink was a non-fat juice, so how could the gallbladder be stimulated? Still, according to the Expanded Commission E, the following contraindications are reported: "Obstruction of bile ducts, gallbladder inflammation, severe liver damage. In case of gallstones, to be used only after consultation with a physician. Preparations containing peppermint oil should not be used on the face, particularly the nose, of infants and small children."[132]

I believe that due to the impressive clinical trials that report the efficacy of peppermint for IBS, it may be a better conclusion that it is a modulator of digestive function rather than an inhibitor or stimulator of motility. Furthermore, with appropriate dosage, clinicians should not dismiss this essential oil for fear of harm.

Oregano Essential Oil

Whereas ingestion of peppermint oil has many clinical trials of efficacy for assisting with digestive distress, oregano oil does not. Yet, it is one of the go-to essential oils for most practitioners in treating gut discomfort related to microbial imbalances. Interestingly, clinical trials on efficacy regarding the popular use for intestinal dysbiosis is lacking.[133,134] There is one lone study on inhibition of enteric parasites.[125]

Its isolated compound, carvacrol, was found in vivo to have protective effects against clostridium difficile associated dirrahea.[135] In another in vivo model using pigs, oregano oil was found to improve intestinal permeability via modulating bacteria and immune status. Interestingly, the oregano oil used, as reported in the analysis found within the supplementary materials, did not contain the two components considered to be most active.[136] Many manufactured oregano oil products are encapsulated and standardized to carvacrol and thymol.

Still, clinicians report benefits and improvements of markers of intestinal dysbiosis for their patients.

As far as safety, it is recommended to be diluted in a fatty oil due to its potentially corrosive properties.

Ginger Essential Oil

Ginger is another well-known herb for its digestive properties and alleviating discomfort. It has evidence of this from a few human trials and many in vitro and in vivo.[137-142] In vitro and vivo, ginger oil has been shown to be microbe inhibiting and have inflammatory modulating properties. The constituents of ginger oil have also shown to be stomach protective,[139] possess antioxidant properties, and modulate inflammation.[137-142]

From my research and experience, I believe that high quality essential oils likely balance microbe activity.

One study review of five trials had compelling evidence that the inhalation of a combination of peppermint oil and ginger oil could assist with nausea, though some methodical issues were reported. The authors stated, "Their results suggest that the inhaled vapor of peppermint or ginger essential oils not only reduced the incidence and severity of nausea and vomiting but also decreased antiemetic requirements and consequently improved patient satisfaction."[142]

Cumin Essential Oil

Cumin essential oil is another essential oil traditionally used for digestive health. A small pilot trial with 57 subjects diagnosed with IBS using ROME II criteria assessed the efficacy of 2% cumin essential oil and had an impressive outcome. The essential oil was administered as 10 drops twice daily for four weeks. The authors concluded, "Abdominal pain, bloating, incomplete defecation, fecal urgency and presence of mucus discharge in stool were statistically significant decreased during and after treatment with Cumin extract. Stool consistency and defecation frequency were also both statistically significant improved in patients with constipation dominant pattern of IBS."[143]

Proprietary Formation

I have had success using combinations of essential oils in proprietary formulations for intestinal health promotion and relief of irritation. One essential oil blend I routinely use contains the following single oils with evidence of digestive support: *Artemisia dracunculus* (tarragon) oil,[144] *Zingiber officinale* (ginger) root oil,[137-142] *Mentha piperita* (peppermint) oil,[128-132] *Juniperus osteosperma* (juniper) oil,[145] *Foeniculum vulgare* (fennel) oil,[110-114] *Cymbopogon flexuosus* (lemongrass) oil,[146-149] *Pimpinella anisum* (anise) seed oil,[150] and *Pogostemon cablin* (patchouli) oil.

This has been very effective in my practice for relief of gastrointestinal discomfort and symptoms. Most report improvement within one month. This is likely due to the synergistic components of the essential oils.[77-78] ➤

Intestinal Discomfort

➤

Dilution and Dosages: A Guide for Essential Oils

Now that I've reviewed the evidence that ingesting essential oils and that their use for intestinal discomfort is science-based, I will now discuss specific dosage guidelines. Although aromatherapists have different viewpoints on dilution amounts necessary for safe application, measurement for what constituents a single dose is a commonality.

In this section, I will provide a dosage guide compiled from the experience of experts and various merchandizers.**

Most essential oils come in 5 ml and 10 ml bottles. This equates to approximately 100 and 300 drops respectively. A general knowledge of equivalency from drops to measurements is necessary for the practitioner to understand, as most often dosage is based on drops rather than liquid measurements of essential oils. Please see Table 1 for these conversions and dilutions of essential oils (EOs).[117-121]

Table 1: Essential Oils Conversion and Measurement Chart

1 oz. = 30 ml
1 oz. = 600 drops essential oils
1 oz. = 2 Tbsp. or 6 tsp.

Using these conversions:
6 drops of EO per oz. of carrier oil = 1% dilution (1% of 600 drops)
3 drops of EO per Tbsp. or 3 tsp. = 1% dilution (1% of 300 drops)
1 drop of EO per tsp. = 1% dilution
1 drop of essential oil = approximately 0.02 to 0.03 grams = 20-30 milligrams = 20000 micrograms (μg)
30 mg = approximately 1 drop*

*Compiled from references 117-121

What the Science Says: Internal Usage and Conversion Measurements for the Application of Essential Oils

With knowledge of which essential oils to use for abdominal pain and a tool for conversions for dosages for administration, I will now review what is in the literature for internal adminstration of these selected essential oils.

Peppermint Essential Oil

According to *Examine*, the dosage for peppermint essential oil "does not follow a particular dosage,"[131] but is often standardized for menthol content. Quality and standards are once again validated as imperative for efficacy by this review. The authors summarize the research on this oil's administration as follows:

> Oral supplementation of peppermint oil for the purpose of gastrointestinal health and motility involves consuming anywhere between 450-750 mg of the oil daily in 2-3 divided doses, and this is around **0.1-0.2 mL** of the oil itself per dosage. The exact optimal dosage of peppermint is not known, and the numbers reflect a menthol content somewhere between 33-50%.*
>
> Usage of peppermint for the treatment of headaches involves having a solution of 10% peppermint oil and applying a relatively thin layer to the front of your head upon the start of a headache, with another application after 15 minutes and 30 minutes (for three applications in total).
>
> Usage of peppermint for aromatherapy does not follow any particular dosing, and similar to other forms of aromatherapy it should be used as either an oil or in a distiller until a pleasant aroma permeates the vicinity.
>
> Any form of peppermint oil should be effective although for persons who experience heartburn (acid reflux) and wish to supplement with peppermint oil for their intestines, then an enteric coated capsule would be useful (since the muscle relaxing effects may affect the esophagous if the capsule breaks prematurely).[131]

The *American Botanical Council's Expanded German E Commission* on peppermint further validates this reported dosage and administration.[132] It states:

> Unless otherwise prescribed: 6–12 drops per day essential oil and Galenical preparations for internal and external application.
>
> **Internal:** Essential oil: Average single dose 0.2 ml.
> Essential oil enterically coated form: Average daily dose 0.6 ml (for IBS).
>
> **Inhalant:** Add 3–4 drops of essential oil to hot water; deeply inhale the steam vapor.
>
> **External:**
> Essential oil: Some drops rubbed in the affected skin areas (may be diluted with lukewarm water or vegetable oil).
>
> **Liniment:** Oily preparation containing 5–20% essential oil in base of paraffin or vegetable oil applied locally by friction method.
>
> **Ointment or unguent:** Semi-solid preparation containing 5–20% essential oil in base of petroleum jelly or lanolin spread on linen for local application.
>
> **Nasal ointment:** Semi-solid preparation containing 1–5% essential oil.
>
> **Tincture:** Aqueous-alcoholic preparation containing 5–10% essential oil for local application.

The German E Commission has more specific quality and internal standards for essential oils than found in the United States. It reports on the constituents and their percentages that must be contained for a bottle of peppermint essential oil to be considered pharmaceutical grade, beyond menthol:

> European pharmacopeial grade peppermint oil is the volatile oil distilled with steam from the fresh aerial parts of the flowering plant. Its relative density must be between 0.900 and 0.916, refractive index between 1.457 and 1.467, optical rotation between –10 and –30, among other quantitative standards. Identity must be confirmed by thin-layer chromatography (TLC), organoleptic evaluation, and quantitative analysis of internal composition by gas chromatography. It must

* Due to FDA regulations, my affiliations, and legalities, I am unable to make specific references or recommendations of brands.

** There is one branded essential oil company with approval for internal ingestion from the FDA. It is the only dietary supplement line of essential oils.

contain 1.0–5.0% limonene, 3.5–14.0% cineole, 14.0–32.0% menthone, 1.0–9.0% menthofuran, 1.5–10.0% isomenthone, 2.8–10.0% menthylacetate, 30.0–55.0% menthol, maximum 4.0% pulegone, and maximum 1.0% carvone (Ph.Eur.3, 1997). French pharmacopeial grade peppermint oil must contain not less than 44% menthol, from 4.5–10% esters calculated as menthyl acetate, and from 15–32% carbonyl compounds calculated as menthone. TLC is used for identification, quantification of compounds, and verification of the absence of visible bands corresponding to carvone, pulegone, and isomenthone (Bruneton, 1995; Ph.Fr.X, 1990).[132]

An example of how to use Table 1 for converting the .1-.2 ml indicated dosage to drops of essential oils is as follows:

- .2 ml of peppermint oil equates to approximately .067 oz (1 oz =30 ml).
- There are 600 drops of essential oil in one ounce.
- .067 oz of 600 drops totals approximately one drop two to three times a day. This equates to six to 12 drops per day.

Fennel Essential Oil

The *American Botanical Council's Expanded German E Commission* reports on the dosage and administration for fennel essential oil[110] as follows:

> Unless otherwise prescribed: 0.1-0.6 ml essential oil or equivalent Galenical preparations for internal use.
>
> Essential oil: 0.1-0.6 ml.
>
> Fennel honey or fennel syrup with 0.5 g fennel oil/kg [=0.5:1000 (w/w)]:
>
> Adult: 10-20 g.
>
> Children 4-10 years: 6-10 g.
>
> Children 1-4 years: 3-6 g.
>
> Duration of administration: Unless otherwise advised by a physician or pharmacist, one should not consume fennel oil for an extended period (several weeks).[110]

Other sources do not contain direct references to dosage.

Oregano Essential Oil

Examine states the following regarding dosage for oregano oil:

> The only study on using oil of oregano for oral supplementation used a dose of 600 mg. To make tea, steep 15 g of oregano leaves in 250 mL of water.
>
> The tea is traditionally used to aid digestion, while the oil has antibacterial properties that may boost the immune system.
>
> Both the tea and oil is usually supplemented once a day.

Since the study cited is based on an emulsified oil, not an essential oil, this information is misleading.[133] Using Table 1:

- 1 drop = 30 mg.
- The dosage reported would be 600 mg/30 mg, which would equate to 20 drops of pure essential oil. This is not an ideal dose.[133, 134]

I did find one human trial of 104 subjects that used oregano oil in a formulation. The study found the efficacy of herbal treatment to be equivalent to Rifaximin for treatment of SIBO. For the intervention, one of the two formulations randomized contained .1 ml of oregano oil. This would be equivalent to approximately .5-1 drop of oregano oil.[151]

I often supplement any gut protocol with a relaxing essential oil to restore the nervous system.

Ginger Essential Oil

Neither of the monographs for ginger in *Examine*[152] and the *American Botanical Council's Expanded German E Commission*[153] state a dosage for the internal usage of essential oil of ginger, as they do the herb. Natural Medicines Database authors report on nasocutaneous administration and inhalation of ginger oil as follows:

> *Chemotherapy-induced nausea and vomiting: An aromatherapy necklace containing two drops of ginger essential oil has been used for 2 minutes three times daily for 5 days starting with chemotherapy.*
>
> *Postoperative nausea and vomiting: A 5% solution of ginger essential oil, administered nasocutaneously, has been used preoperatively. Aromatherapy with ginger alone, or in combination with spearmint, peppermint, and cardamom, has been inhaled through the nose and exhaled through the mouth three times postoperatively.*[154]

The conversion of drops of essential oil in a 5% solution of ginger oil would be as follows:

- 1 oz. = 600 drops
- 6 drops of EO per oz. of carrier oil = 1% dilution (1% of 600 drops)
- 30 drops of EO per oz. of carrier oil= 5% dilution (5% of 600 drops)

Essential Oils and the Microbiome

Since healing the intestinal tract via the "Five R" program includes removing the cause (e.g., microbes) and re-inoculating the good bacteria, it is important to pause and discuss how essential oils, which are often deemed "antimicrobial," impact the microbiome. From my research and experience, I believe that high quality essential oils likely balance microbe activity. Specifically, there is supporting evidence that as they eliminate overgrowth, they also spare commensal organisms and protect our tissues.

➤

Complete article with references is available on our website www.TownsendLetter.com

➤

I will now provide a brief review of the scientific literature regarding this topic. First, I will give a quick summary on their antimicrobial actions and use with antibiotics. Then, I will provide the compelling vivo and in vitro trials. This, in combination with years of clinical experience and experts' opinions, provides support for assisting with positively balancing the intestinal microbiome.

The Antimicrobial Properties of Essential Oils

The antimicrobial activity of essential oils on pathogenic bacteria is diverse. In a review on the effects, the authors differentiate the actions of essential oils (EOs) to their isolates. The authors state:

> The mechanism of action of EOs depends on their chemical composition, and their antimicrobial activity is not attributable to a unique mechanism but is instead a cascade of reactions involving the entire bacterial cell; together, these properties are referred to as the "essential oils versatility". In general, EOs act to inhibit the growth of bacterial cells and also inhibit the production of toxic bacterial metabolites. Most EOs have a more powerful effect on Gram-positive bacteria than Gram-negative species, and this effect is most likely due to differences in the cell membrane compositions.[155]

A proposed mechanism of essential oils on microbe destruction consists of their toxic effects on membrane structure. These include "degradation of the cell wall, damaging the cytoplasmic membrane, cytoplasm coagulation, damaging membrane proteins, increased permeability leading to leakage of cell contents, reducing proton motive force, reducing intracellular ATP pool via decreased ATP synthesis and augmented hydrolysis that is separate from the increased membrane permeability and reducing membrane potential via increased membrane permeability."[155]

Essential oils have also been reported to interfere with quorum sensing (bacteria's regulation of gene expression related to changes in cell-population density) and decrease bacterial virulence factors.[155]

They may also be helpful in combination with antibiotics to prevent resistance. In a 2014 article titled, "Essential Oils, A New Horizon in Combating Bacterial Antibiotic Resistance," the authors explain that essential oils' versatile properties make them a novel approach for a "drug compound." This is because essential oils have more than one therapeutic effect due to their many biological impacts. This contrasts with a drug's mechanism which is skewed to act on one pathway in the body, not accounting for effects on the body's other functions. The article states:

> Various essential oils have been reviewed to possess different biological properties such as anti-inflammatory, sedative, digestive, antimicrobial, antiviral, antioxidant as well as cytotoxic activities. These findings highlight an exciting scientific interest whereby essential oils warrant special attention because they represent a distinctive group of possible novel drug compounds due to their chemical and structural variance that makes them functionally versatile.[156]

Essential Oils Impact on Intestinal Microbes In Vitro

An in vitro study with eight essential oils, the authors sought to determine if essential oils selectively inhibited several microbes that cause intestinal dysbiosis while sparing 12 species of intestinal bacteria. The authors reported:[157]

> The most promising essential oils for the treatment of intestinal dysbiosis are *Carum carvi*, *Lavandula angustifolia*, *Trachyspermum copticum*, and *Citrus aurantium* var. amara. The herbs from which these oils are derived have long been used in the treatment of gastrointestinal symptoms and the in vitro results of this study suggest that their ingestion will have little detrimental impact on beneficial members of the GIT microflora. More research is needed, however, to investigate tolerability and safety concerns, and verify the selective action of these agents.[157]

In a study with swine cecal digesta, the authors tested the antimicrobial effects of 66 essential oils and their impact on swine gut. The authors stated:

> The antimicrobial activity of essential oils/compounds was measured by determining the inhibition of bacterial growth. Among 66 essential oils/compounds that exhibited ≥80% inhibition towards Salmonellatyphimurium DT104 and Escherichia coli O157:H7, nine were further studied. Most of the oils/compounds demonstrated high efficacy against S. typhimurium DT104, E. coli O157:H7, and E. coli with K88 pili with little inhibition towards lactobacilli and bifidobacteria. They were also tolerant to the low pH. When mixed with pig cecal digesta, these oils/compounds retained their efficacy against E. coli O157:H7. In addition, they significantly inhibited E. coli and coliform bacteria in the digesta, but had little effect on the total number of lactobacilli and anaerobic bacteria.[158]

Essential Oils Impact on Intestinal Flora In Vivo

In a 2010 in vivo study, it was demonstrated that ocotea essential oil inhibited inflammatory mediators from microbial byproducts while simultaneously protecting the gastric mucosa of rodents.[159]

In another study with rabbits, thyme oil increased antioxidant status (i.e., GPx activity) and decreased oxidative harm (i.e., lowered malondialdehyde) in the small intestine. It also positively influenced intestinal integrity, aka preventing "leaky gut," as measured by transepithelial electrical resistance (TEER). **Furthermore, there was a tendency "*for thyme oil to stimulate the abundance of some microbes beneficial in the rabbit gut*."** The abstract states:[160]

> In both groups, the bacterial counts were generally lower in the caecum than in the faecal samples. In conclusion, dietary supplementation with 0.5 g/kg DM thyme oil may improve intestinal integrity, and it may have an antioxidant effect. A tendency was also found for thyme oil to stimulate the abundance of some microbes beneficial in the rabbit gut. (Effect of thyme oil on small intestine integrity and antioxidant status, phagocytic activity and gastrointestinal microbiota in rabbits.[160]

A study in chickens demonstrated that five culinary herbs and their essential oils (thyme, oregano, marjoram, rosemary, and yarrow) had negligible effects on gut microflora and beneficially impacted these broiler chicks' digestion. In the

experiment, body mass and feed consumption were measured on a weekly basis. Counts of lactic acid bacteria, coliforms, anaerobes, and *Clostridum perfingens* were assessed at 25 days. Finally, digestibilities were measured via nitrogen (N), dry matter (DM) and organic matter, and sialic acid concentration. The researchers concluded:[161]

> *Generally, dietary thyme oil or yarrow herb inclusion had the most positive effects on chick performance, while oregano herb and yarrow oil were the poorest supplements. Only thyme and yarrow in these diets had a different effect when used as a herb or oil on weight gain and BM. 4. Dietary treatment had no effect on the intestinal microflora populations, apparent metabolisable energy (AME) or the calculated coefficients of digestibility. Sialic acid concentration was greatest in the birds given dietary thyme oil, compared with all other treatments except those birds receiving marjoram oil, rosemary herb and the controls. However, less sialic acid was excreted in those birds given diets with oregano or rosemary oils, or oregano herb, than in the controls. 5. Plant extracts in diets may therefore affect chick performance, gut health and endogenous secretions, although the chemical composition of the extract appears to be important in obtaining the optimal effects. (*The effect of herbs and their associated essential oils on performance, dietary digestibility and gut microflora in chickens from 7 to 28 days of age.[161]

My Clinical Experience: How I Use Essential Oils Internally for Intestinal Discomfort

I find oral administration of essential oils the most effective method of application for clients that are seeking relief from symptoms of irritable bowel syndrome, functional gastrointestinal disorders, bloating and abdominal extension, food poisoning (due to antimicrobial effects noted above), discomfort, gas, dysbiosis, and changes in stool frequency.

I instruct my clients to administer one to two drops of the selected essential oil from a quality supplier. The drops are placed in a vegetable capsule (enteric coated) using pipette droppers. Next, they are asked to fill the remainder of the cap with coconut oil or a non-dairy milk substitute. This is important for sensitive patients, as it will provide coating for the stomach.

Essential oils are alternated every two months or until symptoms have resolved and lab markers are back within normal ranges. I also recommend that my clients take 1-2 days off per week depending on tolerance. If one experiences burping, GI discomfort, or notices loose stools, I will decrease the dose.

I often supplement any gut protocol with a relaxing essential oil to restore the nervous system. The most well-known and most researched essential oil for this is lavender.[162-167]

Lavender has a good reputation for alleviating anxiety Europe. Germany has authorized a preparation of lavender oil, ➤

➤

Silexan, for treatment of restlessness during anxious mood.[162-167] It is branded as LASEA and is standardized for 20-45% linalool and 25-46% linalyl acetate.[162] Two trials have indicated that Silexan has been effective in mood related issues without unwanted sedative effects.[165,166] According to *Examine*, "It is prescribed (or at least used) for Generalized Anxiety disorder in Germany without apparent benzodiazepene actions."[163]

In a comprehensive review, the nervous system effects of lavender were analyzed in animal and human clinical trials. The authors reported that lavender was shown to have in vivo effects of modulating inflammatory pathways in the brain and on the neurotransmitters dopamine, GABA and serotonin. Human studies with functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) also indicated brain imaging evidence for relaxation effects. These calming effects were also shown to have an impact on sleep, pain, and positive mood.[167]

These psychoneurological effects will impact gastro-intestinal function related to the gut-brain connection, stress, and resultant discomfort and pain.[168]

As far as dosage, both *Examine* and the *American Botanical Council's Herbal Expanded Commission E Commissions* report that the internal dosage of lavender oil is between 80-160 mg of essential oil.[162,163] Using the conversions in the table:

- 30 mg = approximately 1 drop of oil
- 80-160 mg would be approximately 3-6 drops of lavender oil

I have often also used this oil internally at these dosages for clients who appear to have hyperactive sympathetic activity, which is most of my IBS and pain clients.

Conclusion: Summarizing the Art and Science of Selecting the "Correct" Essential Oil

Essential oils can effectively remove the obstacles in the way of healing via their multimodal effects while simultaneously and synergistically working with the body to bring it to balance. This is due to their biochemical constituents affecting physiology combined with the instantaneous psychological effect of their aroma.[1-2]

Not only are essential oils synergistic within themselves and with other modalities, they are also the same regarding their action with the human body. One human study provided evidence that the metabolomics and biochemical pathways of individuals were modulated differently by the same essential oil intervention.

In the clinical trial, researchers sought to determine the metabolic changes in thirty-one females with mild anxiety symptoms after exposure to aroma inhalation for 10 days. In several participants, no effect was found in the measurements studied, yet there were minimal disturbances and many benefits reported by all the responsive subjects. This demonstrates the mechanisms of essential oils "innate wisdom" to bring about balance to the human body. The authors concluded:[169]

> A significant alteration of metabolic profile in subjects responsive to essential oil was found, which is characterized by the increased levels of arginine, homocysteine, and betaine, as well as decreased levels of alcohols, carbohydrates, and organic acids in urine. Notably, the metabolites from tricarboxylic acid (TCA) cycle and gut microbial metabolism were significantly altered. This study demonstrates that the metabolomics approach can capture the subtle metabolic changes resulting from exposure to essential oils, which may lead to an improved mechanistic understanding of aromatherapy.[169]

I have now provided evidence that essential oils can address underlying causes of dysfunction while simultaneously alleviating contributors, triggers, and mediators. I have shown this through the example of using them internally for intestinal discomfort. By reviewing what I have learned and my clinical experience for the past seventeen years, my hope is that now clinicians can decipher how to proceed with more informed, safe, and confident decisions on dosage and proper use of this powerful, ancient, innately intelligent, healing modality.

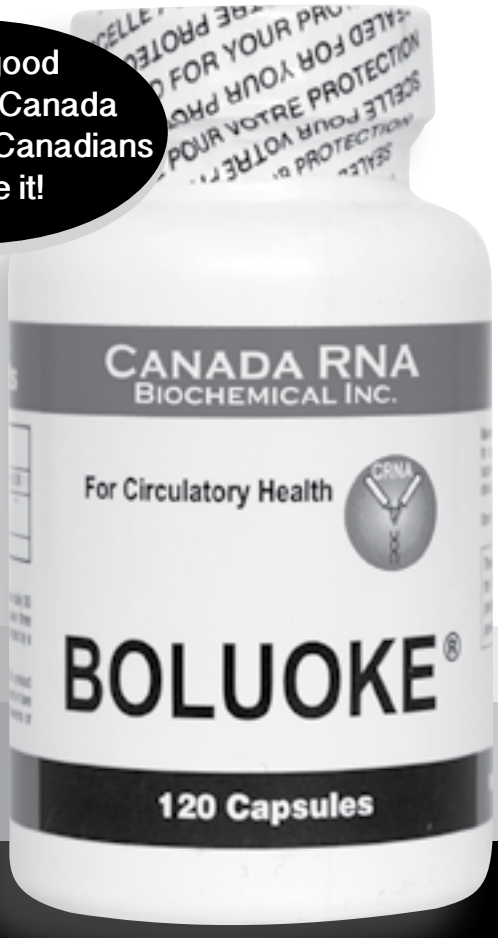
◆

Article and full reference list will be provided on our website www.TownsendLetter.com

Sarah LoBisco, ND, is a graduate of the University of Bridgeport's College of Naturopathic Medicine (UBCNM). She is licensed in Vermont as a naturopathic doctor and holds a bachelor of psychology degree from State University of New York at Geneseo. Dr. LoBisco is a speaker on integrative health, has several publications, and has earned her certification in functional medicine. Dr. LoBisco currently incorporates her training as a naturopathic doctor and functional medicine practitioner through writing, researching, private practice, and her independent contracting work for companies regarding supplements, nutraceuticals, essential oils, and medical foods. Dr. LoBisco also enjoys continuing to educate and empower her readers through her blogs and social media. Her recent blog can be found at www.dr-lobisco.com.

HYPERCOAGULATION

It's so good that Health Canada doesn't want Canadians to have it!



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 INC

antiaging-systems.com

return 2 health

MP Mountain States Health Products, Inc.

Pro Health Network

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

CRNA

1-866-287-4986

www.canadaRNA.com

Letter to the Editor

Re: "Cancer Care: Conventional, Complementary, Alternative?"

I read the article by Dr. Barbara MacDonald in the Aug/Sept 2018 issue of the Townsend Letter with great interest.[1] She gave a good breakdown of the design flaws in the recent article assessing alternative cancer treatment in the *Journal of the National Cancer Institute*,[2] and also made an excellent case for why she advocates proceeding with some form of orthodox therapy for the majority of cancer patients. Based on my own experience working with an alternative cancer therapy, I felt I could add a little information for practitioners about the pitfalls of working in this arena.

I met the late Nicholas J. Gonzalez, MD, in 1983, while he was in the middle of his investigation of the work of William Donald Kelley, DDS. Gonzalez had found a remarkable number of patients with documented terminal cancer who had thrived under Kelley's care.[3] Kelley's regimen involved dietary changes, oral nutritional supplements with large amounts of pancreatic enzymes, and detoxification including coffee enemas.

Gonzalez and I came to New York City in 1987, where Gonzalez set up a practice to recreate Kelley's methods. I completed my internal medicine training, then joined Gonzalez, starting to see patients myself in 1993. While we always had tremendous faith in what we were doing based on Kelley's results and we started to see remarkable outcomes ourselves, we also found that there were a few patients who swore they were completely compliant who nonetheless did not do well. We therefore advised patients who had conditions that could be cured with standard modalities such as surgery, chemotherapy, or radiation that they should do those treatments. It would be a shame for someone to pass up a chance at a cure to pursue something that was experimental.

However, in the early years of Gonzalez' practice, he would also see occasional patients who insisted that they wanted to do a natural-only approach, that they felt it was their right to try, and that they would rather die than get surgery, making such a compelling case that he would decide to treat them. A few of those patients did well. Most of them, however, turned out to be problem patients. An example that sticks in my mind is a patient who had cancer of the larynx, which can be cured by radiation or surgery, but with inevitable alteration of the voice. This patient's career depended on the ability to speak, so a passionate plea was made and the patient was accepted. After four months on the protocol, examination by an otolaryngologist showed that the lesion on the larynx had shrunk by 40%. The patient then opted to discontinue more than half of the supplements prescribed and to cheat extensively on the diet. The patient's spouse explained all that in a call a few months later; the patient was on the phone but unable to speak due to regrowth and progression of the laryngeal mass. The patient was then politely but forcefully referred for radiation, since the voice was gone and radiation could still be curative.

Gonzalez had patients who refused curative surgery who reported that they were taking all their supplements but were not buying enough of the products

to be doing so. In two cases, friends called more than a year after patients died to inform Gonzalez that the patients had been smoking cigarettes or drinking a pint of vodka every night. We finally concluded that for a certain number of the patients who refused orthodox therapy, their real agenda, based on their actions, was not a fervent belief in the power of nature to heal. It was a desire to deny that they were ill. They would try to appease their loved ones, made frantic by their refusal of standard medical care and by their deteriorating condition, by saying they were pursuing a treatment under the direction of a physician. Meanwhile, they would not be following through with the treatment prescribed.

Denial and noncompliance are not confined to cancer patients who refuse potentially curative orthodox therapy, but my experience tells me that more patients in that group exhibit those behaviors. The potential legal ramifications of these patients' poor outcomes are tremendous for the practitioner involved in their care. An informed consent document may or may not protect against malpractice litigation, but disgruntled patients or family members can also file complaints with state regulatory agencies, giving them the opportunity to go on a witch hunt, if they feel so inclined. This is not fearful speculation on my part; it happened to Gonzalez in the 1990s. I have written in a previous Townsend Letter article about those times.[4] Given our reluctance to have a patient refuse a curative option to pursue an experimental treatment they might or might not actually follow, and our horrendous experience of dealing with malpractice cases and state medical board investigations, Gonzalez and I decided to refuse to accept new patients who have curative options they have not received. As I continue our work after his death, I also continue that policy.

Gonzalez and I have been criticized for that decision by other practitioners, mostly naturopathic physicians, who claim they "turn no patient away." MacDonald's statement in her article that "a licensed naturopath who focuses their practice in oncology is not bound by a standard of care like medical oncologists are" helped me understand the perspective of those critics. I hope this letter will help explain my perspective, and that it will be helpful to others as they decide how they want to operate their practice.

Linda L. Isaacs, MD, www.drlindai.com

References

1. MacDonald B. Cancer care: conventional, complementary, alternative? *Townsend Letter.* 2018, Aug/Sep;421:52-57.
2. Johnson SB, Park HS, Gross CP, Yu JB. Use of Alternative Medicine for Cancer and Its Impact on Survival. *J Natl Cancer Inst.* 2018;110(1):121-124. doi:10.1093/jnci/djx145
3. Gonzalez NJ. *One Man Alone; An Investigation of Nutrition, Cancer, and William Donald Kelley.* New York, NY: New Spring Press; 2010.
4. Isaacs LL. In memoriam: Nicholas J. Gonzalez, MD. *Townsend Letter.* 2016, Jan;390:14-19.

◆

Autoimmunity and Your Gut

by Thomas Cowan, MD

Dr. Cowan is a veteran family physician, founding board member of the Weston A. Price Foundation, and author of *Vaccines, Autoimmunity, and the Changing Nature of Childhood Illness* (Chelsea Green Publishing, 2018). His compelling new book reveals his answer to the current epidemic of autoimmunity and chronic disease we are seeing among children today and dives into the latest research in medicine, parenting, the microbiome, and more. He presents a radical new understanding for how vaccines and other environmental toxicants have altered the very nature of disease from acute infectious diseases to chronic autoimmune disorders. And, he argues that certain childhood illnesses can actually help protect against chronic health problems later in life. The following excerpt is adapted from his book *Vaccines, Autoimmunity, and the Changing Nature of Childhood Illness*, and is reprinted with permission from the publisher.

Thanks to the Human Microbiome Project, we know that the human body contains about two to six pounds of microorganisms and that according to some estimates these microorganisms outnumber our own cells by as much as ten to one. Other estimates put the number lower, but the fact remains that we are home to trillions of microbes, the largest number of which are found in our gut. And while the mapping of the microbiome is complex and not yet finished, we know that diversity is everything. As in agriculture, diversity tends toward a state of health and balance; monoculture tends toward one of sickness and disease.

Starting in our nose and sinus passageways, and extending all the way to the anus, our gastrointestinal (GI) tract is filled with an incredible diversity of bacteria, viruses, fungi, and sometimes larger organisms. The GI tract can be thought of as a long, hollow tube, divided into different sections, each with a different function. The entire tract is covered with a layer of microorganisms, as well as a layer of hairlike protrusions called villi. Microvilli are similar and have some of the same functions, but can also be found in some other parts of the body, such as white blood cells.

Like our gut flora, intestinal villi (and microvilli) are critical to our health. On the one hand, they enable good absorption of nutrients from the food we eat. Increasing the surface area of the intestinal wall, the villi absorb nutrients and deposit them in the capillaries that lie just below, eventually delivering them into circulation for use as the building blocks of our cells and tissues. The intestinal villi also create tight junctions that result in the selective permeability of the gut wall, preventing proteins, toxins, and other molecules from gaining access to the bloodstream. Like a well-constructed brick wall, the bricks (read: plump, healthy cells) fit perfectly next to one another. Underneath the villi is a layer of collagen and then a muscular wall, which provides structure and stability to the GI tract. The muscular wall is responsible for the contractile movement resulting in peristalsis and the ability to defecate. Without it, the remnants of our food would not move down and out, and our digestive system would grind to a halt.

I often tell my patients to imagine their GI system like a healthy meadow. Healthy subsoil will provide the structure and foundation upon which the upper layers rest. This subsoil is the muscular layer of our GI tract. Then there is the topsoil (the villi), the meadow's nutritive layer; when healthy, this layer provides the nutrients and habitat for the microbial community. In a pasture or garden, a healthy topsoil gives rise to a thick and vibrant grassy layer filled with an incredible diversity of plant life, everything from perennial grasses, wildflowers, and annual grasses to bushes and trees. Moving in and through these grassy plant layers are insects, butterflies, and animals that together create the diverse ecosystem we call a meadow. While meadows may look static, they are, like our gut, teeming with life.

Our gut lining is also home to a diversity of microbial life, forming a carpetlike inner lining of the gut, lying on top of the plump, healthy cells with healthy villi, and supported by the blood vessels and muscular layer of the gut wall. When healthy – whether a meadow or our gut – the various layers work together to create health for the entire ecosystem. This is the basis of resilience, a state of balance and health that accommodates disturbances without compromising the integrity of the whole system.

In our gut, the feedback system of these layers working together enables microbes to synthesize nutrients that are as important to our well-being as the nutrients provided by our food. The gut microbiome has many more functions, such as aiding digestion, providing bulk to the stool, keeping pathogens in check, and perhaps others we have yet to discover.

When intact, these well-functioning layers – in a meadow or in our gut – prevent the absorption of pathogens – a word I'm using to mean anything, including toxins and agricultural chemicals, that causes disease – into the underlying layers. In a meadow, the rich biodiversity and various soil strata help to prevent toxins or agricultural chemicals from reaching the groundwater. Much will be caught and retained by plants and grasses. If this first layer of the meadow is breached, humus in the soil will bind toxins so they can be digested by the worms, fungi, and other organisms in the topsoil. If the topsoil is breached, then the subsoil will act as a physical barrier to prevent the toxins from reaching the groundwater. Of course, toxins will reach the groundwater in plenty of instances; when you overload a system with toxins, it loses its resilient capacity to absorb, integrate, and maintain homeostasis.

When we are healthy, enzymes in the mouth, acid in the stomach, and microbes in the lower gut will often destroy pathogens. If a pathogen escapes these first lines of digestive defense, then the villi will prevent their access to the bloodstream. If the villi are compromised, we have the physical barrier of the smooth muscular layer of the intestinal wall. In health, these systems function together to screen pathogens from the bloodstream. They are, in essence, guardians of our health. On a more metaphysical level, the gut ecology is the preserver of our integrity. We are not supposed to be a teeming collection of unwanted toxins, proteins, antigens, and pathogens floating around in our blood and settling in our tissues any more than groundwater is supposed to be contaminated with

toxic agricultural products. When this contamination happens, we set the stage for the onset of autoimmune disease, one of the predominant plagues of modernity.

A loss of diversity of the microbiome can happen in a number of ways. One common way is the failure of a child to go through the birth canal during delivery. Babies are inoculated with the healthy microbes from their mothers' vaginas during delivery and these bacteria essentially function as the seeds that will grow into a healthy, diverse gut microbiome. Babies born via C-section initially host more of the flora found in the operating room than the flora found in their mothers. As a result, many American babies have compromised microbiomes during infancy due to the lack of microbial diversity and the paucity of healthy organisms that should populate their gut. Or, if a baby does pass through the birth canal during delivery, but the mother's vaginal ecology is unhealthy due to poor health, chronic antibiotic use, or yeast infections, the child will start life with poor-quality gut flora and thus develop a poor-quality microbiome.

A typical American child is then subjected to numerous other influences that have a negative impact on the formation of a healthy microbiome. One factor is lack of diversity in the family's diet, especially in the diet of the nursing mother. Another factor is the overuse of antibiotics in medicine and their ubiquitous presence in the food chain. Yet another factor is a lack of foods with healthy bacterial cultures, including lacto-fermented vegetables such as sauerkraut and pickles; and cultured dairy such as yogurt and kefir. These and many other factors, including GMOs and glyphosate (Roundup), create the conditions in which it is the rare modern child who is born with and able to sustain a healthy microbiome. Without a healthy microbiome, like a hillside with no grass, the intestinal villi and microvilli deteriorate, compromising the integrity of our inner ecosystem at the most fundamental (cellular) level.

When a cell is healthy, the cytoplasm is a gel, not liquid, and this is particularly relevant for our intestinal villi and microvilli, as they have such an important role to play in both absorption and interception. This gel state is the result of intracellular proteins structuring the water inside the cell into a healthy, consistently robust structure. (Think of Jello.) Side-by-side cells with healthy intestinal villi and microvilli will prevent toxins and large molecules from gaining direct access to the bloodstream. When the structure and integrity of the cytoplasm are compromised, the cells shrink and lose their connection to one another and gaps start to appear between the cells. Through these gaps, large protein molecules that shouldn't show up in the bloodstream pass through. Once in the blood, the body must neutralize these large proteins by the production of antibodies. These antibodies often cross-react with the body's own tissue, and when they do, autoimmune disease will commence. In other words, the root of autoimmune disease can be found in the "leaking" gut. And the root of the leaking gut is the contraction of the cells as a result of unhealthy gel formation within these cells.

What factors interfere with this healthy gel formation? In fact, there are many, the main one being the loss of or imbalance in the microbiome. There are other factors that directly compromise the cells, including cellular poisons such as mercury, aluminum, formaldehyde, and some agricultural chemicals, including glyphosate. These toxins, including glyphosate, are found in modern vaccines. This process of intoxication results in shrinkage of the cells. Shrunken, distorted cells are the hall- mark of celiac disease and other autoimmune diseases. This fact is something that modern medicine is just beginning to appreciate: That is, the etiology of autoimmune disease and allergy can be traced back to distortion of cells and damaged villi and microvilli. And this fact is why diets such as the Gut and Psychology Syndrome (GAPS) diet and the Specific Carbohydrate Diet (SCD) that focus on gut health and repairing leaky gut are so crucial in the treatment of autoimmune disease, autism, allergies, and other chronic conditions.

We are born with an inherent "boundary" in our gut that creates a separation between what is allowed into our bloodstream and what should be kept out. Antigens of all sorts, proteins, bacterial products, heavy metal toxins, and agricultural poisons can breach this gut barrier when the gut lining is inflamed or leaky. This breakdown leads to the production of antibodies that further cellular damage. This process is intrinsic to the process of autoimmune disease.

What does all this have to do with vaccines, which are often administered intramuscularly? The underlying autoimmune phenomenon is the same. And, actually, it has been shown that vaccination does have a direct effect on the microbiome and gut permeability even when given intramuscularly, not orally. The precise mechanism of how this happens is unknown, but I believe that any time you affect the balance of immune response, you affect the largest and most important organ system of immune response that we have – the gut.

Thomas Cowan, MD, has studied and written about many subjects in medicine, including nutrition, homeopathy, anthroposophical medicine, and herbal medicine. He has served as vice president of the Physicians' Association for Anthroposophic Medicine and is a founding board member of the Weston A. Price Foundation. He is the author of numerous books including *Human Heart, Cosmic Heart* and *Vaccines, Autoimmunity, and the Changing Nature of Childhood Illness.*

◆

Genetic Expression and Lifestyle Choices

review by Jule Klotter

Dirty Genes by Dr. Ben Lynch
HarperOne. New York, New York.
ISBN 978-0-06-269814-8; c. 2018; 371 pp; $27.99 (US)

With the discovery that some genetic disease tendencies can be turned off or on with environmental exposures and lifestyle choices (epigenetics), a new paradigm has arisen. Genetic inheritance now offers just possibilities instead of fixed destiny. Even the onset of debilitating inherited diseases like Huntington's can be modulated by nutrition and other factors.[1]

Naturopathic physician Ben Lynch, a graduate of Bastyr University, began delving into the ever-expanding literature on epigenetics over 10 years ago. He looked for specific ways to support health in people who, like his sons and himself, had genetic variations, single-nucleotide polymorphisms (SNPs, pronounced 'snips'), that have far-reaching effects on body and mind. The result is the lay-friendly book *Dirty Genes* that aims "to teach every single interested person how to clean up their genes and achieve a whole new level of health."

Humans have about 20,000 genes with over ten million known genetic polymorphisms, but only a minority of these variations affects gene function. *Dirty Genes* focuses on seven, well-researched genes whose SNPs have important health consequences: "MTHFR, the methylation master gene; COMT, whose SNPs help determine whether you're focused and buoyant, or laid-back and calm; DAO, the gene whose SNPs can make you supersensitive to certain foods and chemicals; MAOA, the gene that affects mood swings and carb cravings; GST/SPX, the genes that can create detox dilemmas; NOS3, the gene that can create heart issues; PEMT, the gene that supports your cell membranes and liver." If one of these genes is "dirty" or not functioning in a health-producing way, it will affect the function of other genes. "All our genes interact with one another," says Lynch. "When one gene gets dirty, it doesn't work properly, so several more genes step up to help – and now suddenly they get dirty too. Your body isn't a set of discrete compartments that each work separately. It's one amazing *interactive* system in which problems spread and multiply with amazing speed."

For better or worse, diet and lifestyle factors significantly affect each of these seven genes, causing them to function in a health-promoting or illness-promoting way. Lifestyle factors that shift genetic expression towards illness include too much sugar, unhealthy fats, too much or not enough protein, nutrient shortages, too little or too much exercise, irregular sleep patterns and non-restorative sleep, environmental toxins, and physical and psychological stress.

A "normal" result on a genetic test does not mean that the gene is being expressed in a health-producing way. "Most of the folks who send away for genetic testing are unaware that a gene born clean can easily become dirty," says Lynch. "When they read that their MTHFR is normal, they celebrate instead of realizing that – due to diet and lifestyle – it might in fact be super dirty." Although *Dirty Genes* includes a list of laboratories that test for genetic SNPs in its resource section, testing isn't necessary in order to use this book. The book gives good descriptions of the physical and behavioral characteristics of the "dirty" expression for each of the seven genes, along with patient examples, and a questionnaire to help readers identify their own problem areas.

> "This book covers a far more advanced approach to genetics than is currently practiced in medicine today. The information you now have at your fingertips is not a Get Healthy Quick scheme. It's a lifetime tool that you can revisit any time you need to tweak you dirty genes."

Instead of prescribing a supplement to shift genetic expression, Lynch recommends starting with a two-week "Soak and Scrub Clean Gene Protocol" that uses basic naturopathic principles. In Week 1 (Soak and Scrub week), for example, he urges readers to track their meals and reactions, to fast 12-16 hours a day, and to eat nutritious food until 80% full, chewing the food thoroughly, and not drinking cold beverages with meals. He also gives suggestions for relieving stress, improving sleep, and removing chemicals from the environment. Week 2 builds on the first week with additional ways to improve digestion, indoor air quality, and reduce stress. At this point, a multivitamin and electrolytes – and possibly liposomal glutathione, molybdenum, or digestive enzymes, if needed – are the only supplements he recommends.

I found Dr. Lynch's advice on supplements quite interesting. Instead of routine supplementation, he says to "tune in" and pay attention to how a supplement makes you feel. Does it have the hoped-for effect? He advises reducing or stopping the supplement upon the point of feeling "great." "People who feel depressed often take supplemental methylfolate," he explains. "In a few days, they feel great! Then they begin feeling irritable, snappish, wired, they experience that 'jumping out of their skin' feeling...they need to cut their methylfolate dose right away.... Because your body is always changing, the 'right amount' of any supplement is always changing too."

After the Soak and Scrub Protocol come suggestions for 'spot cleaning'. A questionnaire helps readers identify which of the seven genes still need more support via additional lifestyle, dietary, and environmental changes and supplements. Instead of focusing on the 'dirtiest' gene first, Lynch has found it more effective to address them in the following order: DAO, PEMT, GST, COMT, MAOA, MTHFR, and NOS3.

Although *Dirty Genes* does have some references, it is primarily written with a lay audience in mind. The book is a very accessible and practical introduction to epigenetics, and the advice for supporting gene function is sure to improve health.

1. Mo C, Hannan AJ, Renoir T. Environmental factors as modulators of neurodegeneration: Insights from gene-environment interactions in Huntington's disease. *Neuroscience & Biobehavioral Reviews.* May 2015;52:178-192.

◆

Curmudgeon's Corner

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

SIO-ASCO and the Difference Between Type I and Type II Errors

A recent American Society of Clinical Oncology (ASCO) decision to adopt a set of guidelines developed by NDs for SIO has me missing Steve Austin as he was the one who could explain why this all feels so crazy to me.

In June 2018, ASCO officially adopted guidelines for the integrative care of breast cancer patients that were initially created by a committee of naturopathic physicians for the Society of Integrative Oncology (SIO). Some consider this adoption to be good news, a mile marker in integrative cancer care. For we perpetually underdog naturopaths even to be noticed by ASCO is exciting, something like being offered a seat at the grownup's table. To have ASCO endorse ND work, well this sounds fantastic, at least when you're reading the headlines.

Reactions have varied depending where on the medical spectrum the viewer seems to practice. Some have heralded this as a landmark achievement for integrative medicine: Fred Hutchinson's website describes "… ASCO's endorsement represents a milestone in the integrative oncology field,"[1]

And for others this adoption is solely an excuse to try out new derogatory terms: "The advance of quackademic medicine in oncology continues apace."[2]

For most of us as we read the actual guidelines, we can't help but be left feeling puzzled, surprised by how much good information just seems to have been left out.

All this sadly reminds me of the late Steve Austin. He explained all of this decades ago, and this only serves to remind me of how much I miss him.

The best way to make sense out of ASCO's adoption of SIO's Guidelines for Integrative Care of Breast Cancer is to go back to when Steve Austin, ND, explained the difference between NDs and MDs was what each profession was afraid of. I think I read this in his and his wife Cathy Hitchcock's 1994 book *Breast Cancer*.[3]

This is far enough back that I may need to find a real copy of the book and type the text by hand. Before I do that, let me back up and provide some more details so you understand what has me thinking about all this.

ASCO, the association of the very straight MDs who specialize in cancer treatment, made a shocking step recently by accepting a series of guidelines from SIO, that is the Society of Integrative Oncology, the relatively open-minded group that investigates and sometimes incorporates alternative therapies into their care of cancer patients. There is normally a wide gulf between the two groups. SIO lets naturopathic doctors become members.

SIO was founded in 2003 as a professional organization for those practicing integrative oncology, so still a relatively young group. Claiming to be integrative, they were obligated to start accepting naturopathic doctors as members. Eager beavers that we are, naturopathic doctors quickly rose to take leadership positions in the group. Heather Greenlee, ND, served as president in 2014, and Suzanna Zick, ND, in 2015. In fact, it was Heather Greenlee, ND, PhD, who co-chaired the SIO guideline task force that developed the set of guidelines for integrative adjunctive care for during and after breast cancer treatment. These guidelines were published in 2017. In June 2018, ASCO pretty much adopted them, with a few added caveats.

This is a massive achievement from the perspective of naturopathic medicine building bridges and working across the spectrum of medical thought. There has been a great deal of back patting and congratulations. Indeed, this congruency of thinking is unprecedented in the realm of naturopathic and conventional medicine. I'll buy Dr. Greenlee a drink next time I see her, for sure.

There is a slight problem with the recommendations, at least from the perspective of anyone who actually practices naturopathic oncology and sees patients; the guidelines are underwhelming to say the least. They are so conservative and so dismissive of so many interventions that naturopathic medicine takes for granted that Heather and her ND colleagues who were part of this task force are getting equal parts abuse along with their deserved congratulations.

According to the guidelines the only acceptable therapies aside from the standard medical interventions are yoga, meditation, and

➤

➤

acupuncture. Diet, exercise, or supplements do not have adequate data in the view of the straight oncology world to be suggested.

The SIO guidelines were based on an analysis of peer-reviewed randomized controlled trials published between 1990 and 2013. More than half of the patients in any study considered had to have breast cancer. The integrative therapy being studied had to be used along with standard therapy and it had to have a noticeable effect on symptoms or side effects of treatment. The bar was set high.

It is hard to believe these few recommendations are all that were found supported by adequate enough evidence to satisfy the members of the ASCO task force that took up this challenge. Medical oncology has standards for the level of evidence that are incomprehensible to the average ND or even for those who focuses on naturopathic oncology in practice, even for those who claim that their practices are evidence based.

In fact, various colleagues of my acquaintance are in such disbelief they are questioning the wisdom of these eminent colleagues on the other side of the spectrum.

Thus, I come back to Steve Austin, ND. He believed that the difference between MDs and NDs all boiled down to different types of error and our respective needs to avoid them.

In statistics there are two fundamental types of error, labeled simply Type I and Type II errors. In statistical hypothesis testing, a type I error is the incorrect rejection of a true null hypothesis (a "false positive"), while a type II error is the failure to reject a false null hypothesis (a "false negative"). A null hypothesis is the statement being tested, usually that there is no difference between two populations.

Let's try an example. There's an ongoing debate on whether taking oral curcumin will reduce radiation dermatitis. Back in 2013, a paper written by Julie Ryan and colleagues told us that they had given 6 grams oral curcumin per day to 30 breast cancer patients during their course of radiotherapy.[4] The null hypothesis for their study was that there would be no difference in frequency or intensity in radiation dermatitis between the placebo and the curcumin groups of women.

In this example, a Type I error would be incorrectly concluding that the null hypothesis was false and that frequency of dermatitis differed between the groups, that is the curcumin did something when, if truth be known, it didn't. In simple words, it is a false positive, believing curcumin is useful when in fact it isn't.

A type II error, "is the failure to reject a false null hypothesis (a "false negative")" so in this example it would be thinking there was no difference between the two groups when in reality there is. Again, in simple language a false negative.

Ryan et al reported that "… fewer curcumin-treated patients had moist desquamation (28.6% vs. 87.5%; P = 0.002)." and that is where the matter has stood until this year when Ryan and her team reported the results of a second study.

In a second much larger study that included 686 patients, the statistical analysis did not show a significant difference in skin damage from radiation so the null hypothesis, the curcumin did not help, stands. A type II error would be if we failed to find a reduction in dermatitis in the experimental group when in fact curcumin did help.[5]

In the late Steve Austin's words,

> Many medical doctors tend to make the philosophical mistake of unconsciously assuming that if something is not proven, it doesn't work. Consciously we can all understand the fallacy of this position. It's tantamount to suggesting that before the link between vitamin C deficiency and scurvy was proven, people who ate foods rich in vitamin C were no better off than sailors on hardtack….As a result of the 'If it's not proven, it can't work' philosophy numerous effective treatments and preventive agents have been and are currently being ignored by many conventional medical doctors. Scientists refer to the mistake made when a useful intervention is considered useless because of lack of absolute proof as a 'type II error.'
>
> Conventional medical doctors make many type II errors, but not without good reason. If you deal with dangerous substances, you must be sure that these therapies do something useful before prescribing them to patients. The implementation of a therapy may be postponed by a few years while it's being proven. Although some precious time is lost in the process, the alternative---employing dangerous treatments, some of which turn out to be useless—could be a disaster….
>
> But this kind of thinking doesn't make the same sense when talking about vitamin D. It's not chemotherapy. If a substance is inexpensive, has been proven safe, and reduces the risk of cancer in animals, should you really wait ten years for proof to develop before taking it, especially when you may not have ten years to wait?[3]

The difference between naturopathic medicine of the sort practiced by naturopathic oncologists and the standard of care world views practiced by ASCO's membership is what sort of errors we are willing to risk because of the difference in therapies we choose to use. We are fairly certain that there is little risk in taking curcumin for pretty much any patient. We do not mind taking it by accident, that is thinking it will help when in fact it does us little good. We are willing to risk a false positive. If in the end it turns out to provide no benefit, then as they say "no harm done."

If instead of curcumin we were contemplating starting the patient on a three-month course of doxorubicin, a particularly unpleasant form of chemotherapy, we would want to be absolutely certain it will provide benefit to the patient.

So, this is the difference between us and them. We are both interested in improving patient outcome. It's just a difference in the tools we are accustomed to using. For naturopathic doctors, the starting assumption is that the tools are safe and won't hurt. For the medical oncologist, the starting assumption is that the tools are dangerous and should only be used with the utmost of caution. For the naturopathic oncologist, the equation is the opposite: "It won't hurt, and it might help."

Perhaps this explanation will help some understand the SIO-ASCO breast cancer guidelines. They attempt to bridge two vastly different world views, and translating between these different paradigms does not come easy.

References

1. The full ASCO integrative breast cancer guidelines can be read here: https://www.fredhutch.org/en/news/center-news/2018/06/asco-endorses-integrative-oncology-guidelines-for-breast-cancer-patients.html
2. https://sciencebasedmedicine.org/asco-endorses-the-integration-of-quackery-into-breast-cancer-care/
3. Hitchcock C, Austin S. *Breast Cancer: What You Should Know (But May …)*. Prima Publishing. 1994:208-209.
4. Ryan JL, et al. Curcumin for radiation dermatitis: a randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients. *Radiat Res*. 2013 Jul;180(1):34-43.
5. Wolf JR, et al. Oral curcumin for radiation dermatitis: a URCC NCORP study of 686 breast cancer patients. Support Care Cancer. 2018 May;26(5):1543-1552.

◆

Healing with Homeopathy

by Judyth Reichenberg-Ullman, ND, MSW; and Robert Ullman, ND

www.healthyhomeopathy.com

Finding the Remedy from the Miasm

What Exactly Is a Miasm?

When I (Judyth) was first introduced to philosophy of homeopathy in my first year of *Bastyr* naturopathic college, I heard the term *miasm.* It was defined as a hereditary layer of disposition, literally a *miasma* or swamp. Dr. Samuel Hahnemann, the founder of homeopathy, postulated that through healing miasms it would be possible to eliminate chronic and recurrent disease. In other words, the *similimum*, or best/exact homeopathic remedy for the individual would relieve symptoms and the removal of the miasm would keep that individual healthy rather than falling sick again and again due to the hereditary tendencies. At that time, we learned there were only FIVE miasms: *psora* (defined then as itch), *sycosis* (gonorrhea), *tubercular* (tuberculosis), and *syphilis*. And there was little information available about how to actually use the miasms to treat patients.

I never really learned, until I went to India ten years after receiving my ND degree, what to do with the concept. Bob and I, in the late 80s, were traveling in Mexico and visited the clinic of the famous Dr. Proceso Sánchez Ortega, famous for his work in miasms. We were invited to sit in on a case, along with several of his students. At the end of the case taking, a list was made of each symptom of the patient and each was categorized according to miasms. We found this process interesting, but overwhelming, and confusing. During that early stage of our practice, pre-computer, grid sheets with remedy names and symptoms were, believe it or not, common.

We were in our homeopathic infancy in those days. We rarely ventured out beyond the *polycrest* (forty-five or so "most commonly prescribed remedies") and heard about the use of miasms to select remedies in obvious cases like patients needing *Thuja, Medorrhinum, Tuberculinum*, or *Syphilinum*. There was talk about using these miasmatic remedies as *intercurrent* remedies – in other words, in between the so-called constitutional remedy. I never prescribed that way because it didn't really make sense to me. I would have to say, in retrospect, that we found the *simillimum* (one best remedy for the patient) only by effort and luck, and only periodically, in those early days.

Mumbai Changed Our Practice Dramatically

Having read *The Science of Homeopathy* by Dr. Rajan Sankaran in 1993, we realized how much we had to learn despite our previous training and a decade of practice. Rajan and his colleagues, having practically memorized the homeopathic literature and taken off from that point, were leaps and bounds ahead of us in all ways. We were humbled, inspired, challenged, impressed…. more than anything we were blown away. Older than these Indian homeopathic colleagues by a good ten years and having been in practice ourselves about the same number of years, we were novices. Fortunately, that became patently obvious to us immediately on beginning our Indian training, and we became sponges soaking up this new material.

I would say that we tossed out about 80% we had learned previously and started afresh. That included case taking, case analysis, breadth of *materia medica*, and potency selection. Our practice, our writing for the *Townsend Letter*, our subsequent books… all were affected and transformed dramatically by that course in Mumbai, by the eight other times we studied with Rajan in India, and by the many seminars in the US and Hawaii that presented complementary material. Our understanding of patients, remedies, and the unfolding of the cases over time shifted radically. Many of our readers, colleagues, and students were as dazzled by the new information as we were. Those homeopaths who were committed solely to the previous methods, which they called "the real Hahnemannian approach" were less impressed, and still are by Rajan's new system. What one person considers avant garde and revolutionary, another considers heresy.

The Sensation Method and Miasms

Rajan's Sensation Method has revamped, enriched, and made much more meaningful and practical the miasms. The masterful work written by our colleagues and friends, Nancy Herrick, PA, and Roger Morrison, MD, *Miasms of the New Millenium*, has elaborated on this method beautifully. This book is so indispensible that I have a copy both in Washington and Chile. Rajan explains that miasms are indicators of the level of intensity, desperation, depth, perception, and pace of the patient's state. He has also expanded the number of miasms, which progress from immediate to deeper as follows:

➤

➤

1. *Acute*: Think life or death. Someone who perceives herself to be in sudden and extreme danger, do or die, at great risk. Remember that this is the perception of the individual rather than, necessarily, what is happening.
2. *Typhoid*: A concentrated, intense, brief, do-or-die effort and struggle that ends in exhaustion, collapse, burnout.
3. *Psora*: Optimism, effort within one's ability. Literally an itch.
4. *Ringworm*: Trying again and again. Alternation between struggle and resignation.
5. *Malaria*: The patient uses words like *limited, harassed, miserable, stuck* to describe this state.
6. *Sycosis*: An inherent, unfixable flaw or weakness that requires hiding or covering up. The patient feels he must live with this unavoidably.
7. *Cancer*: The task is insurmountable, beyond all effort, chaotic and requires a superhuman effort and perfectionism to achieve.
8. *Tubercular*: A suffocative, intense, desperate, hectic pace leading in burnout.
9. *Leprosy*: A profound feeling of being dirty, shunned, avoided, disgusted. The scarlet letter syndrome.
10. *Syphilis*: All hope is lost. The situation is beyond survival. There is only destruction, withdrawal, suicide, or death.

Rajan's *Schema* method further categorizes remedies from many mineral, animal, and 33 plant families according to miasm. This is not definitive but rather a work in process. There are, of course, far more members of each kingdom to fit into any chart. But for me, since I have used this method for the past 25 years or so, as it has continually evolved, so has my use and comprehension of it. The system has allowed me to prescribe countless remedies with which I was previously unfamiliar. The following is one case, out of many, to bring meaning to this method in clinical practice.

Joe: A Case of Severe Depression

This patient has come faithfully for homeopathic care for 25 years. He worked as a manager for a utilities company until he retired a couple of years ago, but what he earned just covered his expenses. He has just enough resources to make ends meet so that he enough money to last for the rest of his life. He is now 65 years old and retired. I tried many remedies with this man over the years. I will summarize the case beginning 18 years ago. At that time, and for some years, I was giving Joe the remedy *Chocolate*, which actually belongs to the acute miasm. Even though I knew about miasms, I had somehow become confused in this case – just overwhelmed by Joe's level of despair. It goes to show how a homeopath can miss the obvious, or, at least, the forest for the trees.

Joe: I am feeling really isolated from people. All my friends are withdrawing. No one wants to be around me. I am not fit to be around. I just turned 54. I was told I'll live a long time but, if I'm screwed up, I don't know if I want to live that long. I take things too seriously. And I eat chocolate all the time. When I was younger it gave me mood swings. I was addicted to it and I still am. I feel separate. I've had herpes in the past and sometimes I still get an outbreak.

When I was in grade school, I'd be left out. My siblings would go off and I'd be left behind. Loneliness. I didn't feel part of things. I had three siblings. My father was an alcoholic and fought with my mother all the time. My mom used to beat me up as a kid. She suffered from manic depression. There were times when she threatened to kill me. I never understood why she hated me so much. I actually felt sorry for her. I spent a lot of my younger years trying to get my parents to love me…. being a martyr. I'm told that I'm too hard on myself. I always think I'm wrong and that I don't deserve love. I've been seeing a therapist off and on for years. I guess alienated is a good word to describe how I feel. Unloved. Unacceptable. Alone.

I get some neck, shoulder, and thigh pain. Like I've strained it. It started last year and chiropractic hasn't helped. I've cried a lot recently. I tell myself that I'm alienating myself from my friends. That I don't do a good job at work. The feeling of isolation didn't improve much from the last dose of the Chocolate*.*

I had chosen the remedy, *Chocolate*, a member of the *Malvale* family, whose members feel estranged and indifferent, along with Joe's longstanding addiction to chocolate. I subsequently gave Joe *Magnesium muriaticum*, a remedy for profound loneliness, abandonment, and the feeling of being orphaned, alone in the wilderness – as well as a number of different remedies over the years, including *Aurum metallicum, Thuja,* and, once, *Hura,* which is a plant belonging to the *Euphorbiaceae* or spurge family. I was close but never found the simillimum for Joe at that time. I was, I hate to admit, all over the map with the kingdoms and miasms. But Joe was a loyal patient who stuck with me over time until I did find just the right remedy for him. It was many years ago that I did hit on the right family, *Anacardiaeceae*, but not the right remedy. It is embarrassing to admit my longstanding failure in Joe's case, but, fortunately, it turned out, eventually, quite well.

Right Family, Wrong Miasm

Joe: I never measured up to what my mother wanted me to be. Even she couldn't say anything nice about me. I don't feel the worst I ever have felt. But I isolate myself and think there's something wrong with me. That nobody likes me. I'm disgusted about my weight. I get occasional episodes of diarrhea. I overwork. Long hours. I feel like a martyr, but I rarely show my anger. Just to myself.

Joe was extremely hard on himself. All of his anger was turned inward rather than to his family or to anyone else. The *Anacardium*, from the cashew family, covered Joe's self-hatred, his extreme demand on himself in all situations (cancer miasm), his joint symptoms for which he received chiropractic care, and the periodic bouts of diarrhea. The remedy helped a great deal, helping to improve Joe's spirits even dramatically at times. But there remained a tremendous self-reproach, even self-hatred that bubbled up often, to the point of his screaming at himself, either internally or aloud. Despite the *Anacardium*, this came whenever stress was intensified.

Joe was doing "well enough" and continue to have tremendous trust in me to help him. It was six years ago when it dawned on me that the *Anacardium* had been helping, but that Joe was clearly leprosy miasm, not cancer miasm. From the beginning of his life he had felt discarded, disgusting, like an outcast. Although I knew nothing about the remedy, I prescribed *Comocladia dentata*, a member of the *Anacardiaceae* family but belonging to the leprosy miasm.

According to Rajan's volume on plants, this remedy covers leprosy. Mental rubrics include "indifference, apathy to ordinary matters, malicious" (with Joe, the malice was self-directed). And from a 2001 Indian proving of the remedy:

> Tremendous sadness. She felt stuck, at a standstill, not progressing, not reaching anywhere, not going ahead… unable to think about the future, to see a ray of hope ahead. She felt like a failure… lost interest in life. Wanted to give up altogether. Indifference, total depression. She felt like nothing would change. She did not feel like talking with anyone, would avoid people.

The summary of the feeling in the proving (which has an Indian societal overlay, but still applies in Joe's case): "People from lower castes are stuck. They have to struggle a lot, but there is no progress. Other people may at least have relatives who are financially well off, but with lower castes, the cycle continues… there is no going ahead, no progress."

Joe's Long-Term Response to *Comocladia*

As I typically find, to my great relief, after landing upon the simillimum remedy, Joe has done quite well for the past six years. I continue to have appointments with him every six weeks, since I am an important member of his support network. He has some relationship now with a sibling, still has a few close, long-term friends, and feels considerably more positive about himself and his life. He still has intermittent periods of anger directed towards himself, but to a much lesser extent than previously. Some excerpts from his follow-up visits over the past six years post-*Comocladia*:

> I'm doing much better with sugar and chocolate. I'm walking every day. I've lost a lot of weight… I haven't needed to take the backup remedy that I am holding… I have actually been having periods of elation and joy since my job is ending. Better than feeling crabby and alienating everyone like I've felt sometimes in the past.

He has been able to decrease his chocolate consumption much of the time, though he still has some temporary setbacks. Joe is generally more positive and less self-deprecating and maintains a better outlook on life. Now that he has retired, he is spending more time with close friends and has been able to enjoy some traveling. Retirement has brought tremendous relief, though he still has to manage his money carefully. Over the past six years, he has taken three doses of *Comocladia* 200C, six doses of 1M, and four doses of 10M. We continue to have regular appointments, and he considers me an important support in his life. Joe is much happier, treats himself much better, eats chocolate periodically, and his physical symptoms are quite manageable. I sincerely wish I had known enough to find his simillimum earlier, but I am grateful that I have done so. Better late than never. Never underestimate the impact of miasms. Dr. Hahnemann was no fool!

Judyth Reichenberg -Ullman and Robert Ullman are licensed naturopathic physicians, board certified in homeopathy. We have written eight books on homeopathy as well as *Mystics, Masters, Saints and Sages – Stories of Enlightenment*. We also have an app: Natural Travel Doctor. Apple version: https://tinyurl.com/l7song8 and Android: https://tinyurl.com/m7cnexh**.** We are more passionate than ever about homeopathy and we never seem to tire of traveling.

We practice in Edmonds, Washington, and by Skype and Zoom and are happy to accept new patients. The Edmonds office address has changed, as you will see on our website. We live on Whidbey Island, Washington, and in Pucón, Chile. Visit our website www.healthyhomeopathy.com. Please friend us on Facebook at Healthy Homeopathy. Call us at 425-774-5599 or email us at drreichenberg@gmail.com or drbobullman@gmail.com.

◆

Ask Dr. J

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

To B or Not To B

William Shakespeare had a great existential question in *Hamlet*, which I want to modify for use in functional medicine genetics. Do we want two of our more important B vitamins, folate and B12, to be expressed in forms that contribute to health and well-being or not? This is my question.

Within the nuclei of our trillions of cells lies a genetic roadmap. If we utilize that roadmap intelligently, we can express genes that contribute to longevity and functionality in our bodies. Not using our reading glasses with this genetic road map can lead to chronic disease and mediocrity within the various cells and organs of our body. Nutrigenomics determines how diet affects the expression of genes. Nutrigenetics establishes how genes affect dietary needs and responses. I will be expanding on the latter in this article.

A single-nucleotide polymorphism, abbreviated as SNP, is the most common type of genetic variation among people. Each SNP represents a difference in a single DNA building block, called a nucleotide, and occurs at a specific position on a chromosome. The genetic code of a chromosome is represented in its base sequence. There are four bases present in DNA. They are adenine (A), guanine (G), cytosine (C), and thymine (T). For example, a nucleotide may contain cytosine in most individuals; but in some distinct number of individuals, the position may have changed to adenine. This means that a SNP has occurred at this specific condition and now there are two possible nucleotide variations, C or A for this position. The C and A are defined as different alleles.[1]

SNPs occur in everyone's DNA, at approximately every 300 nucleotides on average. Some, not all, can affect a gene's function, which can affect health or development. Some SNPs developed in response to environmental pressures, such as the sickle cell hemoglobin in response to malaria. Other SNPs can be utilized to predict how each person will react to certain drugs, their susceptibility to various environmental chemicals, how to optimize common biochemical reactions in their cells, which type of food is optimal for them, and their risk of developing particular diseases.[2]

For me professionally, I am particularly interested in identifying SNPs for common biochemical pathways in our cells and how to optimize these pathways for maximal performance in digestion, cognition, and detoxification. Identifying these SNPs can direct a person on how to correctly choose food for their unique constitution, exercise in a way that doesn't harm their body, and customize supplementation without the usual trial and error period. No more saying "I feel like this could be the best food/supplement/mode of exercise for you"; your specific genetic profile points us to these very precise recommendations.

One key here is to focus on SNPs that are clinically relevant for us and our patients. Knowing this genomic information leads us to some valuable benefits. First is to help reduce trial and error. Much of the clinical guesswork can be removed by studying a person's genomic package. Next, you can also explain how a treatment regimen from another practitioner was unsuccessful, which has the added benefit of making you look smart. This should also maximize patient compliance, which is one of the biggest road blocks in successful resolution of a patient's complaint. They see in black and white and beautiful colors in a "scientific" report what will work for them. Finally, the genomic report can justify costs of monitoring the patient further and why they might need higher doses and/or long-term supplementation.

An example of this would be a patient who comes to you and says they are taking cod liver oil every day and knows that their vitamin D levels are just perfect. Their genomics report on the other hand shows that they are homozygous GG for their vitamin D binding protein, which means they are almost 50% more likely to have vitamin D at a level of < 20 mg/ml and have a compromised benefit of sunlight in northern latitudes. (They also happen to live in Boston.) Now they are much more likely to allow you to run a serum vitamin D and find out if their daily cod liver oil is going to be sufficient to optimize their vitamin D levels or maybe they will require extra supplementation.[3,4]

The mechanism of cellular action of various SNPs is quite variable. They can cause the enzyme produced to be less stable as can occur with COMT or catechol O-methyl transferase. The SNP may also increase/decrease the enzyme's activity in managing its cellular activity as happens

with CBS (cystathionine beta-synthase). In addition, it can reduce nutrient transport into a cell as happens with TCN (transcobalamin carrier protein), which decreases vitamin B12 entry into the cell. Finally, it may alter the location of a protein within a cell as occurs with SOD (superoxide dismutase).[5]

Now there exist multiple companies presently performing genetic testing. Who to use or recommend is also a huge question plus the testing can be prohibitively expensive. I happened to be intrigued by what is called PureGenomics (www.puregenomics.com) at the Pure Encapsulation booth during the Institute of Functional Medicine's annual bash in Hollywood, Florida, this year. I was intrigued because they analyze your 23 & Me or Ancestry information for free! You input the information to their website, and they magically transform that information in what seems like a matter of seconds into these categories: Methylation SNPs, Vitamin and Mineral SNPs, Detoxification SNPs, Weight Management SNPs, Glucose Homeostasis SNPs, Immune SNPs, and Cognitive Health and Memory SNPs. Nothing is free so what is the catch? I happened to be at their booth at the same time as a very smart ophthalmologist from Florida, Shalesh Kaushal. He laughed and said the tests are like turkeys at Thanksgiving: loss leaders. Pure Encapsulation is giving you extremely valuable and clinically useful genomic information for free, but they then recommend one of their products that will help where you have SNPs that can be problematic.

First, I like anything that is free, especially if it is clinically useful. Second, I feel the five categories above are important pieces of the clinical puzzle I am trying to solve for each of my patients. I uploaded my information and received a well-organized and, particularly important for me as I'm a visual learner, visually stunning download. Attempting to translate all the information into a clinically useful dialogue appeared a little daunting. Fortunately, Pure Encapsulations is thinking ahead. They are offering one-day training seminars. I attended the one in Seattle on September 22, 2018, entitled "Nutritional Genomics: The Future Is Now."

At the seminar, we discussed the various SNPs in the five categories above. There are many SNPs that you can incorporate into your practice the next week. One that caught my eye was in the weight management section. The gene is titled APOA2. It regulates postprandial response to a saturated fat overload in the meal. There are two alleles, C and T. If you have the CC variant and consume greater than 22 grams of saturated fat/day, you will have a mean increase in BMI/body mass index of 6.2% and thus higher obesity. You also will have a higher rate of ghrelin release, which will lead to increased appetite and more calories being consumed. Finally, you will be more efficient at absorbing fat in your small intestine. This fact can definitely explain some people's weight gain with fatty foods and point us in a dietary direction that will maximize their weight loss.[6]

Another was TPH2 (tryptophan hydroxylase 2). This gene produces an enzyme that catalyzes the conversion of L-tryptophan to 5-HTP. There are two alleles, T and G. If you have the TT variant, this genotype is associated with reduced enzyme activity. These people would not benefit from taking L-tryptophan for their depression; 5-HTP, since it is downstream from the enzyme, would be a much better choice.[7] My wife has this SNP, and 5-HTP is helping her sleep better in her post-menopausal, funky sleeping pattern!

I could go on ad nauseam, but I'll stop here and let you contact Pure Encapsulations and set up an account and see your genetic profile. The chief medical officer, Nathan Morris, MD, was an excellent presenter. He also gave us the four common mistakes that practitioners make when educating themselves on genomics which I found quite useful:

- Assumption that the SNP matters in clinical practice,
- Questionable sources of information,
- Assumption that addition of a new test in a practice will add complexity to the practice,
- Assumption that the learning part is time-consuming and complicated.[5]

Dr. Morris also didn't shuck and jive us like many presenters do at conventions where their supplement or realm of expertise is the best and never fails and every clinical example they give is a 100% success story. He related that genomics is just part of a complex puzzle that is each and every patient. Looking at their genetic profile will allow clinical doors to open and can lead us in directions that will help us to customize clinical recommendations for each patient. This will then allow for much more successful treatment regimens and for patients who feel better and are more satisfied. Sounds great to me!

Finally, Dr. Morris made a statement that I embraced 40-plus years ago, and I wish most people would also: food/supplements/herbs are like a retirement plan. You mostly don't immediately feel the beneficial effects of supplements/herbs/good food. Thus, there aren't feelings of health generated daily through supplementation and the consumption of good food. Forty years later that daily, rigorous regimen you followed will pay its benefits just like a retirement plan. All of a sudden you won't look or feel like most people. Then you'll really be able to smile, internally and externally.

Thanks to Victoria Coleman, DC, for the title to my column. I was originally going to use "To Be Or Not To Be," but she suggested I use just B as a metaphor for the B vitamins.

References

1. https://en.wikipedia.org/wiki/Single-nucleotide_polymorphism
2. What are single nucleotide polymorphisms (SNPs)? https://ghr.nlm.nih.gov/primer/genomicresearch/snp
3. Signorello LB, et al. Common variation in vitamin D pathway genes predicts circulating 25-hydroxyvitamin D Levels among African Americans. *PLos One.* 2011;6(12): e28623.
4. Wang T, et al. Common genetic determinants of vitamin D insufficiency: a genome-wide association study. *Lancet.* July 17, 2010; 376(9736):180-8.
5. Notes from Nathan Morris presentation at seminar, "Nutritional Genomics: The Future Is Now," September 22, 2018.
6. Notes from Penny Kendall-Reed, ND, presentation at seminar "Nutritional Genomics: The Future Is Now," September 22, 2018.

◆

Please Support the Advertisers in this Issue

Classified Ads

Calendar

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

JANUARY 9-13, 2019: 16th ANNUAL NATURAL SUPPLEMENTS: AN EVIDENCE-BASED UPDATE in San Diego, California. CEs available. CONTACT: http://www.scripps.org/naturalsupplements

JANUARY 24-27: HAWAII DOC TALKS 2019 in Kona Beach, Hawaii. CEs available. CONTACT: https://www.events.syncopatemeetings.com/hawaii-doc-talks/

JANUARY 25: RUBIMED THERAPIST TRAINING LEVEL 1 in Toronto, Ontario. Also, **APRIL** in Los Angeles, California. CONTACT: https://biomedicine.com/education/all-event-listings

JANUARY 25-FEBRUARY 8: INTENSIVE CLINICAL TRAINING in India. 200+ live cases demonstrated to show homeopathy in gross pathologies. CONTACT: http://www.homeopathy-course.com/index.php/training-courses/india-homoeopathy-training/2-week-clinical-training-in-calcutta

JANUARY 26-27: RUBIMED THERAPIST TRAINING LEVEL 2 in Toronto, Ontario. Also, **APRIL** in Los Angeles, California. CONTACT: https://biomedicine.com/education/all-event-listings

FEBRUARY 1-3: 16th INTERNATIONAL ISLA CONFERENCE FOR MEDICAL LASER APPLICATIONS AND REGENERATIVE MEDICINE in San Diego, California. CONTACT: 954-540-1896; http://www.islalaser-us.com; sharon@islalaser-us.com

FEBRUARY 8-9: CONTROVERSIES IN INTEGRATIVE THERAPIES in Costa Mesa, California. CEs applied for NDs. CONTACT: http://www.events.syncopatemeetings.com/cit/

FEBRUARY 8-10: GREAT PLAINS LABORATORY ACADEMY PRACTITIONER WORKSHOPS – Organic Acids Testing & Environmental Toxins Testing in St. Petersburg, Florida. Also, **FEBRUARY 22-24** in Scottsdale, Arizona; **APRIL 26-27** in San Francisco, California. CONTACT: http://www.GPLWorkshops.com

FEBRUARY 15-17: 8th ANNUAL OncANP NATUROPATHIC ONCOLOGY CONFERENCE in San Diego, California. CONTACT: https://oncanp.org/conferences/

FEBRUARY 15-17: FLORIDA HOMEOPATHIC SOCIETY 2019 ANNUAL CONFERENCE – Homeopathy for Women's Health with Gabrielle Traub in Orlando, Florida. CONTACT: cicamp7@gmail.com; http://www.floridahomeopathicsociety.org/

MARCH 1-3: CALIFORNIA NATUROPATHIC DOCTORS ASSOCIATION 21ST MERGING MEDICINE CONFERENCE – Autoimmunity in Palm Springs, California. CONTACT: https://www.calnd.org/ce-events

MARCH 7-9: THE FORUM FOR INTEGRATIVE MEDICINE "Exploring Practical Solutions for Complex Conditions" in Seattle, Washington. CONTACT: https://forumforintegrativemedicine.org/

APRIL 12-14: ENVIRONMENTAL HEALTH SYMPOSIUM (EHS) – Endocrine Disruption: The Solution in Scottsdale, Arizona. Endocrine disruption correlation to chronic disease and solutions. CMEs available. CONTACT: 855-347-477; http://environmentalhealthsymposium.com

APRIL 22-23: TRADITIONAL MEDICINE 2019 – Exploring New Horizons in Traditional & Alternative Medicine in Rome, Italy. CONTACT: https://www.meetingsint.com/conferences/traditional-medicine

APRIL 26-27: THE GREAT PLAINS LABORATORY, INC. presents GPL ACADEMY PRACTITIONER WORKSHOPS in San Francisco, California. Organic acids testing, toxic chemical testing, and mycotoxin testing, among others. CONTACT: http://www.GPLWorkshops.com

MAY 3-5: KLINGHARDT BRAIN MASTERS – Science and Solutions in Morristown, New Jersey. Neuro Lyme, Autism, MS, ALS, Parkinson's, Retrovirus with Dr. Judy Mikovits, Boyd Haley PhD, Dietrich Klinghardt, MD, PhD. CONTACT: 908-414-0769; info@klinghardtacademy.com; www.klinghardtacademy.com

JUNE 7-9: LDN 2019 CONFERENCE in Portland, Oregon. CONTACT: https://www.ldnresearchtrust.org/conference-2019

JUNE 7-9: COLLEGE OF NATUROPATHIC DOCTORS OF SASKATCHEWAN HEALING SKIES CONFERENCE in Saskatoon, Saskatchewan, Canada. CONTACT: http://sanp.ca/healing-skies-conference.html

JUNE 14-16: 4th HRI INTERNATIONAL HOMEOPATHY RESEARCH CONFERENCE in London, United Kingdom. CONTACT: https://www.hrilondon2019.org/

JUNE 21-22: THE GREAT PLAINS LABORATORY, INC. presents GPL ACADEMY PRACTITIONER WORKSHOPS in Minneapolis, Minnesota. Organic acids testing, toxic chemical testing, and mycotoxin testing, among others. CONTACT: http://www.GPLWorkshops.com

JUNE 22-29: ALLEN COLLEGE OF HOMOEOPATHY SUMMER SCHOOL in Chelmsford, Essex, United Kingdom and online. CONTACT: https://homoeopathy-course.com/images/pdf/reasons-to-join-summerschool.pdf

JUNE 28-30: 14th ANNUAL JOINT HOMEOPATHIC CONFERENCE – Homeopathy and Brain Health in Baltimore, Maryland. CONTACT: https://www.homeopathycenter.org/2019-joint-american-homeopathic-conference

AUGUST 15-17: AMERICAN ASSOCIATION OF NATUROPATHIC PHYSICIANS 2019 ANNUAL CONVENTION in Portland, Oregon. CONTACT: https://www.naturopathic.org/

SEPTEMBER 20-29: KLINGHARDT IMMERSION WEEK - Injection Techniques, Neural Therapy, and Autonomic Response Testing Workshops in Kenmore, Washington. CONTACT: 908-414-0769; info@klinghardtacademy.com; www.klinghardtacademy.com ◆

Women's Health Update

by Tori Hudson, ND
womanstime@aol.com

Safety Issues of Hormone Therapy in Transgender Patients

Many transgender individuals desire hormone treatment; estrogen for male-to-female (MTF) and testosterone for female-to-male (FTM) individuals. The purpose is to accomplish the physical characteristics of their desired gender identity. A total of 2842 MTF adults were followed for an average of four years and 2118 FTM adults for an average of 3.6 years. Each transgender individual was matched to data for 10 cisgender men and 10 cisgender women.

The greatest concern was a significantly higher incidence of venous thromboembolism (VTE) in all the MTF individuals when compared to the cisgender men and cisgender women. All rates of ischemic strokes and myocardial infarction were similar in the MTF individuals and the comparison groups. In MTF individuals who initiated estrogen therapy, the significant increases of VTE started at year 2 whereas ischemic stroke risk started at year 6. The hormone regimen most commonly prescribed to MTF individuals was oral estrogen, and an average dose of 4 mg/day.

Commentary: It is not surprising that oral estrogen elevates the risk of VTE in MTF individuals, because that is true in postmenopausal women who take oral estrogen and is also true of oral contraceptives in reproductive aged women. The average dose of oral estrogen in menopause management is 1 mg/day, so the average dose of oral estrogen for MTF individuals is four times higher. If transdermal estrogen were used more in MTF individuals, the risk would likely be less, as it is in menopausal management, although the doses again, would be different.

Getahun D, et al. Cross-sex hormones and acute cardiovascular events in transgender persons: A cohort study. *Ann Intern Med*. July 10, 2018; e-pub.

Myo-Inositol Plus Selenium Reverses Thyroid Antibodies in Those with Subclinical Hypothyroidism

Chronic autoimmune hypothyroidism is one of the most common autoimmune diseases affecting more than 10% of women and 2% of men. It primarily affects those who are 30-50 years old. An elevated thyroid stimulating hormone (TSH) and autoantibodies such as anti-thyroglublin (TgAb) and anti-thyroid peroxidase (TPOAb) are the typical features of this condition. Most hypothyroid disease is an autoimmune process, Hashimoto's being the most prevalent. A mild hypothyroid condition is called subclinical hypothyroidism with a TSH between 3-6 IU/ml. The American Thyroid Association's guidelines have a TSH upper limit of 4.12. Some professionals have proposed the TSH should be no higher than 2.5 or 3.0, while others are even steering more towards 1.5-2.0.

In the current study, a total of 168 patients with Hashimoto's hypothyroidism with TSH levels between 3 and 6 IU/ml were randomized into two groups: one received Myo-inositol 600 mg daily plus 83 mcg of selenium (75 women and 9 men); the other group received just the 83 mcg selenium per day (74 women and 10 men). This was done for six months.

TSH, TPOAb and TgAb levels were significantly decreased in patients treated with the combined myo-inositol/selenium after six months. There was also a significant increase in free thyroxine (free T4) in the combination supplement group, as well as an improvement in quality of life and subjective symptomatology. The increase in thyroid hormones concentration was observed in both treatment groups, but it was significantly higher in those receiving the combination.

Commentary: The take home in this study is that these doses of myo-inositol plus selenium can improve TSH levels, reduce thyroid antibody levels, and improve subjective symptoms in women and men who have subclinical (a TSH of 3-6) Hashimoto's thyroid disease. This is great news for those individuals for whom their doctor will not prescribe thyroid hormones because their TSH is normal or normal enough, but yet have symptoms without other explanations, including fatigue, muscle weakness and mood related issues. TSH is a very sensitive marker of thyroid function, more so than thyroid hormone levels such as free T3 and free T4. This is especially

➤

➤

true in individuals with subclinical cases. When the TSO is above 10, thyroid hormone prescriptions are a well proven treatment. Of the many mechanisms of myoinositol in thyroid function, it is involved in one of the first steps of thyroid hormone production. Previous trials have reported reduction of TPOAb with selenium after six months and we know that selenium deficiency leads to glutathione peroxidase inactivity, which may induce oxidative harm for thyroid cells leading to thyroid damage and fibrosis.

Basciani N. Myo-inositol plus selenium supplementation restores euthyroid state in Hashimoto's patients with subclinical hypothyroidism. *European Review for Medical and Pharmacological Sciences*. 2017;21(2):51-59.

Cost Effectiveness of Emergency Contraceptions

The average cost of emergency contraception options are varied including $29.00 for oral levonorgestrel; $43.00 for ulipristal acetate; and upwards of $887.00 for a copper intrauterine device (IUD) and $917.00 for the oral levonorgesterol for immediate need and then with the addition of the levonorgestrel IUD placement. The advantage of the IUD approach, while it might appear obvious, is that women who use one of the two oral medications are more likely to become pregnant during the following year than those who receive the IUD. When looking at cost effectiveness issues, this year of increased health care costs is part of the calculation. When factoring this in, and reduced pregnancy rates during the year following emergency contraception use, both the copper IUD and the combination of oral levonorgestrel plus the immediate levonorgestrel IUD is more cost effective than either of the two oral medications. The copper IUD was the most cost effective unless a clinic has access to special pricing for the levonorgestrel IUD ($50.00) in which case the combination of the oral levonorgestrel and the immediate levonorgestrel IUD placement was the most cost effective.

Commentary: There are multiple options for emergency contraception, but it is important to weigh the short-term and long-term costs, especially if working in a clinic where these services are a significant part of the patient care population. Surprisingly, it turns out that the two options involving IUDs are the most cost effective over a 12-month period because it results in fewer unintended pregnancies.

Bellow B, et al. Cost-effectiveness of emergency contraception options over 1 year. *Am J Obstet Gynecol*. May 2018; 218:508.

◆

It Doesn't Always Have to Be Complicated

With the many advances in both conventional and integrative medicine, we have a wide range of options available for assessing and treating our patients. In some cases, particularly in those who are chronically ill and have complex problems, a comprehensive laboratory analysis might help identify treatable conditions that would not otherwise be suspected, and a comprehensive treatment program might be more successful than a simpler intervention. It is important to remember, however, that not all cases are complicated. In many instances simple, low-cost, low-tech, low-risk interventions can be quite successful. Following are a few examples.

Nature Will Castigate Those Who Don't Masticate

A 26-year-old male had a long history of heartburn. A gastroenterologist had performed an upper GI endoscopy and diagnosed gastroesophageal reflux disease. Treatment with proton pump inhibitors and other medications had provided only partial relief. When the young man consulted me, questioning revealed that he ate his food extremely rapidly. He was advised to chew each mouthful thoroughly, and this change alone resulted in an 80% improvement in his symptoms. Subsequently he removed most of the "junk food" from his diet and became symptom-free.

Temporomandibular Joint (TMJ) Syndrome

Temporomandibular joint (TMJ) syndrome is a common disorder of the joint that connects the mandible (jawbone) to the temporal bone of the skull. Symptoms may include pain or aching of the jaw or surrounding muscles; difficulty chewing; locking of the jaw; and a popping, clicking, or grating when the mouth is opened or closed. The cause of TMJ syndrome is multifactorial and may include chronic teeth grinding, trauma to the area, arthritis in the joint, or displacement of the articular disc that is present between the mandible and the temporal bone. Treatment may include anti-inflammatory medications, analgesics, muscle relaxants, mouth guards, and physical therapy. In severe cases, surgery may be recommended.

A few years ago, I took my 11-year-old daughter to a chiropractor for various minor musculoskeletal problems. During the visit, I mentioned that she had been experiencing uncomfortable clicking and popping sensations on both side of her jaw for about three months, along with a feeling that her jaw was out of alignment. I was not aware that there was a chiropractic treatment for TMJ disorders. The chiropractor examined the area and then used an "activator" to deliver a gentle force directly over each of the TMJ discs. This maneuver resulted in immediate and complete resolution of the symptoms. My daughter has had to return a few times over the ensuing three years, but each time the benefits of the adjustment lasted at least six months.

The chiropractor told me he has seen about 50 TMJ patients (mostly acute cases) over an 18-year period, and about 80% of them experienced very good results. Another chiropractor I have spoken to reports similar results. Presumably, patients with more advanced disease, significant arthritis, or various other predictors of a poor outcome would be less likely to respond to this type of TMJ adjustment. However, more widespread use of this intervention (particularly in early cases) would likely decrease the need for high-cost, invasive procedures.

➤

Editorial

➤

A Case of Chronic Fatigue

A woman in her 30s had a chief complaint of longstanding fatigue. She had previously seen another "alternative" doctor, who told her she had an increased body burden of heavy metals, as demonstrated by a 24-hour urine collection following an EDTA challenge. She underwent 15 sessions of EDTA chelation therapy, which cost a lot of money and appeared to make her fatigue worse.

Questioning at my office revealed that the fatigue was better when she did not eat and was often worse after eating. That observation, as well as some aspects of her past medical history, suggested the possibility of hidden food allergy. Her fatigue disappeared on an elimination diet and recurred when she reintroduced soy, which had been a regular part of her diet. She remained symptom-free as long as she avoided soy-containing foods.

Anxiety in an Elderly Woman

A 77-year-old woman had a six-month history of persistent anxiety. She had tried several anxiolytic drugs, which were not well tolerated and not particularly effective. When she consulted me, I ascertained that her symptoms had begun about a month after she started treatment with a thiazide diuretic for hypertension. Thiazide diuretics are known to deplete magnesium, and magnesium deficiency is, in my experience, a common cause of anxiety. She was advised to take 400 mg per day of supplemental magnesium. Symptomatic improvement was noticeable within a couple of days, and the anxiety was markedly better within two weeks.

Conclusion

These case reports are presented to remind us that the practice of medicine does not always have to be complicated, and that simple and straightforward solutions to problems are often available. A famous medical philosopher (whose name escapes me) once said that, all else being equal, we should try the least heroic interventions first.

Alan R. Gaby, MD

Monthly Miracles

by Michael Gerber, MD, HMD
Practitioner of Homeopathic Medicine
contact@gerbermedical.com

16th International Integrative Oncology Conference – "Cancer, Cannabis & Keto," Day 3

Annie Brandt, founder of the International Organization of Integrative Cancer Physicians (IOICP), the Best Answer for Cancer Foundation, and 18-year survivor of breast cancer, brought a great selection of speakers and exhibitors for her 16th annual conference in Orlando, Florida, on May 17-19, 2018. A summary of Day 1 appeared in the August-September 2018 issue and Day 2 appeared in December 2018. This article covers Day 3.

Care and Feeding of Mitochondria

Dr. Nalini Chilkov, LAc, OMD, the founder of the American Institute of Integrative Oncology and author of *32 Ways to Outsmart Cancer: How to Create a Body Where Cancer Cannot Thrive,* instructs us that there is more to mitochondrial function and cancer than the Warburg Effect and the shift from oxidative phosphorylation to aerobic glycolysis. Mitochondria are crucial cell monitoring sentinels governing cell death through autophagy, mitophagy, and apoptosis.

The overexpression of the Bcl-gene is associated with cancer cell survival and inhibition of apoptosis. The pro-apoptotic Bcl-2 family members Bax and Bak are recruited to mediate mitochondrial outer membrane permeabilization (MOMP), resulting in pore formation and cytochrome c release from mitochondria into the cytosol to activate caspases, the executors of programmed cell death. Tumor cells escape apoptosis by downregulating pro-apoptotic Bcl-2 genes and/or upregulating anti-apoptotic Bcl-2 genes.

Phytochemicals in food and spices that promote normal apoptosis by inhibition of Bcl-2 include the following: allicillin, apigenin, carnosol, sulforaphanes, I3C, curcumin, gingerol, chrysin, EGCG, resveratrol, pterostilbene, quercetin, genistein, capsaicin and gallic acid. These compounds are found in garlic, parsley, celery, broccoli, kale, turmeric, ginger, rosemary, oregano, cayenne, grapes, red onions, red apples, pomegranate, red berries, blackberries, blueberries, green tea, soybeans, Botanicals that promote normal apoptosis by inhibition of Bcl-2 include the following: *Curcuma longa*, *Panax ginseng*, *Polygonum cuspidatum*, *Rabdosia rubescens*, *Camelia sinensis*, Magnolia cortex, *Andrographis paniculata*, *Taxus brevifolia*, *Scutellaria baicensis*, *Salvia miltiorrhiza*, Dioscorea spp, *Ganoderma lucidum*, *Pleurotus pulmonarius*, *Inonotus obliquus*, *Rosmarinus officinalis*, *Tanacetum parthenium*, Tababueia spp, Zingiber off., *Withania somnifera*, *Berberis vulgaris*, *Coptis chinensis*, and *Viscum album*.

Nutraceutical supplements that promote normal apoptosis by inhibition of Bcl-2 include the following: curcumin, EGCG, resveratrol, pterostilbene, Honokiol, indole-3-carbinol, quercetin, berberine, Tanshinone, reishi mushroom, chaga mushroom, and chrysin, all in 500-1000 mg tid dosing.

Tumor suppressor gene p53, guardian of the genome, induces apoptosis in response to stress. Upon activation, p53 leads to cell-cycle arrest and promotes DNA repair or induces apoptosis. Loss of wild-type p53 function is often associated with aggressive tumor growth, poor prognosis, and resistance to chemotherapy. Restoration of p53 function in mice suffering from lymphomas or sarcomas has been shown to induce tumor regression.

More than 50 percent of human tumors contain a mutation or deletion of the p53 gene. Natural compounds that normalize p53 function are very similar to the Bcl-2 herbs and include 5-methyl-tetrahydrofolate, tocotrienols and vitamin E succinate.

Hexokinase II derived cell penetrating peptide targets mitochondria and triggers apoptosis in cancer cells. Curcumin inhibits aerobic glycolysis and induces mitochondrial-mediated apoptosis through hexokinase II in human colorectal cancer cells in vitro. Resveratrol also induced apoptosis and inhibited tumor growth in mice.

MicroRNA (miRNA) are a class of single-stranded non-coding RNA molecules, approximately 22 nucleotides that play crucial roles in gene expression. The same phytochemicals upregulate these miRNAs, which help regulate apoptosis in cancer cells.

Dr. Chikov's presentation was heavily documented and is available from her study guide, lecture summary notes and lecture slides. Download at www.aiiore.com/ioicp2018. Email: drchilkov@aiiore.com.

Creating Genomic Stability in Patients with Cancer by Disabling ENOX2 Proteins and Restoring Microbiota Balance

Mitchell J. Ghen, DO, PhD, discussed the ENOX family of cell surface proteins, which is very complex and has far reaching influences upon certain areas of plant and animal biochemistry. These include being responsible for setting the length of periods of activity and inactivity within cells in the body, acting as an internal biological clock. Over 250 peer-reviewed papers have been published on the ENOX proteins. (Morré &Morré (2013) *ECTO-NOX Proteins: Growth, Cancer, and Aging*).

➤

➤

Why ENOX2? Research has detected ENOX2 proteins four to ten years before development of clinical symptoms. It is cancer specific, elevated early, and useful for screening early intervention. (Morré et al. (2016) *Clin. Proteom*. 13:2). ENOX2 comes from thiol interchange/cell enlargement in cancer cell membranes to promote unregulated growth. EGCg is a polyphenol that binds to ENOX2 receptor sites, disables them, and is synergistic with the vanilloid component of a specific chili pepper. Ghen gives a summary of outpatient infusion protocol for Capsol-T/ElimENOX2.

Dr. Ghen also reviewed the role of bacteria causing toxic carcinogenic metabolites, increased inflammation, antigen driven lymphoproliferation, and induction of hormones that increase epithelial proliferation. Microbial waste products and mycotoxins weaken the immune system and are causative in prostate cancer, chronic prostatitis, cervical cancer-chlamydia, (HPV), PAL (pyothorax associated lymphoma), Hodgkin's B cell lymphoma, leukemia, and MALT lymphomas. EBV is found in 70-85% of the PAL tumors in Asia. Ghen lists over 300 pathogens capable of enhancing or relating to oncogenesis, including *H. pylori, Chlamydophilia psittaci*, *Borrelia burgdorferi*, and mycoplasma.

Treatment with silver hydrosol products has two key advantages: they are broad-spectrum antibiotics and are not yet associated with drug resistance. (Lansdown AB, "Silver. I: Its Antibacterial Properties and Mechanism of Action." *J Wound Care*. 2002 Apr 11:125-30) Size makes a difference; at 23 parts per million (ppm), there may be over 300,000,000 particles of active silver in every drop of pharmaceutical-grade silver. Silver improves or stimulates the rate of bone marrow WBC production. Indirect mechanisms of action include an increased production of reactive oxygen species, and it induces or catalyzes increased WBC production of myeloperoxidase. Silver has an excellent safety record in these nanosized particles.

Without removal of microbes, the cancer can return. He emphasizes no raw meat, no sushi and reduce sugar. Microbe-killing foods and spices include onion, garlic, allspice, oregano, thyme, tarragon, curcumin, clove, bay leaf, and cayenne pepper.

In summary, cancer treatment aims to block ENOX2 proteins, restore microbiome, decrease inflammation, decrease free radicals, increase nutrition, decrease blood viscosity, disrupt reproductive cycle, improve healthy stem cell function and immune response, and institute positive lifestyle changes.

Contact Mitchell Ghen, DO, PhD, in Boca Raton, Florida, Email: ghenm@mac.com.

The Unmet Need

Travis Christofferson has degrees in molecular biology, material engineering, and science. He is the author of the best-selling *Tripping Over the Truth: How the Metabolic Theory of Cancer is Overturning One of Medicine's Most Entrenched Paradigms*. He is the founder of the Foundation for Metabolic Cancer Therapies, and the CEO of Care Oncology USA. He spoke about off label uses for common drugs in cancer therapy

Christofferson commences with the quote from Lewis Cantley, the director of the Cancer Center at Weill Cornell Medicine: "Metformin may have already saved more people from cancer deaths than any drug in history." Nobel laureate James Watson (of DNA-structure fame), who takes metformin off-label for cancer prevention, once suggested that the drug appeared to be "our only real clue into the business" of fighting the disease.

Metformin may have broad utility in cancer treatment. Researchers at MD Anderson found that among 2,529 women with early-stage breast cancer, the pathological complete response rate after chemotherapy was higher by 24% in diabetic patients who had received metformin than in diabetic patients who had not received metformin (8%) and in nondiabetic patients (16%). In the second study, a group in Department of Gastrointestinal Medical Oncology found that among 255 diabetic patients, the risk of developing pancreatic cancer was 62% lower in those who received metformin than in those who did not. Studies at the University of Pennsylvania reported dramatic improvement in local recurrence in 16 lung cancer patients who received chemoradiation while taking metformin. A study followed 87,344 men diagnosed with prostate cancer between 2000 and 2008. The median overall survival for non-diabetic (not taking metformin), diabetics on metformin, and diabetics not on metformin was 7.1, 9.1, and 7.4 years, respectively. The study concluded that both overall survival and cancer-specific survival was significantly prolonged among the diabetics on metformin.

Statins have also been associated with cancer risk reductions. Several observational studies and meta-analyses have shown reduction in risk of multiple cancers with statin therapy. A recent Danish study showed a 15% reduction in all-cause and cancer specific mortality in statin users as compared to non-users. Improved survival with statin exposure was seen in 13/17 cancer subtypes, including the four most common cancers; lung, prostate, colorectal and breast.

Statins could reduce risk of breast cancer death by 38%, research shows. Overall statin use was associated with a 27% reduction in both cancer-specific and overall mortality. However, those who took the same drugs for more than four years did not appear to show the same protective association, with only a 16% reduction in cancer-specific death, or death from all other causes. A VA retrospective case-control study of 483,733 patients from 1998 to 2004 showed a reduction of lung cancer by 55%. Statins appear to be protective against the development of lung cancer.

Pravastatin seems to be more effective than Simvastatin on the growth of tumor cells from different organ sites. Pravastatin increased survival time in unresectable hepatocellular carcinoma. Median survival was 18 months in the pravastatin group versus 9 months in controls. (Kawata S. et al. *Br J Cancer.* 2001 Apr 6;84(7):886-91).

Statins (HMG-CoA reductase inhibitors) are well know cholesterol-depleting agents. It has been shown the statins may inhibit the cell cycle by influencing both expression and activity of proteins involved in cell-cycle progression such as cyclins and cyclin dependent kinases. By inhibition of the synthesis of cholesterol, statins may destabilize the cell membrane. The following study reviews several other proposed mechanisms for anti-cancer activity: Matusewicz, et al. The effect of statins on cancer cells – a review. *Tumor Biol*. 2015 Jul; 36 (7): 4889-904.

The combined metformin-statin program reduced hepatitis B risk for developing cancers nearly in half.

Targeting cancer stem cells with antibiotics is another new treatment modality. Antibiotics that target mitochondria effectively eradicate cancer stem cells across multiple tumor types, treating cancer like an infectious disease. New analysis shows that four to five different classes of FDA approved drugs can be used to eradicate cancer stem cells across 12 different cancer cell lines, including breast, DCIS, ovarian, prostate, lung, pancreatic, melanoma, and glioblastoma. These five classes of mitochondrially targeted antibiotics include the erythromycins, the tetracyclines, the glyclycyclines, as well as the anti-parasitic drug chloramphenicol. Data were presented for one antibiotic in each drug class: azithromycin, doxycycline, tigecycline, pyrvinium pamoate, as well as chloramphenicol. Mebendazole and a non-steroidal anti-inflammatory combined to reduce tumor initiation in a colon cancer preclinical model (Williamson T, et al. *Oncotarget*. 2016 Oct 18;7(42):68571-68584).

An oncology clinic from the UK developed COC Protocol™, using metformin, atorvastatin, doxycycline, and mebendazole. Using individualized doses of the above medications gave improved results in a METRICS trial on glioblastoma. Two-year overall survival was 55% in the standard of care + COC protocol™ versus a 28.7% survival in the standard of care alone group. Advantages to the proprietary off label protocol include the following: decades of clinical use establishing safety, targets ubiquitous metabolic dysregulation, provides critical need for adjunctive therapy, provides a treatment option when no other exists or has been exhausted and provides a treatment option to prevent recurrence.

"Even James Watson, one of the fathers of molecular biology, is convinced that targeting metabolism is a more promising avenue in current cancer research than gene centered approaches. At his office at the Cold Spring Harbor Laboratory in Long Island, Watson, 88, sat beneath one of the original sketches of the DNA molecule and told me that locating the genes that cause cancer has been 'remarkably unhelpful'. If he were going into cancer research today, Watson said, he would study biochemistry rather than molecular biology." (An Old Idea Revived: Starve Cancer to Death. *New York Times*, 2016)

Cannabinoids and Terpenoids

Dr. Steve Ottersberg is the founder of Green Lab Solutions Company (Durango, Colorado), operating as Colorado's 11th certified cannabis testing laboratory. He has a BS in biochemistry and an MS in biochemistry from Arizona State University and has an honorary ND from Southwest College of Naturopathic Medicine. He shared his knowledge of human genetic testing in medicine to an audience of physicians, expanding understanding of the biochemical connections between polymorphisms of key enzymes associated with multiple disease states.

Endocannabinoids are fatty acid esters that act upon cannabinoid receptors. Terpenes include isoprenes, monoterpenes and sesquiterpenes. All are parts of cannabis in varying strains.

Alpha-Pinene, found in cedarwood, pine, rosemary oil and *Boswellia serrata,* is anti-inflammatory, broncho-dilating, stimulating, antimicrobial, and nootropic. It is also found in cannabis.

Camphene is found in camphor, mothballs, *Zingiber officinale*, *Rosmarinus officinalis,* and *Salvia officinalis*. It is analgesic, anti-inflammatory, sedative and antimicrobial.

Beta-Pinene is found in pine, polish, wood and also in parsley and nutmeg. It is analgesic, anti-inflammatory, stimulating, and nootropic.

Beta-Myrcene, found in Balsamic, fruit, geranium herb, cardamom, *Piper nigrum*, and *Boswellia sacra*, is anti-nociceptive, anti-inflammatory, sedative, euphoric, and anti-mutagenic.

Delta-3-Carene is found in pine, *Piper nigrum*, *Thymus vulgaris*, and star anise. It is anti-inflammatory, sedative and nootropic.

D-Limonene is found in citrus, mint, *Vitex agnus-castus*, *Citrus limon*, and celery. It is anti-tumor, anti-inflammatory, a cannabinoid agonist, antidepressant, stimulant, calming agent, nootropic and euphoric.

Ottersberg made a big point that limonene, lemon peel in hot water, will counteract cannabis overdose!!!!

This reviewer has confirmed the efficacy of this treatment very recently in a patient who accidently overconsumed an edible cannabis product. He was quite focused, non-communicative, not moving, and apparently holding on to his consciousness.

After sipping lemon peel in hot water, he immediately started to come back into regular consciousness and was able to walk. A peppermint oil drop, which is a stimulant and demulcent, licked from the back of his hand, was also very helpful. His nausea was helped by applying pressure to the acupuncture point Pericardium 6, four fingerbreadths above the inner wrist creases. Bringing him back into his body was helped by apply acupressure to Liver 3, at the junction of the large toe and second toe joints bilaterally.

I have seen several cases of cannabis overdose and have employed Governor Vessel 26, one-third of the distance between the nose and the upper lip in the midline, if consciousness is deteriorating. An acupuncture needle insertion is ideal, but a ball point pen stimulating the point, a hat pin, a sharp finger nail, and on one occasion an umbrella from a tropical drink helped bring a patient back from waning consciousness. Death or debility from overdose is highly unlikely, but the experience of the event may be disconcerting.

D-Limonene and its metabolites, perillic acid, dihydroperillic acid, uroterpenol and limonene 1, 2-diol, may inhibit tumor growth via inhibition of p21-dependent signaling and apoptosis resulting from induction of the transforming growth factor beta-signaling pathway. D-limonene induces apoptosis via the mitochondrial death pathway and suppression of the PL3K/Akt pathway in human colon cancer cells. Animal studies show activity of D-limonene against pancreatic, stomach, colon, skin, and liver cancers. Ottersberg presented 22 citations to support these data.

Cancer incidence has been accelerated by post WWII hydrocarbon toxicity created by extensive use of chemicals in food sources, water, clothing, plastics, pesticides and heavy metals.

Fifteen more terpenoids were presented with therapeutic potentials similar to the above terpenoids in their effects.

In addition to terpenes, Ottersberg discussed cannabinoids. Cannabinoids, represented by Delta 9 Tetrahydrocannabinol are analgesic, anti-inflammatory, and antiemetic. Cannabidiol is anxiolytic, analgesic, antipsychotic, anti-inflammatory and antispasmodic. Cannabigerol is an appetite stimulant and neuroprotective. Delta9-Tetrahydrocannabinol decreases turnover of brain histamine. (Oishi R et al. *J Pharmacol Exp Ther*. 1985 Feb; 232(2):513-8.)

Ottersberg included a very large bibliography for his presentation.

Immunotherapy

Antonio Jimenez, MD, ND, CNC, Chief Medical Officer, Hope4Cancer Treatment Centers in Baja California, and Cancun, Mexico, spoke about what makes cancers difficult to treat with conventional therapies: tumor heterogeneity, genetic variability from tumor formation to metastasis, and the difficulty of targeting diverse metabolic pathways.

He utilizes therapies that target specific cancer-related molecular receptors/antigens, hormone therapies, signal transduction inhibitors, gene expression modulators, apoptosis inducers, angiogenesis inhibitors, monoclonal antibodies that deliver chemotherapy, cancer vaccines, gene therapy, and immunotherapies.

If the immune system has it all figured out, why do we get cancer? Cancer cells are survivors and masters at immune evasion and may not present recognizable antigens. Pluripotent cancer stem cells display virtually no antigens on their surfaces. Inflammation triggers the expression of protective antigens on cancer cells, e.g. PD-L1, that suppress T cell activity. Tumors subvert macrophages and other immune cells to create its own toxic, self-defense system in the tumor micro-environment.

There are several types of immunotherapy drugs that target cancer cells and tumors:

➤

➤

- Monoclonal antibodies are engineered to target specific antigens and may be used to deliver chemotherapies to targeted cancers cells. The first, Rituximab, was approved in 1997 and targets CD20 on malignant B lymphocytes.
- Cytokines are substances released by T cells to kill cancer cells. The first cytokine IFN-a was approved for the treatment of cancer in 1986.
- Autologous cell therapy/cancer vaccines are immature antigens presenting cells extracted from the body, which are engineered to contain a cancer-specific antigen and are reintroduced as a vaccine. The first vaccine: Sipuleucel-T was approved in 2010 for prostate cancer.
- Oncolytic virotherapies uses viruses to locate, infect, and kill cancer cells. The first genetically unmodified oncolytic virotherapy, Riga virus, was approved in 2004; Amgen's T-VEC was the first engineered oncolytic virotherapy.
- Immune checkpoint inhibitors (ICIs) are antibodies engineered to bind to ligands on cancer cells or block receptors on T cells that inhibit their ability to kill cancer cells. The first approvals: Ipilimumab (Yervoy), a CELA-4 inhibitor: Nivolumab (Opdivo), a PD1 inhibitor.
- Adoptive T cell transfer: TCR and Car T cell therapies are personalized therapies based on modifying T cells from the patient. They involve amplification of T cells in the laboratory. Pre-treatment of patients with chemotherapy to kill immune system cells and the transfer of the CAR/TCR containing T cells to the patient is the treatment paradigm.

Jimenez raises concerns surrounding effectiveness and safety of the new immunotherapies. Serious adverse events are common and include autoimmune and inflammatory reactions, endocrinopathies, dermatitis, colitis, hepatitis, immune evasion and resistance. Currently, about 70% of patients cannot be prescribed immunotherapies at all. Hyperactivation of T cells cause unexpected organ damage, severe neurotoxicity, lowered blood pressure, and patient death from treatments. Cytokine storms from overactivation of T cells cause labored breathing, rapid pulse, high fevers, decreased blood flow to organs and coma. Pre-administration of chemotherapy/radiation is needed, resulting in the killing of the existing immune system to clear the path for engineered T cells. They are also poorly penetrating into solid tumors.

Immune checkpoint inhibitors (ICIs) have a similar panoply of side effects. ICI immunotherapy drugs will not benefit over 90% of patients of cancer patients.

Jimenez advocates 7 Key Principles of Cancer Therapy™. Non-toxic cancer therapies, immune modulation, oxygenation, full spectrum nutrition, restoration of the microbiome, detoxification and emotion and spiritual healing are the foundation of his therapy program. He uses Sono-Photo Dynamic Therapy, Interstitial PDT Laser Application, GcMAF, mistletoe therapy, and oncolytic virotherapy.

Mistletoe releases cytokine transmitters (e.g.IL-1, IL-6, TNF-a, IFN-g, GM-CSF). Immunomodulatory effects include increased amount and activity of many types of immune cells (e.g. dendritic cells, B-cells and T-cells). It causes indirect immune-mediated tumor inhibition and lowers susceptibility to infections.

Oncolytic virotherapy is classified as an immunotherapeutic agent in Latvia because of its specific ability to cause immune-mediated damage to tumor cells. In peripheral blood, cytotoxic CD38+, CD95+, and activated T cells are elevated along with apoptosis receptors. Repeated courses of oncolytic virotherapy taken by a patient are designed to encourage a sustained immune system response that in the long-term favors tumor rejection. It has been shown in clinical situations that repeated application of oncolytic virotherapy results in the gradual regression of lymph node micro metastases and subcutaneous metastasis in melanoma patients.

Also, hyperthermia (local and full body), autologous antigen receptor specific oncogenic targeted acquisition (AARSOTA), vitamin C IV therapy, nutrition therapy, ATP-1 personalized supplementation and nutrients, including vitamin D and propolis, lymphatic massages, and hormonal optimization are routine therapies in his clinics.

Beat Cancer and Win the Fight by How You Live

Leigh Erin Connealy, MD, graduated from the Chicago Medical School and received post-graduate training at the Harbor/UCLA Medical Center in Los Angeles. She founded The Center for New Medicine in Irvine, California, and wrote *The Cancer Revolution*, many articles, and appears on *Dr. Detective*, airing on KDOC, Roku, and Apple ETV. Her newsletter can be found at NewportNaturalHealth.com. She regards healing as caring for the whole person – body, soul and spirit – sharing the healing power of faith, hope and love while advancing science and medicine to put an end to cancer one person at a time.

Cancer is a multi-factorial disease. One particularity of cancer cells is their refusal to die. They escape apoptosis because of the failure of tumor suppressor genes that control cell cycle apoptosis. P53 is the guardian of the genome and mutation occurs in more than 50% of cancer.

The *British Medical Journal* of October 4, 2017 said that there was no clear evidence that most cancer drugs extend or improve life. Dr. Connealy states that the majority of cancer drugs approved in Europe between 2009 and 2013 entered the market without clear evidence that they improved survival or quality of life for patients.

Cancer is the number one killer of people, ages 1 to 85. In 1900, one person out of 100 developed cancer; today we have reached one person out of three. Very soon we will be one out of every two. Currently 1,647 die from cancer every day or 601,000 cases in the US alone annually. There are 14 million new cases per year with 8.2 million deaths every year. There has been no significant increase in survival rate over the past 35 years. Resistance to chemotherapeutic drugs is considered the greatest obstacle to the successful management of cancer patients.

Dr. Connealy cites the lack of digestive enzymes, stress, over-acidic environment and diet, toxins, bugs, biological factors, and DNA methylation irregularities as primary causes of cancer.

Toxins include rradiated food, additives, mercury toxicity, dental factors, electromagnetic fields, sick building syndrome, ionizing radiation nuclear radiation, pesticides, industrial toxins, heavy metals, xenoestrogens, phthalates, polluted water, chlorinated water, fluoridated water, tobacco and smoking, immunosuppressive drugs and all drugs increase cancer risk.

Bugs, such as bacteria, fungus, molds, mildews, and candida, parasites and viruses, need to be addressed to reduce the infectious load on the immune system.

Emotional Stress. Good stress increases B-endorphins, enhances immune system function, and increases immune response. Bad stress decreases B-endorphins and decreases immune system function, causing depression and fatigue. These emotions increase inflammation in the body and enhance development of illness and infection.

Biological Factors. Dietary and nutritional deficiencies, toxic emotions, depressed thyroid, gluten allergy, heavy metal toxins, intestinal toxicity, hormone therapies, (birth control, synthetic estrogens, hormone blockades), blocked detoxification (bad

circulation, scars, calluses), cellular oxygen deficiency (acidity, lack of exercise, pollution, cellular terrain), free radicals and vaccines block P53 activation.

P53 mutation is associated with every step of tumor growth, metastases, and invasion. This mutation is associated with aggressive cancer, angiogenesis, resistance of cancer cells to chemotherapy/ radiation, breast, glioma, pancreatic, and colon cancers.

Root Canals. Over 40,0000,000 Americans receive root canals every year. Ninety-eight percent of breast cancer patients have had one or more root canals. Root-canaled tooth bacteria are extremely dangerous and release toxins that can travel in the blood stream and cause cancer, stroke, and heart attacks, among many other diseases.

Dr. Connealy discussed cancer profile tests. She recommends HCG blood and urine tests, PHI (autocrine mobility factor) CEA, carcinoembryonic antigen, GGTP, very sensitive liver enzyme, TSH (basic thyroid screen) I also recommend free T3 and free T4 , and DHEA-S, the adrenal anti-stress, pro-immunity, longevity hormone. Dr. Connealy likes circulating tumor cells blood test, RGCC, serum ferritin, and CRP.

Thermography should be considered as an alternative to mammograms. It measures infrared heat radiating from the body and can detect 86% of non-palpable breast cancers up to ten years before a cancerous tumor can be found. It can differentiate cancer from other breast diseases and is completely safe, non-contact, pain- and radiation-free.

Ivy Gene test is a blood test for the presence of cancer and quantification of cancer presence and uses advanced DNA sequencing methods to detect DNA methylation patterns of cell free DNA in blood. Unlike many genetic tests that use DNA to determine the propensity or possibility of developing cancer over time, the Ivy Gene test identifies DNA methylation pattern consistent with actual disease presence at the time of testing.

Cancer therapies and treatments include the following: SOT/ RGCC, dendritic vaccination, insulin potentiation therapy (IPT), low-dose chemotherapy after insulin pretreatment, high-dose vitamin C with K2, hyperbaric oxygen, nanovated bath therapies, EVOX emotion therapy to resolve negative emotions via frequencies sent through a medical device hand cradle, targeted nutritional supplements, PEMF, far infrared sauna therapy, total body ozone, cryotherapy, hyperthermia, light beam with ozone, IV vitamin C, Salicinium, Poly MVA, artemisinin, DCA, sodium bicarbonate, mistletoe, dendritic cell vaccine, curcumin and other detox therapies such as coffee enemas which reduces toxicity by 700%. Resveratrol activates NF-kB. In addition, CoQ10, omega 3s, melatonin, curcumin, genistein, lycopene, poly mannose extract from aloe vera, modified citrus pectin, fucoidan, quercetin, selenium, Boswellia, green tea (ECGC) and D_3.

Cryoablation can be used in place of open surgery to ablate tumors if the tumor, because of its location, would have been challenging to reach surgically and if radiation would have caused considerable collateral damage to surrounding organs. Cryosurgery can be used to treat both external and internal tumors. To treat internal tumors, argon gas is delivered into the tumor through a cryoprobe. Ultrasound or MRI is used to guide the probe's placement. A ball of ice forms, freezing nearby cells. Cells die as they thaw. Sometimes cryotherapy must be combined with chemotherapy.

Targeted low-dose therapy was developed in the 1930s and has been used in cancer therapy since 1946. It uses insulin followed by glucose to deliver drugs more efficiently and to make them work in smaller doses with reduced or no side effects. It is gentler, safer (1/10 dose), more effective, less expensive with no surgery or radiation and usually no side effects.

Monthly Miracles

Gc Protein-derived Macrophage Activating Factor (GcMAF) acts as a director of the immune system and instructs macrophages to kill malignancies. Nagalase is an extracellular matrix-degrading enzyme that is secreted by cancerous cells in the process of tumor invasion. Nagalase activity is directly proportional to viable tumor burden. The nagalase test measures the activity of alpha-acetylgalactosaminidase in the blood. Patients should have their blood tested before treatment, after three weeks of treatment, and again following eight weeks of treatment. There should be a significant drop in nagalase level (a level below .65 indicates the body will be able to begin to produce its own GcMAF).

Thermography … measures infrared heat radiating from the body and can detect 86% of non-palpable breast cancers up to ten years before a cancerous tumor can be found.

Vitamin C IV. Dr. Mark Levine led a team of researchers to analyze the cancer-killing effect of high-dose vitamin C treatment. They discovered that by utilizing high dose and rapid intravenous infusion of vitamin C, large concentrations of vitamin C can be reached in the extracellular space. There, vitamin C reacts spontaneously with the molecular oxygen within tumors and generates large amounts of hydrogen peroxide, which is lethal to tumor cells. Tumor cells produce small amounts of protective catalase. Vitamin C given in high doses intravenously to a group of human subjects found that it effectively eradicated cancer cells while leaving healthy cells intact. (University of Kansas). High-dose IV vitamin C can stop new blood vessels from growing in cancer by creating an inhospitable, highly oxygenated environment.

Total body ozone therapy. Ozone has been used in Germany since 1950 and is considered one of the main treatments for a variety of diseases. It is a potent regulator of the immune system, increases oxygenation to the tissues, improves circulation, increases antioxidant production, and is anti-microbial. Being a powerful stimulant to the mitochondria it is helpful in detoxing ETOH, improves microcirculation and is beneficial for diabetic patients.

IV Treatments. Curcumin, silymarin, resveratrol and mistletoe strongly effect natural killer cells which help promote tumor cell death and reduce cancer recurrence. Salicinium is a natural plant-based extract. Amygdalin (also known as Laetrile or Vitamin B17) is found in raw nuts and the pits of many fruits, particularly apricot kernels and can be of benefit. Artesunate, from artemisinin (wormwood) has a similar effect to gemcitabine and causes significant tumor regression in human pancreatic cancer cells. Hydrogen peroxide, very diluted has a similar activity to high-dose IV vitamin C. Glycyrrhizin is derived from the licorice plant and has therapeutic potential against prostate cancer say researchers from the University of Illinois.

Glutathione is one of the body's chief antioxidants. Cancer patients have lower levels of this powerful antioxidant, especially those using conventional therapies (chemotherapy, radiation and surgery) which can lead to cell damage and negative health effects.

EDTA Chelation Therapy. Ethylenediaminetetraacetic acid (EDTA) is a synthetic amino acid related to vinegar. EDTA is taken intravenously (Also topically, orally and rectally) and removes heavy metals. A study published in the *Journal of Advancement in Medicine* found a 90% reduction in mortality in 59 cancer patients during the 18 years follow-up when treated with EDTA. Reviewer's note: It also removes the toxicity of platinum after chemotherapy with cisplatin or carboplatin. ➤

Monthly Miracles

➤

Dendritic Cell Therapy is an immune therapy that harnesses the body's own immune system to fight cancer. The dendritic cell (DC) is an immune cell whose role is the recognition, processing and presentation of foreign antigens to the T-cells in the effector arm of the immune system.

The creation of an individualized DC vaccine involves the harvesting of patient's own blood cells to be processed in a lab to isolate cancer cells and identify the most frequently expressed "epitope" (protein) on the surface of cancer cells and imprint dendritic cells with that "epitope." The new DC population is augmented (increased in numbers) in preparation to be introduced back into the patient's body. The goal of DC is to educate T and B cells to identify the cancer cells and mark them for destruction for macrophage clean-up. If the vaccine "takes" it will give long term immunity against cancer cells.

Stage IV breast cancer patient treatments include the following: EVOX, emotional evaluation, nutritional consult, hemosonic infrared sauna daily, hyperbaric treatments (three times weekly), nano bath (twice weekly), LBG (light beam generator to stimulate lymph flow, three times weekly), PEMF daily, IV vitamin C, Vitality C (1 tsp twice daily), pancreatic enzymes (five, three times a day on empty stomach), liver flush (once per month), and coffee enemas.

"Peace begins with each of us taking care of our bodies and minds every day." - Thich Nhat Hanh.

New Perspectives on Salicinium for Integrative Cancer Treatment

Virginia Von Schaefer, MD, discusses the rationale for using Salicinium as an integrative cancer treatment.

Cancer incidence has been accelerated by post WWII hydrocarbon toxicity created by extensive use of chemicals in food sources, water, clothing, plastics, pesticides and heavy metals. Polypharmacy causes (all drugs, too many drugs) "Magic Pill" obsession. Electromagnetic fields, nuclear radiation, ionizing radiation and EMFs all enhance cancer formation. In addition, chronic/sub-acute infections from bacteria, viruses, parasites, fungi, and candida all make energy via anaerobic fermentation metabolism and contribute to creating microenvironment conducive to cancer cell growth.

Stress is another contributor. It arises in response to forces either within us or in our environment that are beyond our control and triggers a "fight or flight" syndrome. It increases chronic levels of blood glucose, sympathetic nervous system overdrive, decreases parasympathetic driven functions of regrowth and repair, as well as decreasing oxygen tension.

The challenges are greater now than ever before because cancer is pandemic. In the USA estimates are that 50% of males and 41-45% of females will develop cancer in their lifetimes. Worldwide these numbers are growing daily. Treatment results are abysmal with no significant increase in five-year survival over the past 50 years using the current mainstay of treatment with surgery, chemotherapy and radiation therapy.

What are we missing? How can we overcome seemingly insurmountable odds? Dr. Von Schaefer's focus is to treat the whole person and apply principles of biochemistry and cell biology to medical problem solving.

She revisits Otto Warburg's phenomenon of cancer cells being anerobic, utilizing fermentation. Fermentation metabolism involves a neutral pH (7.0) and extrudes lactate. Leaky membranes cause a loss of electrochemical gradient across the membrane, and when "leaky" the delicate electron transport chain of the mitochondria fails. Warburg concluded that cancer is a disease of mitochondrial dysfunction promoted by environmental hydrocarbon toxicity.

Cancer tissue also has upregulated glucose receptors +GLUT-4 and excess iron (400 x the amount of iron needed for DNA replication). Increased extracellular acidity increases angiogenesis, fibrin coating, and nagalase, which blocks GcMAF activation.

Trophoblast cells come from the fetus, not the mother. They cause arterial remodeling to attach cells to the maternal spiral arteries, invade and remodel them to create adequate blood supply to the fetus. The trophoblast causes phagocyte repulsion, masking them from maternal lymphocytes. This masking is affected by the release of "fibrinoid sialomucin," which was demonstrated to be nagalase. (Simon & Russel 1962: Carrie & Bagshawe, 1967/ Peter W. Stackpoole, 1971, *Trophoblastic Nature of Cancer*)

Nagalase (alpha-N-acetylgalactosaminidase) creates a protective fibrin coat on cancer cells and repels phagocytes. It blocks vitamin D binding protein complex (GcMAF), which is required to activate tissue macrophages. Elevated nagalase indicates increased tumor activity and possibly indicates aggressiveness of the tumor. Serial monitoring can tell the progression of therapy.

When cancer cells are deprived of energy and cannot perform functions to maintain protective microenvironment, decreasing nagalase leads to reduction of the fibrin coat, reduces angiogenesis, and increases effective GcMAF. Thus, cancer cells are starved, de-cloaked, and vulnerable to the immune system.

Salicinium targets cells conducting fermentation/anaerobic respiration. It saturates tissue especially in areas of pleural space, peritoneal cavity, crosses the blood-brain barrier and changes abnormal cellular microenvironment that protect the cancer cell via blocking nagalase release, acid extrusion, angiogenesis, fibrin coating, and deactivation of GcMAF. The Salicinium blocks progression of glycolysis to produce 4 ATP/net2 ATP and blocks acid extrusion/lactic acid formation.

Salicinium contains a benzaldehyde ring. The glucoside/complex glycome of 4-hydroxy-benzaldehyde is extracted from the plant *Helicia nilagirica*. In the early 1970s, the Japanese researched and demonstrated the anti-tumor effect of benzaldehyde via several different mechanisms. It causes disruption of cytosol glycolysis and increases NK cell activity. Benzaldehyde reduces phosphorylation of a class of "HUB" signaling proteins.

When using Salicinium, the following need to be avoided: oxidative therapies, ozone, H_2O_2, artemisinin, genistein, SOD, IP6, MMS, cell food, and high-dose vitamin C. Compatible therapies include glutathione, Meyers cocktail, HBOT, EDTA, IPT/APT and ERT. Synergistic therapeutics include mistletoe, hyperthermia, sound therapy, and gallium maltolate. Dr. Von Schaefer presented seven cases of positive response from Salicinium treatment in conjunction with other modalities.

Von Schaefer reminded attendees that the therapeutic demise of cancer cells with Salicinium may be proceeded by their expansion. Meningeal metastases may expand during treatment and cause optic nerve damage. Liver tumors may expand and cause obstruction. Pancreatic tumors may expand and cause duct obstruction.

This ends a very great meeting presented by Annie Brandt. These 28 speakers offered state-of-the-art integrative cancer therapies and increased our repertoire of responses to this plague. ◆

The diagrams associated with Dr. Gerber's article can be found on our website www.TownsendLetter.com

Salicinium®

PHYTO-NUTRICEUTICAL

Salicinium has recently been added to the R.G.C.C. Circulating Tumor Cell test as well as the BioFocus Labs Cellular NK test:

to order test: Research Genetic Cancer Center info@rgccusa.com or www.atmctx.com/cancer-test

to order test: Bio Focus Labs www.prix@biofocus.de

The Science of Glycobiology

Salicinium changes the way the macrophage of the immune system recognizes diseased cells through immune modulation. The Nagalase enzyme produced by anaerobic cells shuts down the natural function of the immune system providing safety for these diseased cells.

The composite Salicinium molecule will only affect anaerobic cells destroying the enzymatic "cloak" which allows them to hide from the immune system's NK cells. Salicinium stops the production of Nagalase and lactate removing their protection while simultaneously stimulating the the innate immune macrophage to eliminate these diseased cells.

Circulating tumor cells are at the forefront of an ongoing or escalating malignant process. CTC testing has shown Salicinium affects these cells first therefore halting the spread of malignancy. Continued use of Salicinium will allow the immune system to steadily attack remaining malignant cells. The same testing also induces the death of cancer stem cells and Salicinium therapy, whether I.V. or oral, should be continued without interruption until testing shows no further indicators of malignancy.

- **In a study by R.G.C.C. of 967 patients Salicinium showed a 26.28% average apoptosis rate from a single dose with 82% sensitivity. A much higher cumulative apoptosis rate is recognized with ongoing treatment as the level of Salicinium builds within the tissues.**
- **Salicinium can be used alone or as an adjunct to other complementary therapies or as an integrative therapy to allopathic treatments.**
- **Salicinium is completely targeted - it will only enter anaerobic cells.**
- **Salicinium allows Gc-Maf to resume operation, greatly increasing Immunoglobulins**
- **Salicinium does not kill the malignant cells - the immune system does. Only the immune system can destroy anaerobic cells, Salicinium increases immune natural killer (NK) cells/Gc-Maf**

for more information about Salicinium:

(888) 262-5903 info@salicinium.com

The First and Only CBD Formula Produced Exclusively for Doctors.

*Douglas Laboratories® is a registered trademark of Atrium Innovations, Inc. and not affiliated with TruGen3®
† 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.

Personalized labeling available

- The only hemp oil product in the professional channel lab-tested using ICH standards that support and validate two-year shelf life.
- Exclusive VESIsorb® Technology provides up to 6x more CBD hemp oil bioavailability †
- Solvent-free SMB chromatography extraction for undetectable THC levels (unlike lipid-based and other extraction methods used in substandard CBD products that retain THC).
- 25mg of CBD & 6mg of beta-caryophyllene

Your Patients Deserve the Best.

TruEase® is truly today's best-in-class CBD product for discriminating Health Care Professionals. A TruGen3® exclusive, TruEase® delivers an ideal concentration of CBD, enabling bioactives like betacaryophyllene (BCP) to deliver synergistic interaction between phytocannabinoids and terpenes. This superior ratio of 4:1 (CBD:BCP) supports each other's function perfectly as BCP is directly linked to activating CBD in the body via CB2 receptors. (Beware inferior CBD products with zero levels of BCP and low-potency hemp oil (as little as 5% CBD, compared to 60% found in TruEase®).

TruGen3® continues Douglas Laboratories' family legacy, with our third generation and more than half-century of nutraceutical experience. All TruGen3 products are produced under the highest ethical standards and available only through Health Care Professionals.

Contact us today for FREE SAMPLES and to find out how you can put our innovative, one-of-a-kind products to work for your patients, and your practice, today.

Seeing is Believing

See for Yourself at www.trugen3.com/vesisorb

Patented VESIsorb® technology is clinically proven to provide up to 6X more bioavailability via multiple PK studies measured in human subjects.†

Competing Softgel

Formula does not go into solution; note separation of ingredients.

VESIsorb® Softgel

100% in solution; completely homogenous colloidal solution for optimal absorption.

TruGen3®

Three Generations of Truth in Nutrition

www.trugen3.com 1-844-387-8436