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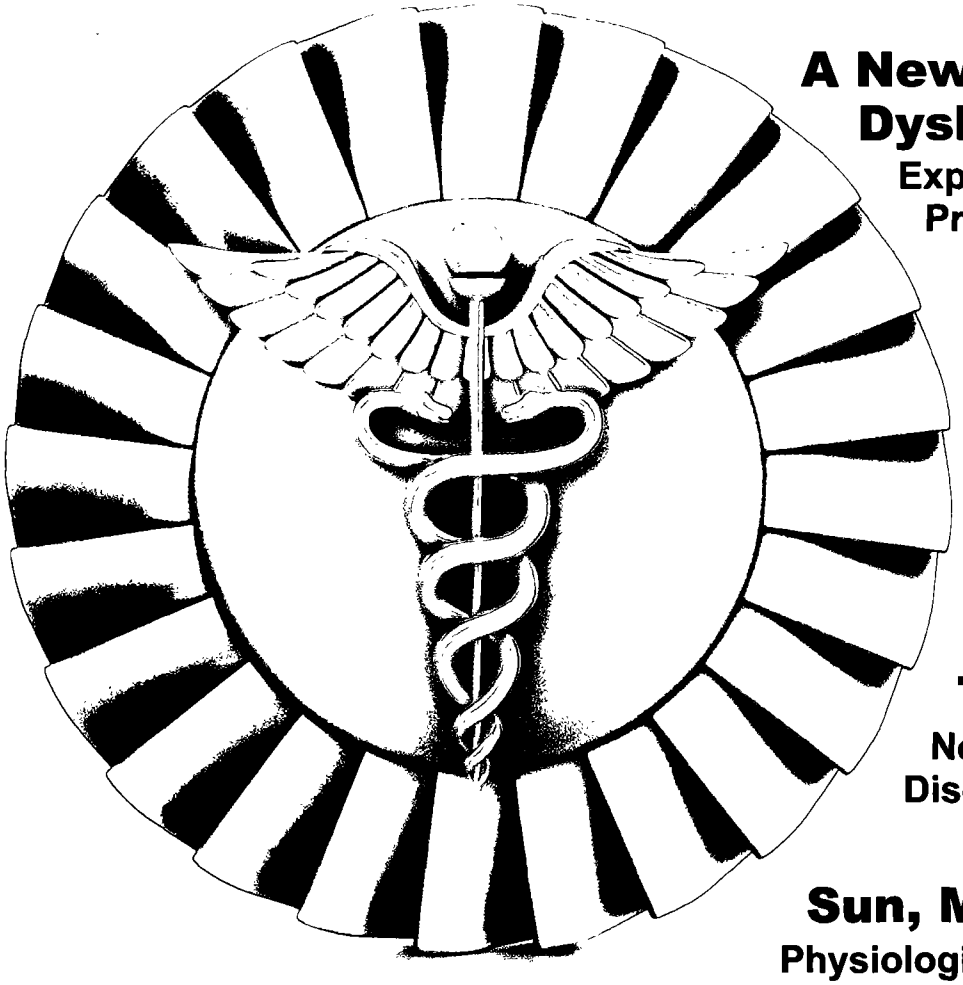

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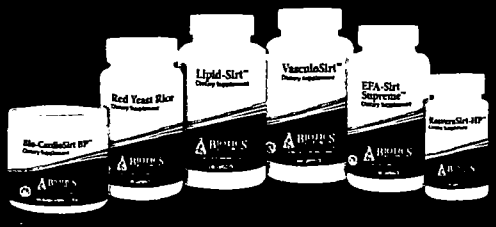

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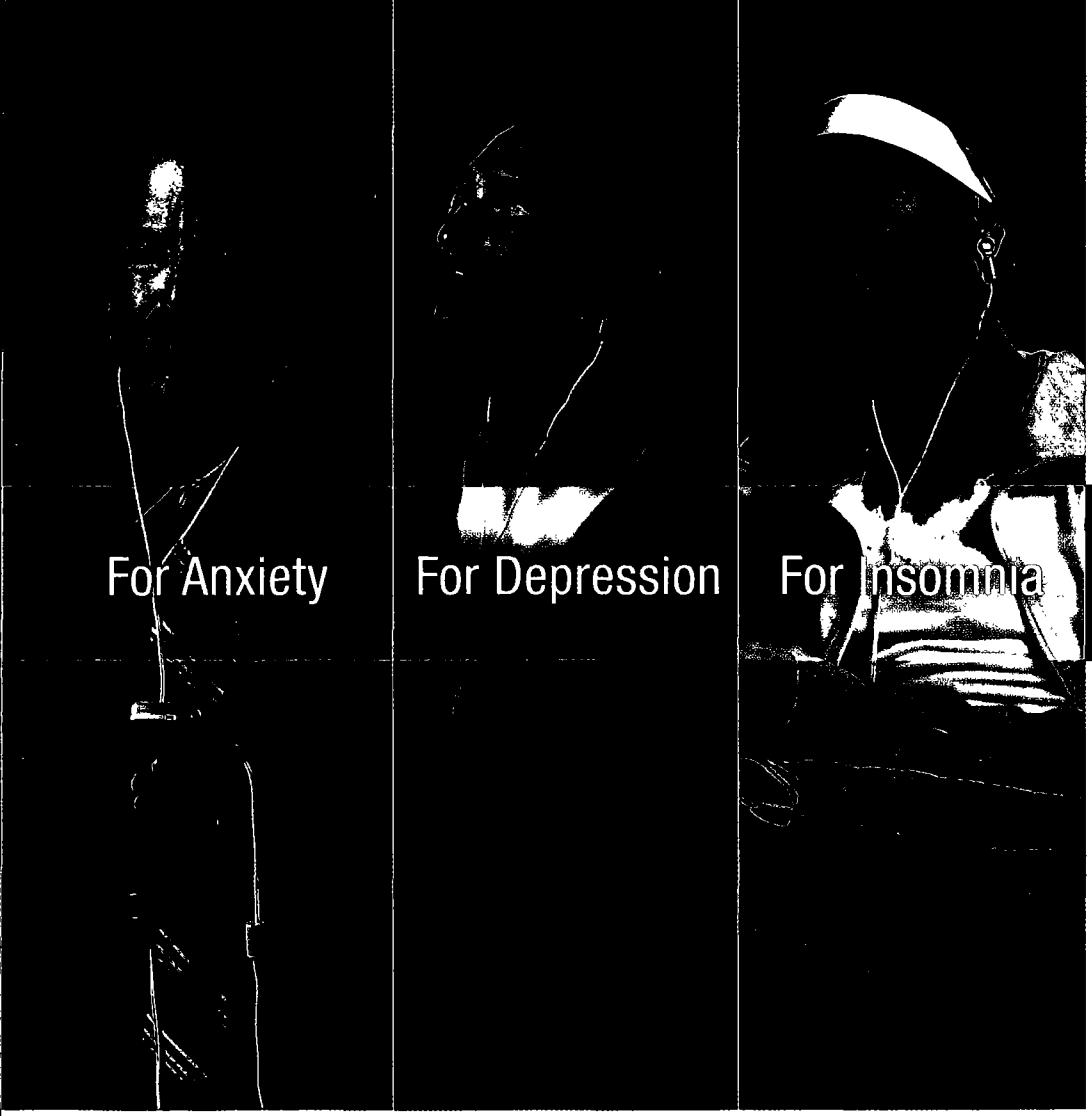

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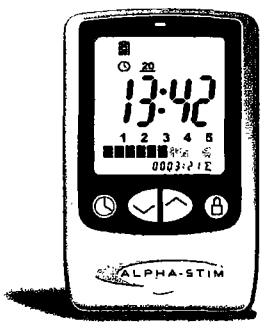

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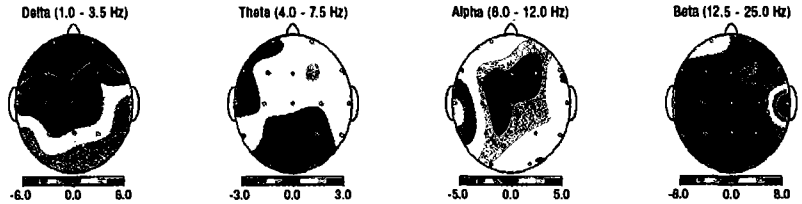

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*Kennerly R. Changes in quantitative EEG and low resolution tomography following cranial electrotherapy stimulation. PhD Dissertation, the University of North Texas. 2006;529 pp., 81 tables, 233 figures, 171 references.

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Letter from the Publisher

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Holmes believes that a laboratory test does not need multiple specimens of blood removed by venipuncture. Instead, a simple finger stick is sufficient for completing a lab panel. What's more, Holmes's laboratory model offers testing stations to be conveniently located in pharmacies operating seven days per week, throughout the day, making lab testing as convenient as a trip to the supermarket. The laboratory technique depends on a proprietary method known as "lab-on-a-chip." Rather than using the large equipment manufactured by Roche Diagnostics and Siemens, lab testing is done on machinery designed by Holmes's company, Theranos. Its equipment is much smaller and presumably more efficient in assessing a lab result with minimal blood. Theranos has perfected the assessment of dozens of laboratory tests all done with a simple lancing of the blood performed in less than 2 minutes. It offers the testing at a fraction of the cost of its competitors – below the amount approved by Medicare. The lab testing is CLIA approved, but it has not been subject to medical peer review – it doesn't have to, because the instrumentation and testing methodology have been developed in house (the FDA does not require peer review for in-house testing, but this may change in 2015).

Holmes, who owns 50% of the stock of Theranos, has an impressive team of statesmen and CEOs for her board of directors because of her friendship with Palo Alto neighbor and former Secretary of State and Treasury George Shultz. Working on the board with Holmes is Bill Frist, a cardiac surgeon and former Senate Republican majority leader. Other board members include former Secretary of State Henry Kissinger; Sam Nunn, former Democratic senator; William Perry, former defense secretary; and William Foege, MD, former director of the CDC. Holmes has convinced Cleveland Clinic president and CEO Dr. Delos Cosgrove that her testing will not only upend lab science but will also be a "major change in how we deliver health care." Currently, a Walgreens store in Palo Alto as well as 30 Walgreens stores in Phoenix offer Theranos testing. Individuals are required to have a physician prescription to have testing done. Holmes hopes to get lab testing available at all 8400 Walgreen stores in the future as well as at competitor pharmacies. Couriers pick up lab specimens several times daily and are shipped to the Palo Alto laboratory for processing.

Quest argues against Holmes's claim that it continues to use the technology of the 1940s – the company's instrumentation and testing methodology

continued on page 13 ➤

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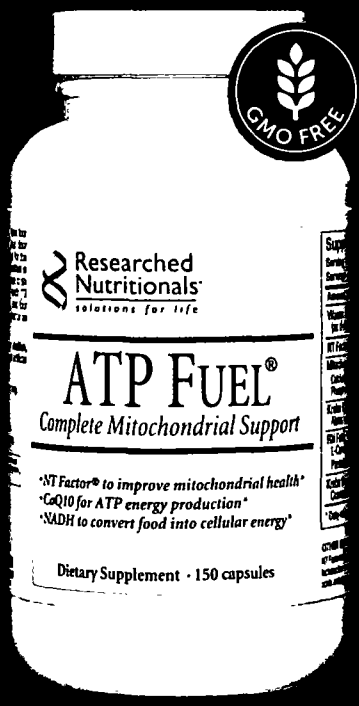

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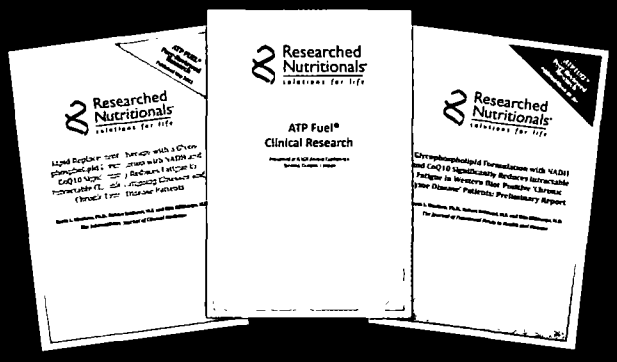

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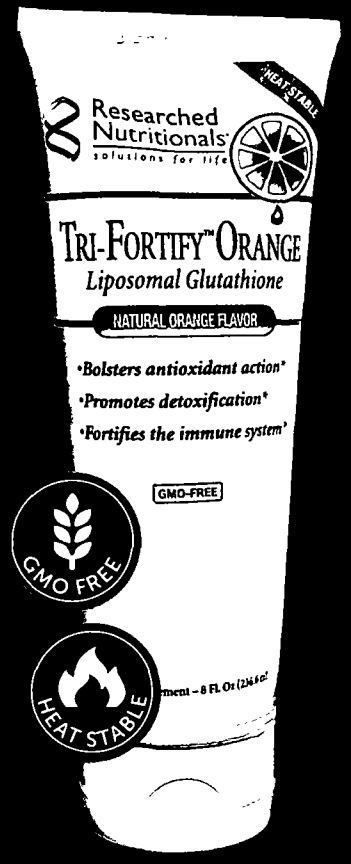

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Letter from the Publisher

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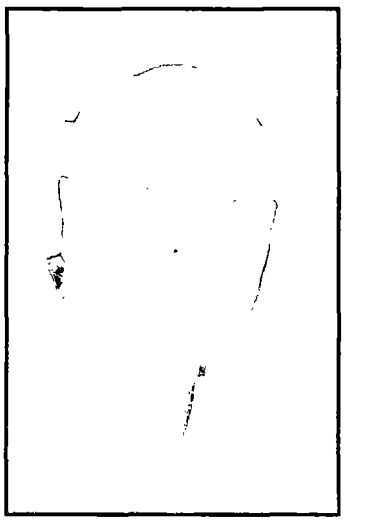
have greatly reduced the volume of blood required for testing. Further, Quest's senior scientist, Nigel Clarke, disputes that the lab assessment from a capillary finger stick is the same as a venous specimen. Laksmann Ramamurthy, former associate director of the FDA, is concerned that the technology does not have peer review. Although Theranos has applied for FDA approval, it has never received any official response from the agency. Some critics worry that patients will not be able to understand laboratory test results without physician oversight. Holmes counters, how difficult could it be to interpret a cholesterol score or a blood count?

J. Craig Venter, PhD

Perhaps the most intriguing speaker at the A4M December meeting at the Venetian Hotel in Las Vegas was J. Craig Venter, PhD. Venter is one of the first to sequence the human genome. He is the first to transfect (introduce DNA or RNA into) a cell with a synthetic genome. As an example, a bacteriophage is a virus capable of infecting a bacterial cell, causing bacterial cell lysis. Venter's group analyzed and sequenced the genome for Phi X 574 bacteriophage that kills *E. coli*. When the synthesized genomic material was implanted in *E. coli*, viral particles accumulated and the bacteria were lysed. The phage was able to further infect adjoining *E. coli* bacteria. Venter thinks of the phage transfecting process as viral software that enables it to build its own hardware. He sees the process of synthesizing artificial genomes, DNA assembly tools, as the process by which one can convert one species into a different species. Venter explains that the donor genome encodes restriction enzymes that degrade the recipient cell's genome. Once the synthetic DNA is implanted the activity of the DNA in the recipient cell is changed permanently.

In 2010 his group was successful in creating the first synthetic life form. Venter thinks that transfected organisms with implanted DNA will be the key to developing new vaccines, medicines, biofuels, waste remediation technologies, and other scientific advances. When Venter began his work gene sequencing required massive computers and hours of time to sequence hundreds of DNA/RNA pairs. Now the technology is available with lab bench instrumentation that is capable of sequencing 10,000 pairs in a similar period of time. The speed of the genomic sequencing with these portable instruments means that medical workers could sequence an emerging virus in a jungle environment and with the synthesis of small fragments of the viral genome proceed to create vaccines. Effectively this would enable vaccines to be made in "real time" as new viruses are encountered. Venter discusses the role of synthesizing phages for difficult-to-control hospital bacterial infections; for example, a phage could be synthesized for resistant pseudomonas in hospital burn units. He sees a role for synthetic genomic sequencing in transplantation work. Lung transplants have been extremely expensive and difficult. He thinks that we can "humanize" pig cells for organ transplantation. If pigs could go through genomic editing, pig cells would be available for lung transplantation. Venter sees the application of portable genomic sequencing in space exploration for life; genomic sequencing can be made of a suspected Martian life form and the sequencing can be messaged to earth, then the genomic sequencing can be synthesized here.



J. Craig Venter, PhD

Venter's most ambitious project to date is his joint venture Human Longevity Inc. The company was formed in March 2014 with the goal of expanding quality human life expectancy. Venter's group intends to use "big data" from genomics, microbiomics, metabolomics, and proteomics to determine how best to use stem cell therapy and other treatments for life extension. Venter is the author of a book telling his personal story, *A Life Decoded*. Venter reviews his work and predictions for the future of science in *Life at the Speed of Light: Double Helix to the Dawn of Digital Life*.

Best of Naturopathic Medicine Competition 2015

Our February/March 2015 issue publishes the winners of our "Best of Naturopathic Medicine" competition held every two years. This year we have awarded the first-place prize to Jonathan Prousky, ND, chief naturopathic medical officer and professor at the Canadian College of Naturopathic Medicine.

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Letter from the Publisher

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Jonathan Prousky has spent more than 16 years treating patients with mental disorders. He has employed orthomolecular medicine and naturopathic treatment in managing patients with anxiety, depression, bipolar disorder, and schizophrenia. As editor of the *Journal of Orthomolecular Medicine*, he has examined and reviewed the work of Abram Hoffer, MD; Linus Pauling, PhD; and others, incorporating their work in his practice. His article on assessing vitamin B12 published in the February/March 2011 issue of the *Townsend Letter* offers a well-documented rationale for administering high doses of B12 in managing mental disorders. Prousky's article in this issue examines the triggers of mental breakdown and the need for the patient to have effective resilience to cope with stress. Prousky argues that the majority of psychiatric medications not only fail to reverse mental disorders but render the patient less motivated and capable to actively seek strategies that restore wellness and mental health. The psychosocial support that patients need includes effective counseling, proper shelter, regular meals, employment, exercise, connection to nature, religious/spiritual practice, sufficient sleep, and orthomolecular interventions.

Second place has been awarded to Steven Sandberg-Lewis, ND, and Allison Siebecker, ND. Dr. Sandberg-Lewis is a professor at the National College of Naturopathic Medicine and cofounder of the SIBO Center. Dr. Siebecker is an instructor at the National College of Naturopathic Medicine and co-founder and medical director of the SIBO Center.

Steven Sandberg-Lewis has devoted his academic work to teaching gastroenterology; he is the coauthor of *Functional Gastroenterology*. Sandberg-Lewis and Siebecker have founded a clinical center in Portland, Oregon, to treat dysbiosis and irritable bowel syndrome. They have conceptualized dysbiosis as small intestinal bacterial overgrowth (SIBO) – an abnormally high number of microorganisms typically found in the large colon populating the small intestine. These commensal bacteria include *E. coli, Bacteroides, Clostridium, Streptococcus, Enterococcus,* and *Campylobacter.* Because carbohydrates and fats are not fully digested until passing through the small intestine, bacteria ferment the carbohydrates, yielding vast quantities of hydrogen, hydrogen sulfide, and methane. Sandberg-Lewis and Siebecker contend that it is only by measuring the gas production that one may make a diagnosis of SIBO and advise an appropriate treatment strategy. They differentiate IBS symptoms of diarrhea and constipation based on the predominant gas production; excess methane leads to constipation and excess hydrogen leads to diarrhea. The treatment of SIBO includes a carbohydrate-restrictive diet, antibiotics, herbal antibiotic alternatives, and biofilm disruptors. Prevention of SIBO relapse includes a modification of the restrictive diet, a "prokinetic" agent to mobilize the intestine, and further supplementation. Sandberg-Lewis and Siebecker offer strategies to prevent treatment failures.

Jonathan Collin, MD

Integrative Medicine Conference Covers Pain

The fall conference of International College of Integrative Medicine (ICIM) was titled "End Pain." A comprehensive approach was outlined by Jacob Teitelbaum. Special features of pain were discussed by Robban Sica on migraines, Vladimir Tomljanovic on neck disorders, Derrick Lonsdale on thiamin, Bill Faber on the lightning reactions, Robert Rowen on ozone for healing, Ed Kondrot on microcurrent, Sahar Swidan on compounding, and David Kohns on the role of the brain for pain.

Especially high ratings were scored for Helene Leonetti on the path to vibrant health, David Nebbeling on a holistic approach to musculoskeletal pain, Guy Chamberland on a master herbalist's approach, and David Pawset on mindfulness. A rousing debate was held between Bruce Holub and Brain Peskin on fish oils vs. PEOs for inflammation. John Huniston described many years of amazing results using IV amino acids to treat addictions. Al Augustine continued to remind us of the legal aspects of integrative medicine.

David Brownstein gave a detailed workshop on iodine, and Terry Chappell chaired one-day workshops on basic and advanced chelation therapy. A lifetime achievement award honored John Trowbridge. Executive director Wendy Chappell made sure that we had fantastic food, great music, and a fascinating tour of the African American museum in Detroit.

Recordings of lectures and copies of PowerPoint slides can be purchased by e-mailing wendy@ICIMed.com.

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Transforming Patient Care Takes Center Stage at 2014 Metagenics Lifestyle Medicine Summit

Health care is evolving as an ever-growing body of research and clinical experience demonstrate the effectiveness of lifestyle medicine therapies in helping to manage, prevent, and reverse some of today's most challenging and prevalent chronic illnesses – including type 2 diabetes and cardiovascular disease. Lifestyle medicine protocols are also evolving, as are strategies to personalize these protocols for individual patients. Metagenics Inc., a nutrigenomics and lifestyle medicine company, hosted its third annual Lifestyle Medicine Summit, held September 26–28, 2014, in Nashville, Tennessee. Nearly 600 health-care practitioners attended the summit to connect with peers and opinion leaders to discover the most effective lifestyle medicine protocols and advancements in nutritional science – and learn how to implement them in clinical practice.

This "shift" in health care was the theme of this year's summit: "Transformational Patient Care: Powering the Paradigm Shift." This landmark event included discussions and breakout sessions led by 16 world-class research clinicians, physicians, and other respected practitioners across a variety of fields. Each year the summit becomes larger – attracting more exhibits, sought-after speakers, leading research scientists, and new attendees.

"For over 30 years, practitioner education has been a driving force behind the Metagenics mission to improve patient health. It is an honor each year to host the Lifestyle Medicine Summit, the highest-caliber educational event in our industry," said Fred Howard, chief executive officer of Metagenics Inc. "This unique collaborative forum also fosters connections between like-minded health-care providers – the ones who are truly powering the change for the future of health care."

The goal of these annual summits is to inform and inspire practitioners with innovative nutritional and lifestyle medicine strategies. As in years past, presentations began with Jeffrey S. Bland, PhD, founder of the Personalized Lifestyle Medicine Institute and well-known functional medicine pioneer, research scientist, and educator. His discussion mirrored his latest book, *The Disease Delusion: Conquering the Causes of Chronic Illness for a Healthier, Longer, and Happier Life*. Other notable speakers included:

- **Mark Hyman, MD**: Chairman, Institute for Functional Medicine (IFM); practicing family physician; eight-time #1 *New York Times* best-selling author; internationally recognized leader, speaker, and educator.
- **Osama Hamdy, MD**: Director of the Inpatient Diabetes Program, Joslin Diabetes Center; assistant professor of medicine at Harvard Medical School; clinical researcher and author of more than 150 publications.
- **Mimi Guarneri, MD**: President, American Board of Integrative Holistic Medicine; founder, Scripps Center for Integrative Medicine; noted physician, speaker, and health-care adviser.
- **David Katz, MD**: Director, Yale Prevention Research Center; clinical instructor of medicine at the Yale School of Medicine; ABC News medical consultant and author of numerous scientific articles.
- **Robert Martindale, MD, PhD**: Professor of surgery, chief of the division of gastrointestinal and general surgery, and medical director for hospital nutrition at Oregon Health & Science University; author of over 200 publications, coeditor of a major textbook on ICU nutrition; editorial board member for several surgical and nutritional journals.
- **Mark C. Houston, MD**: Associate clinical professor of medicine at Vanderbilt University School of Medicine and director of the Hypertension Institute and Vascular Biology; medical director of the division of human nutrition at Saint Thomas Medical Group; has published six best-selling books and over 200 articles and scientific abstracts, and completed over 80 clinical studies in hypertension, hyperlipidemia, and cardiovascular disease.

"The Metagenics Lifestyle Summit was amazing! It taught us how to position ourselves as the 'lifestyle experts.' I can now better serve my patients and attract more new patients," said Fabrizio "Fab" Mancini, DC, president emeritus of Parker University and a well-known author, television health expert, and integrative chiropractor. This was his first year as a featured speaker at the conference.

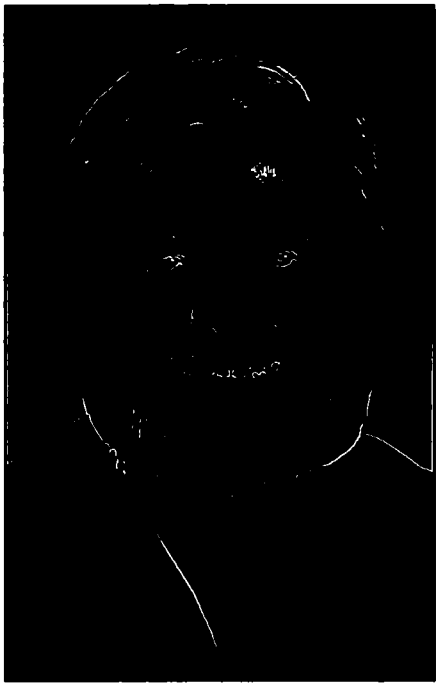
Other presenters and workshop leaders included Alison Monette, ND, RD; Michael Nova, MD, PhD; Dane Donohue, DC; Eamonn Quigley, MD, PhD; Bob Rakowski, DC, CCN; Samantha Eagle, ND; Robert Silverman, DC; and Michael Kyrchman, MD.

A special award was also presented to Naomi Judd – country music superstar, television personality, actress, humanitarian, former RN, and mother of two successful daughters – for her contributions to health and wellness. She has helped increase awareness of the benefits of lifestyle therapies through publicly sharing her own personal journey to better health.

The 2015 Lifestyle Summit will be held on September 25–27, 2015, at the JW Marriott Desert Ridge Resort & Spa in Phoenix, Arizona. The theme is "Healthy Aging – 100% vitality for your first 100 years: Restoring and Maintaining Optimal Health." Early registration at metagenics.com/education is encouraged to guarantee participation. ◆

2014 ICIM Lifetime Achievement Award: John Parks Trowbridge, MD, FACAM

Dr. John Parks Trowbridge earned the rank of Eagle Scout before he attended Stanford University as a National Merit Scholar and California State Scholar, graduating in 1970 with an AB degree in biological sciences. He attended the School of Medicine at Case Western Reserve University (CWRU), finishing in 1976 with an MD degree. Serving as the first National Trustee for the American Medical Student Association (AMSA), he was privileged to address the House of Delegates of the American Podiatry Association (APA) in 1975, where he received its Special Commendation for sponsoring closer interprofessional relationships, complementing a similar award that year from the American Podiatry Students Association (APSA). As a student associate in the Division of Research in Medical Education, he completed a series of 12 color-videotapes on congenital heart disease, still used in teaching medical students around the world.



John Parks Trowbridge, MD, FACAM

In 1978, he started a general medical practice in Humble, a Houston suburb. Always curious, he expanded into industrial medicine, serving the needs of over 50 light- and heavy-manufacturing companies, with concerns ranging from preemployment determinations to on-the-job injuries to toxic chemical exposures. In 1980 to 1982, Trowbridge was the chief medical consultant for Texas International Airlines, which bought and merged into Continental Airlines. By 1981, Trowbridge was turning to the intensive study of how nutritional changes – with supplements and diet – could improve the condition of patients with chronic degenerative diseases.

In 1985, he was awarded a Diplomate in Preventive Medicine by the Medical Research Institute of the Florida Institute of Technology for master's-level graduate studies in nutrition. Trowbridge became certified as a specialist in the removal of toxic heavy metals by the American Board of Chelation Therapy (now the ABCMT) in 1985 and as a specialist in treating arthritis/sports injuries by the (now defunct) American Board of Biologic Reconstructive Therapy (arthritis and pain medicine) in 1993; he served as an examiner for both boards. In 2006, he was named a director and then secretary of the American Board of Clinical Metal Toxicology (ABCMT). The International Academy of Biological Dentistry and Medicine (IABDM) elected Trowbridge a director in 2007; he became the first physician president in 2009. He served as director and officer of the American College for Advancement in Medicine (ACAM, 1984–1991) and was awarded highest recognition as a Fellow of the College (FACAM) in 1991.

Trowbridge also served as chairman of the board of governors of the National Health Federation (NHF) in 1989 and as president of the Great Lakes College of Clinical Medicine (GLCCM, now ICIM) in 1995–1996. From 1996 through 1998, Trowbridge was program chair for the advanced chelation training seminars in "Heavy Metal Toxicology: Diagnosis and Treatment"; he has lectured at the advanced training as a founding faculty member since 1993. In 2000, he was reelected to the board of directors of GLCCM and appointed editor of its newsletter; in 2001, the society changed its name to the International College of Integrative Medicine (ICIM) and Trowbridge was named as board secretary, a post that he held through 2008. From 1992 through 1998, he served as a charter member of the board of directors of the American Preventive Medical Association (now the American Association for Health Freedom, AAHF). Since 1995, he has served on the Medical Advisory Board of the Arthritis Trust, having become skilled in using this specialized treatment program in his practice since 1983. He served as president of the NCR Doctors Association, a group promoting a safe and effective treatment for migraine and other headaches and painful neck, back, and posture problems, from 2002 to 2003; in 2003, the group reformed as the NCR Research Institute, and Trowbridge served as its president through 2011.

Popular as a public speaker and radio/TV guest, in 1990 he hosted his own nationally syndicated AM radio talk show – *Finally Feeling Better* – and more recently hosted a Houston AM radio talk show, *Feeling Better ... Naturally, with Dr. John Trowbridge*. Trowbridge serves as an editorial adviser for several health newsletters and magazines. Among his several books are three best-sellers: Bantam Books' million-copy *The Yeast Syndrome* (1986), *The Healing Powers of Chelation Therapy* (1985), and *Do What You Want to Do* (1996). A unique "book on tape" (now on CD) on chelation therapy, titled *Living Well Past 50: Rejuvenate Your Heart and Arteries*, was released in 1998, featuring 3 hours of patient interviews and "plain English" explanations of the extraordinary chelation program. *The Rumble in Humble: Heart Surgery and All That Jazz!*, published in 1997, reviewed diagnostic and treatment issues in the modern treatment of heart and blood vessel diseases, including "alternative" or "complementary" approaches.

Trowbridge's recent projects include books in preparation covering innovative and effective treatment strategies for those suffering with heart and blood vessel and other degenerative diseases. He remains a board adviser for the International College of Integrative Medicine.

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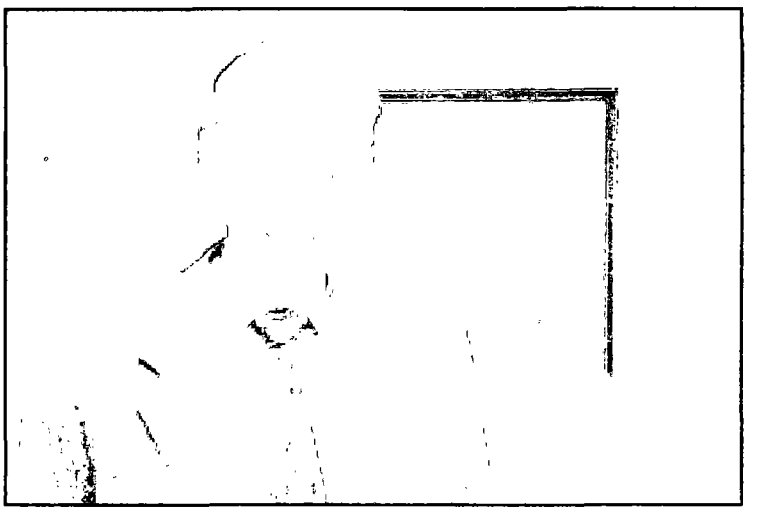

In Memoriam: Hal Alan Huggins, DDS, MS

Dr. Hal Huggins passed away peacefully at his Colorado Springs home on November 29, 2014. He was 77.

Dr. Huggins rightfully earned the title of "elder statesman" of holistic dentistry. He is also known as a leading pioneer and the "grandfather" of identifying and treating medical problems caused by toxic dental materials.

Dr. Huggins received his DDS degree over 50 years ago at the University of Nebraska and practiced for decades in Colorado Springs. Continuing his education in 1990, he received his postdoctoral master's degree from the University of Colorado, with an emphasis on immunology and toxicology.

He presented over 2500 lectures in 47 of the US states and 16 foreign countries. He authored many books, wrote over 50 articles, and gave over 1000 radio/television interviews, including *60 Minutes Australia* (1989) and *60 Minutes New Zealand* (2007).

As founder of the Multi-Discipline Alliance of Professionals, he ensured continuing education for dentists desiring to learn the Huggins dental protocol. Training includes helping patients avoid and recover from ailments caused by harmful dental procedures.

He devoted his last years to establishing the Huggins Applied Healing center (www.drhuggins.com), but his greatest passion was the recent formation of the Dental DNA laboratory (www.dentaldna.us). This sophisticated facility specializes in the detection of dangerous, disease-causing DNA that resides within root canals, cavitations, implants, and other oral environments.

Dr. Huggins was a caring and sensitive man who dedicated his life's work to helping humanity. He was loved by his patients, professional colleagues, and staff for his compassion, generosity, and willingness to give of himself.

His greatest joy was helping those on their quest to recover from the many degenerative diseases caused by silver (mercury) fillings and heavy metal toxicity from other dental materials.

He is survived by three children, David Huggins and Chip Elizabeth of Colorado, and Holden "Denny" Conover of Alaska; two grandchildren, Patricia and Michael Conover; and one great-grandchild.

Donations in his memory may be sent to the Toxic Element Research Foundation (TERF), 5082 List Drive, Colorado Springs, Colorado 80919.

◆

Pathways to Healing

by Elaine Zablocki

Cleveland Clinic Opens Center for Functional Medicine

In October 2014, the Cleveland Clinic Center for Functional Medicine (CFM) opened its doors. This new program is a collaboration among the Cleveland Clinic; the Institute for Functional Medicine (IFM); and Mark Hyman, MD (IFM's board chair). Although CFM hasn't done a great deal of advertising, its calendar is full; it is currently scheduling appointments three months ahead.

Staff at the Cleveland Clinic Center for Functional Medicine: (Back L-R) Patrick Hanaway, MD; Dirk Parvus, MD; Mark Hyman, MD (Front L-R) Laura Vuicich, RN; Brigid Titgemeier, MS, RDN; Trisha Howell, MSH, RD

Many patients seeking care at the new center have complex chronic conditions that are difficult to diagnose and treat using only the paradigms of conventional medical care. "Our goal is to serve as a gateway program for patients with complex, chronic disease," says Patrick Hanaway, MD, CFM medical director. Using a functional medicine approach means that clinic personnel look at an array of potential clinical imbalances in biological systems that could be the root cause of a particular manifestation of disease. Each patient receives team-based care with a focus on appropriate nutrition and lifestyle changes.

"The conventional medical system looks at symptoms and asks, how do I reduce or eliminate them?" Hanaway says. "But symptoms are like a 'check engine' light; if we focus mainly on reducing them, we may miss the opportunity to investigate an important signal about an underlying imbalance. Functional medicine isn't about trying to reduce symptoms; it is about finding the root cause of disease and helping the person move towards wholeness and wellness. As part of that process, symptoms will often decrease or even disappear."

Hanaway estimates that 50% of the patients he has seen at the center have an autoimmune disease. That's an umbrella term, covering more than 80 different conditions, including type 1 diabetes, rheumatoid arthritis, lupus, and inflammatory bowel disease. "From the viewpoint of functional medicine, autoimmune disease is not some team you've joined and have to play on for the rest of your life," Hanaway says. "Rather, it's a continuum of illness and you can reverse your trajectory so that you are moving toward health rather than toward disease."

From a functional medicine perspective, when someone has inflammatory bowel disease, it may turn out to be related to the gut microbiome, to antibiotic therapies, to toxins, or to a pro-inflammatory diet. "It's different for different people," Hanaway says. "We work with each person to discover and eliminate the root causes of their condition."

The Cleveland Clinic Center for Functional Medicine plans to move forward in four major areas:

- clinical practice
- comparative effectiveness research
- research on total cost of care
- medical education (undergraduate, graduate, and CME)

The initial intake process at CFM includes a 75-minute visit with the doctor, review of care plan and labs with a nurse, an hour-long visit with a nutritionist, laboratory testing, plus a visit with a health coach.

Before the first visit, each patient fills out a detailed 20-page questionnaire. In addition to conventional questions about medical history and current symptoms, it includes unusual and exhaustive questions about nutrition, coping mechanisms, sources of support, plus an environmental assessment. Here are some sample questions:

continued on page 25 ➤

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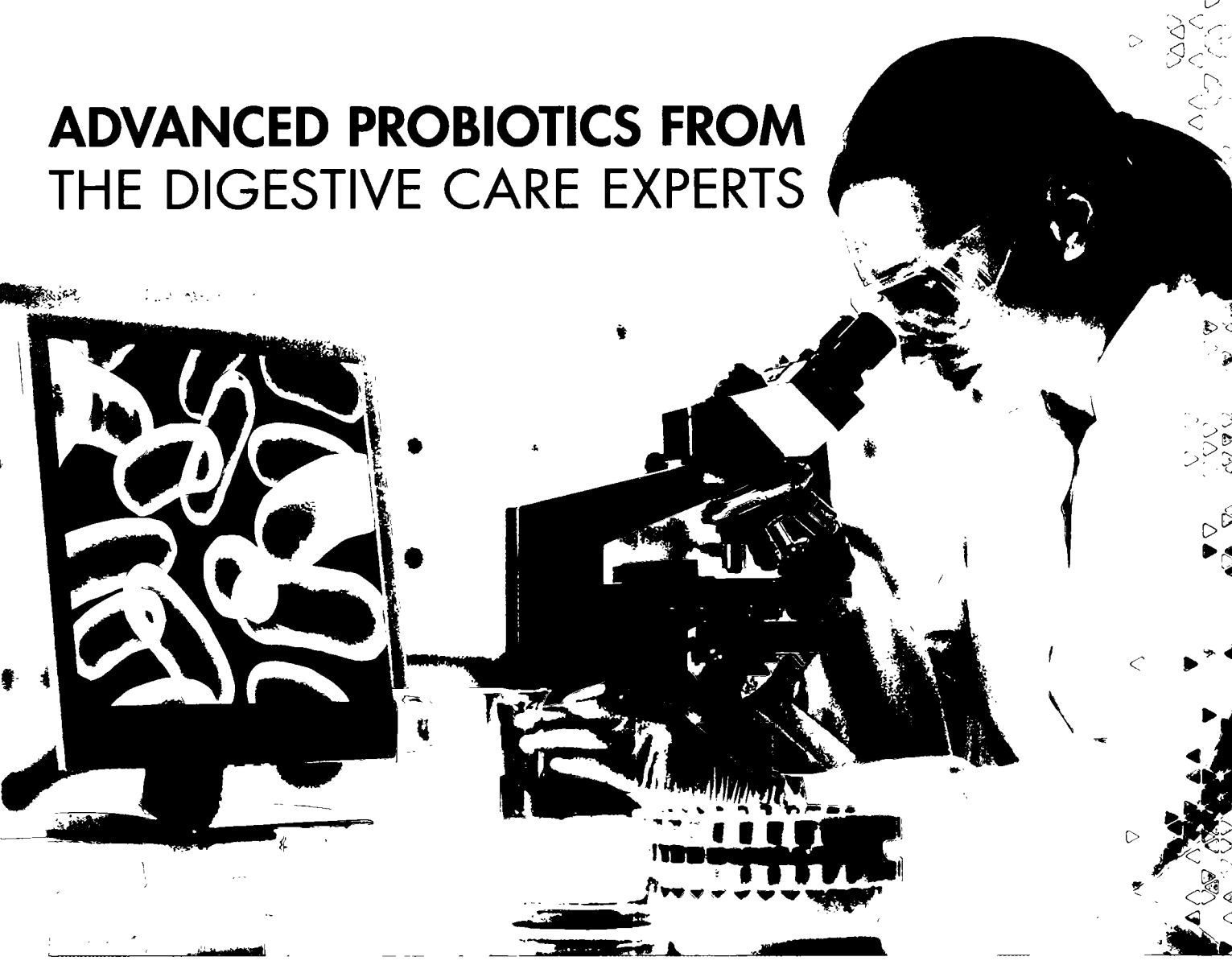

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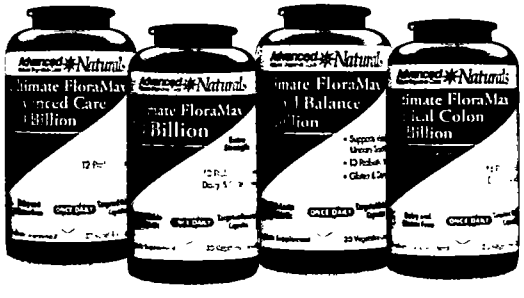

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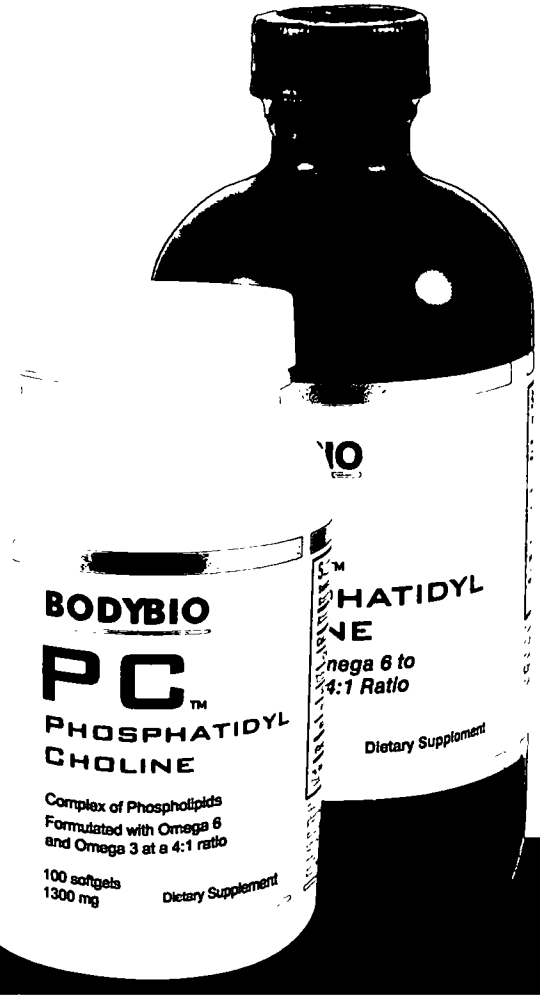

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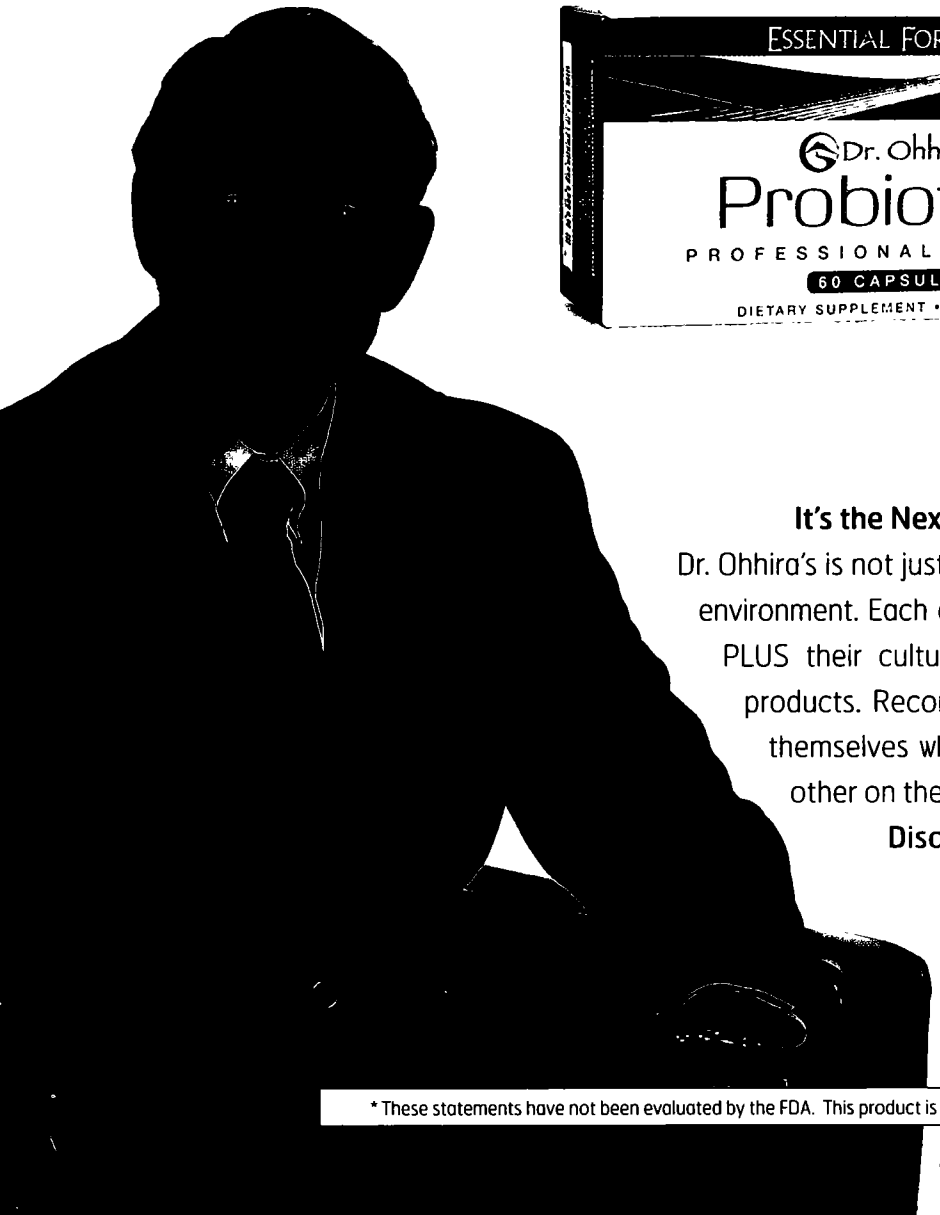

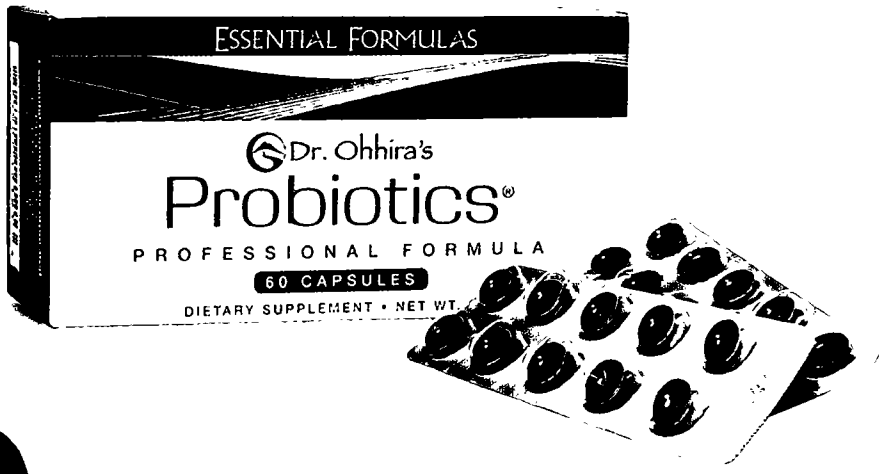

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- If you could eat only a few foods a week, what would they be?
- Do you eat too much/too little under stress?
- Do you ever feel guilty about your alcohol consumption?
- When you drink caffeine do you feel irritable or wired? Or experience aches and pains?
- Do you have an adverse reaction to garlic, cheese, citrus foods, monosodium glutamate, preservatives?
- Have you lived or worked in a damp or moldy environment?
- Do you feel significantly less vital than you did a year ago?
- Do you feel rested upon awakening?
- Do you have resources for emotional support?
- Are you happy?

The questionnaire also includes a "readiness assessment" which asks whether you are willing to:

- significantly modify your diet?
- practice relaxation techniques?
- engage in regular exercise?

It also asks:

- How confident are you of your ability to follow through on health-related activities?
- How supportive do you think the people in your household will be?
- How much support from our professional staff would be helpful to you?

Typically, a patient's first visit to CFM lasts about 4 hours, and there are regular follow-up visits. How is it possible to cover the cost of a 4-hour visit? Conventional insurance usually covers the physician visits. Insurance also covers nutritionist fees for patients who are obese or have diabetes, so about 50% of nutrition visits are currently covered by insurance. Health coach services are offered without a fee. The Cleveland Clinic is investing resources in the functional medicine program, because it expects to demonstrate over time that this approach delivers better clinical outcomes at lower cost.

Research on Comparative Effectiveness

This year, the center will begin prospective randomized clinical trials comparing the effectiveness of a functional medicine approach to a conventional medical approach for four diseases: inflammatory bowel disease, type 2 diabetes, asthma that is nonresponsive to conventional therapy, and recurrent migraines. IFM has drafted a set of consensus statements to codify functional medicine approaches for these four conditions, using this basic structure:

- setting goals of treatment
- understanding the patient's story – identifying key antecedents, triggers, and mediators
- analyzing clinical imbalances around the nodes of the functional medicine matrix
- identifying treatment approaches to address the underlying dysfunctions (clinical imbalances) that lead to disease

In addition to clinical research, CFM will be in an ideal position to examine the cost of functional medicine services compared with conventional care, looking at all inputs. The center will look at the total cost of care for those who choose to be seen at the center and are enrolled in the Cleveland Clinic Employee Health Program.

"Achieving change at the national level requires strategic efforts to create a substantive business case for the potential of functional medicine to improve health outcomes and reduce costs," Hanaway says. "CFM has four big advantages: a well-defined set of clinical approaches to care, an electronic record-keeping system that allows for the collection and analysis of data, a commitment to a research model that allows for the personalization of care, and the side-by-side collection of both outcome and cost data."

Education Based on Functional Medicine

The Center for Functional Medicine will develop educational programs based on functional medicine for three different levels: undergraduate medical education, graduate medical education (residency), and continuing medical education (CME). For example, it is developing enhanced training in nutrition for the Cleveland Clinic's Lerner College of Medicine, in collaboration with Case Western Reserve University School of Medicine. In addition, the center is developing a working relationship with the Heritage College of Osteopathic Medicine, which is based at a Cleveland Clinic hospital. The Heritage College Southpointe campus will open in August 2015, and is developing a pilot curriculum using a systems-based approach to medicine.

The center will collaborate with Cleveland Clinic residency programs for physicians, and it is developing CME programs for Cleveland Clinic physicians. For example, Cleveland Clinic practitioners are interested in learning more about nutritional supplements, including safety and quality considerations such as Good Manufacturing Practices (GMP) and Generally Recognized as Safe (GRAS) standards. "We look forward to developing activities that will educate physicians on how to evaluate nutritional supplements and use them most effectively in clinical practice," Hanaway says.

Inside These Hallowed Halls

The Cleveland Clinic was founded in 1921; it has a reputation as an incubator for new ideas, a model of the best possible health care. Every year it ranks as one of the best hospitals in the US. ➤

The Institute for Functional Medicine was founded in 1991 to promote a systems-biology approach to the prevention and management of chronic disease. Systems medicine reflects a movement away from one-size-fits-all medicine, toward care that is adapted to the individual's unique combination of genetics, environment, and lifestyle. Each specific expression of disease is shaped by continuous, ongoing interactions among these core influences. Over time, IFM has developed sophisticated models that apply these concepts to clinical practice.

For those of us who've been observing integrative and complementary/alternative medicine over the past 20 years, it's something of a surprise to learn that the Cleveland Clinic and the Institute for Functional Medicine are collaborating on a long-term project to evaluate the effectiveness of functional medicine according to academic research standards. It feels like a time for celebration.

But when Hanaway talks about CFM, he does so in the matter-of-fact tones of a health-care leader with a long list of projects and many details that require precise oversight. "Here we are in a forward-thinking clinical environment, having a conversation with thought leaders about the specifics of functional medicine and how to do accurate studies to compare the two approaches." he says. "We're having a pragmatic conversation about the best way to do this."

To have this conversation within the Cleveland Clinic is a new step, he notes. "In the past we've compared ourselves to them anecdotally. Now we'll be able to compare ourselves directly through randomized trials. We are inside the hallowed halls."

Understandably, the main focus for all participants is finding the most effective ways to provide excellent patient care. "Dr. Cosgrove, the Cleveland Clinic CEO, and all the leaders at the various institutes here care most about putting patients first," Hanaway says. "That's their motto. Over the years, one of the hallmarks of the Cleveland Clinic has been its focus on innovation. They care most about helping patients, and now they perceive the functional medicine model as one way to do that."

Resources

The Institute for Functional Medicine: https://www.functionalmedicine.org

The Cleveland Clinic Center for Functional Medicine: http://my.clevelandclinic.org/services/center-for-functional-medicine

The questionnaire that patients fill out before their first CCCFM visit: http://my.clevelandclinic.org/ccf/media/Files/functional-medicine/Introductory%20Patient%20Information%20for%20LV.PDF

Elaine Zablocki has been a freelance health-care journalist for more than 20 years. She was the editor of *Alternative Medicine Business News* and *CHRF News Files*. She writes regularly for many health-care publications. ◆

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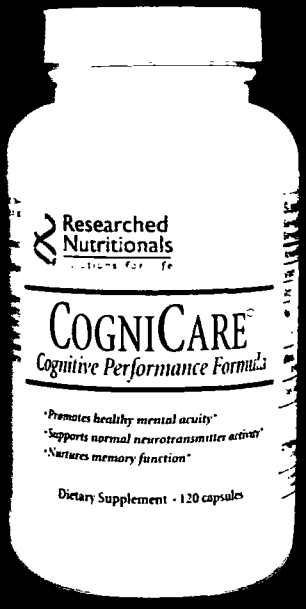

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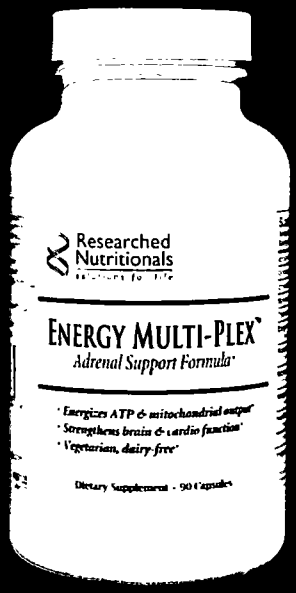

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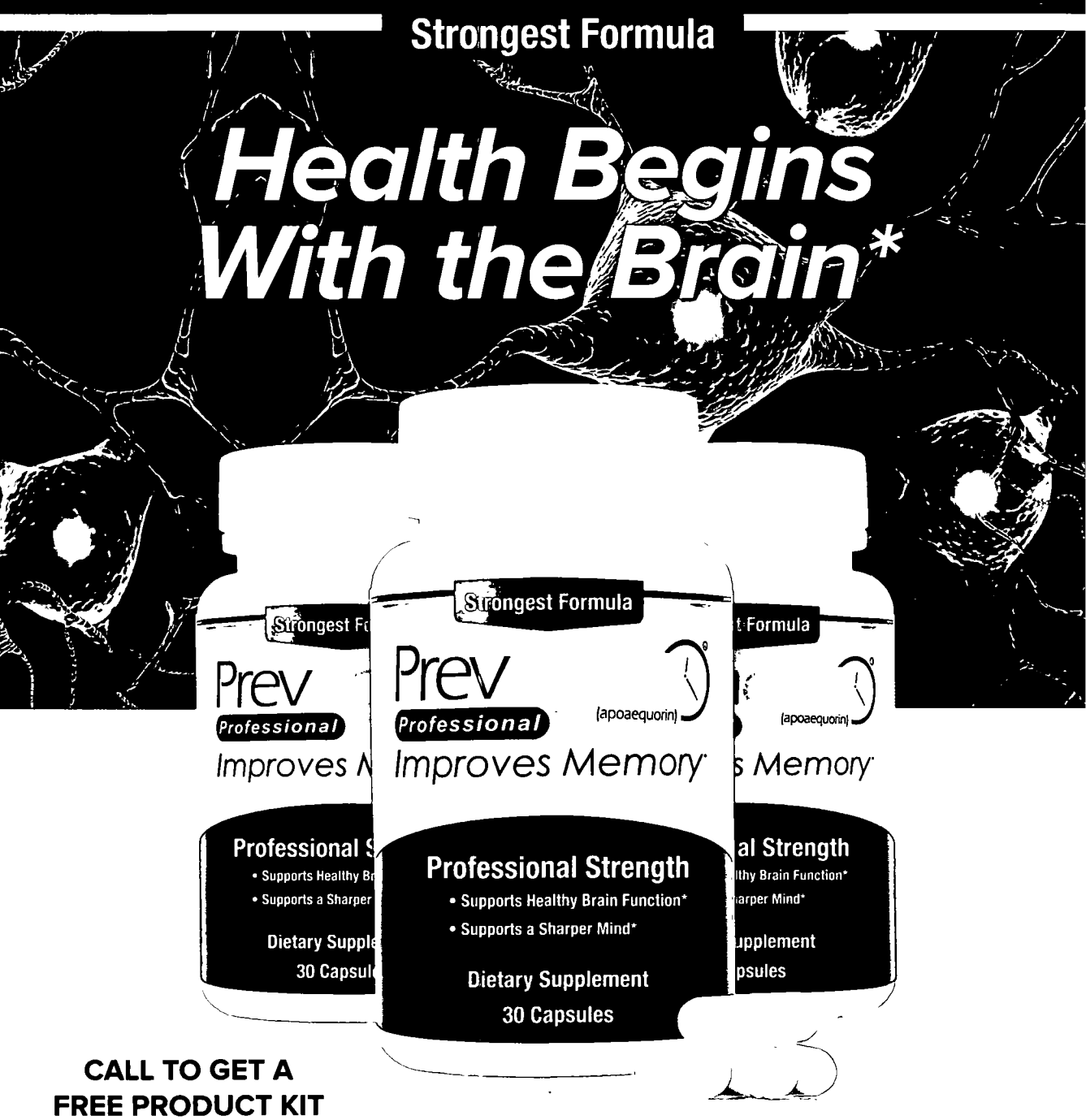

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Shorts

briefed by Jule Klotter
jule@townsendletter.com

Integrating Naturopathic and Allopathic Care

Naturopathic medicine, with its holistic, individualized approach, ill suits randomized placebo-controlled trials, designed to test isolated interventions. "In contrast to traditional Chinese medicine, which the allopathic community reduces to acupuncture, and chiropracty [sic], which the allopathic community reduces to spinal manipulation, naturopathy has defied reduction to a single modality," says Charles R. Elder, MD, MPH. Elder is Physician Lead for Integrative Medicine at Kaiser Permanente Northwest (KPNW). Isolated treatments used in naturopathic care – such as diet, exercise, herbs, and stress reduction techniques – have been studied, but few trials have investigated the effectiveness of naturopathic medicine protocols. As a result, insurers have little data to support the inclusion of naturopathic care.

When Washington State required health insurers to cover the services of naturopathic doctors, KPNW investigators asked respected naturopaths to tell them which conditions were appropriate for naturopathic care. The investigators then searched the medical literature for studies involving those conditions and treatments associated with naturopathy. Using this "modified, evidence-informed approach," KPNW was able to create its medical necessity criteria for naturopathic use. Referrals to naturopathic care are available to KPNW clients with osteoarthritis, menopausal symptoms, irritable bowel, headache, chronic fatigue, eczema, and conditions that have not responded to conventional care.

In his editorial, Elder discusses paradigm conflicts that hamper the integration of naturopathic and allopathic care. When dealing with hypothyroidism, for example, naturopaths often measure T3 and T4 levels in addition to ordering the thyroid stimulating hormone (TSH) test, and they recommend T3-T4 preparations, such as desiccated thyroid, instead of standardized Levothroid T4 supplementation. To a conventional physician, the extra tests are unnecessary and the nonstandardized treatment suspect. Patients may be confused by contradictory advice from medical practitioners with differing paradigms. Patients may also feel forced to choose sides in a tug-of-war between conventional and naturopathic medicine.

Broadening the scoop of allopathic and naturopathic continuing medical education to include both types of practitioners would increase interaction and understanding, making collaboration possible, says Elder. In addition to becoming familiar with naturopathic perspectives and skills, allopathic doctors could learn about herbs and noninvasive treatments for chronic disease. Naturopathic physicians could identify practices that might augment a patient's allopathic care. Both types of practitioners would gain a better understanding of when to consult or collaborate with the other. "Establishing and improving lines of open, respectful, constructive communication," Elder writes, "will be a first step toward developing the type of collaboration between allopathic and naturopathic physicians that our patients deserve."

Elder CR. Integrating naturopathy: can we move forward? *Permanente J.* Fall 2013;17(4):80–83. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3854814. Accessed November 22, 2014.

Naturopathic Care Demographics

Musculoskeletal problems, ill-defined symptoms (e.g., fatigue, malaise), digestive problems, and mental health issues are the most common reasons that people use onsite clinics at naturopathic colleges, according to a 2014 study. The study compared patient visit data from clinics at Bastyr University (Seattle, WA), National College of Natural Medicine (Portland OR), Southwest College of Naturopathic Medicine (Tempe AZ), and the Canadian College of Naturopathic Medicine (Toronto, Ontario, Canada) with CDC data from office-based primary-care (PC) allopathic physicians, PC doctors at community health centers, and PC doctors who reported using CAM methods.

The study's authors reported a 44% overlap between the top 25 diagnoses at naturopathic clinics and the top 25 at allopathic clinics. Routine infant/child health checkups, the most common reason for allopathic care, did not appear on the naturopathic list; malaise, constipation, HIV, insomnia, and menopause did not appear on the allopathic lists. The percentage of patient visits for endocrine and metabolic diseases was similar for naturopathic clinics, office-based PC, and community health centers.

Patients sought naturopathic care despite a lack of economic support. Fifty percent of naturopathic visits were paid for out of pocket. Only about 23% of the naturopathic

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visits were covered by private insurance, compared with over 50% of allopathic visits. The remaining naturopathic visits were discounted or not charged. At this point, naturopathy is not covered by Medicare or Medicaid. These US government programs paid for 32.85% of the PC-CAM visits, 35.15% of the office-based visits, and 55.41% of the community health center visits.

Chamberlin SR, Oberg E, Hanes DA, Calabrese C. Naturopathic practice at North American academic institutions: description of 300,483 visits and comparison to conventional primary care. *Integr Med Insights*. 2014;9:7–15. Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC4039213/pdf/imi. Accessed November 18, 2014.

Naturopathic Medicine and Cardiovascular Disease

Naturopathic care combined with usual care improved cardiovascular-risk biomarkers more than usual care alone, according to a 2013, 1-year, randomized clinical trial. The trial involved 246 Canadian postal workers, ages 25 to 65, living in Toronto, Vancouver, and Edmonton, who showed risks for cardiovascular disease. (207 completed the study.) All participants received usual care plus biometric measurement (weight, waist circumference, blood pressure, lipid and glucose levels) at baseline, 26 weeks, and 52 weeks from their family physicians. In addition, the naturopathic group received individualized health-promotion counseling and recommendations for nutritional medicine or dietary supplements from licensed naturopaths during work-site clinic visits.

"For consistency with naturopathic practice, treatment recommendations were individualized from a predetermined menu of interventions based on which risk factors were present and patient preferences," explain Dugald Seely, ND, and coauthors. The "menu" consisted of weight-loss counseling (via calorie restriction and physical activity); dietary recommendations based on the Mediterranean and portfolio diets; and supplements such as omega-3 fatty acids, soluble fiber, coenzyme Q10, and plant sterols.

The study's primary outcomes were measured using the Framingham risk algorithm to assess the 10-year risk of having a cardiovascular event and the Adult Treatment Panel III diagnostic criteria to assess for metabolic syndrome. At 52 weeks, the naturopathic group had a 3.07% lower risk of having a 10-year cardiovascular event, compared with the control (control: 10.81%; naturopathic care: 7.74% [95% confidence interval (CI) −4.35% to 1.78%], $p < 0.001$). The naturopathic group also had a lower frequency of metabolic syndrome (control: 48.48%; naturopathic care: 31.58%; risk reduction −16.90% [95% CI −29.55% to −4.25%], $p = 0.002$). Adverse events reported in the naturopathic group included fishy-tasting eructation from fish oil capsules (n = 3), indigestion from phosphatidylcholine (5 g/day; n = 2), and heart palpitation (n = 1).

This study did not determine the relative benefits of lifestyle modification vs. supplementation. It would be interesting to see three-arm studies that compare full naturopathic care to naturopathic care with placebo supplements, and to supplements alone.

This Canadian study was also the basis for a cost-effectiveness analysis. The economic study, led by Patricia M. Herman, ND, PhD, used data from 156 of the study participants (63.1% of the original control group (n = 77); 63.7% of the original naturopathic care group (n = 79). With participants' consent, the researchers totaled all medical claims that were submitted 6 months before baseline through study's end for each individual, including prescription medications and visits to chiropractors, physiotherapists, massage therapists, and acupuncturists. In addition, they collected the amount of sick leave paid by the employer. Work productivity (presenteeism) was assessed using the World Health Organization Health and Performance Questionnaire.

Participants receiving naturopathic care in addition to usual care spent an average of C$715 for visits to doctors and other practitioners, prescription medication, and natural health products, compared with C$413 for the usual care control group. (Average cost of a naturopathic doctor visit at that time was C$152.50 per hour compared with C$42.35 per hour for a conventional doctor visit.) Work productivity was significantly better in the naturopathic group. The researchers calculated a net saving for employers of C$1187 per participant, even if the employer paid the full cost of naturopathic care and biometric screening. Follow-up for a longer period is needed to see if risk reductions and cost savings continue.

Herman PM, Szczurko O, Cooley K, Seely D. A naturopathic approach to the prevention of cardiovascular disease. *J Occup Environ Med*. February 2014;56(2):171–176. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3921268/pdf/joe. Accessed November 19, 2014.

Seely D, Szczurko O, Cooley K, et al. Naturopathic medicine for the prevention of cardiovascular disease: a randomized clinical trial. *CMAJ*. June 11, 2013;185(9):E409–E416. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3680587/pdf. Accessed November 19, 2014.

Patient Perspectives of Naturopathic Care

A 2012 study, supported by the National Institutes of Health National Center for Complementary and Alternative Medicine, looked at the perceptions of 37 patients who engaged in naturopathic care (NC) for the first time during a year-long observational study. This observational study asked Group Health clients with suboptimally controlled type 2 diabetes to consult with a naturopathic doctor (ND) in the community. (Naturopathic care was included in their health coverage.) Naturopathic care was adjunctive, not integrated with the primary care that patients were already receiving. The observational study reported "improvements in patient-reported outcomes (e.g., glucose monitoring, diet, self-efficacy, motivation, and mood) and reductions in blood glucose that exceeded those for similar patients who do not receive [adjunctive naturopathic care]." Negative responses to NC in the observational study included adverse reactions to dietary supplements (n = 2), guilt for not following recommendations (n = 1), higher blood pressure (n = 1), and complaints about the high cost of supplements.

When the observational study ended, 22 of the 37 patients agreed to take part in a focus group or a telephone interview to elicit their opinions about the naturopathic care experience. The authors noted that those who agreed to participate were

also the ones who were most satisfied with naturopathic care: "As a result, the views of the participants described in this study are almost certainly more positive than would have been the case had we had a higher participation rate."

Many interviewees found the combination of conventional and naturopathic care beneficial for helping them manage diabetes. The NDs provided information in a relaxed, personal way that helped patients understand their condition more holistically: "Several commented that the ND attended not only to their diabetes but also to other aspects of their health and life [including psychosocial factors] that might impact their diabetes and their ability to engage in self-care." This additional information helped some "re-engage with their conventional primary care providers and/or improve their adherence to prescription medication."

Naturopathic physicians worked collaboratively with patients, encouraging them to experiment with diet, exercise, and stress reduction techniques and then observe the effect on glycemic levels. By encouraging patients' active participation, the NDs were able to help them come up with an individualized management plan that increased patients' engagement, optimism, and feeling of having more control. The NDs also suggested practical tips and supplements for improving glycemic levels, such as eating a small piece of protein at bedtime to bring morning levels down. "Many participants emphasized that the diet, exercise, and stress management strategies they learned differed in quantity and specificity from those they had previously received in diabetes education classes or from their primary care provider," state Oberg et al.

The high cost of supplements, which are not covered by insurance, was the only complaint from the interviewed patients.

Bradley RD, Sherman KJ, Catz S, et al. Adjunctive naturopathic care for type 2 diabetes: patient-reported and clinical outcomes after one year. *BMC Complement Altern Med.* 2012;12. Available at www.biomedcentral.com/1472-6882/12/44. Accessed December 12, 2014.

Oberg E, Bradley R, Hsu C, et al. Patient-reported experiences with first-time naturopathic care for type 2 diabetes. *PLoS ONE.* November 2012;7(11):e48549. Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC3492455/pdf. Accessed November 18, 2014.

Public Health and Naturopathic Medicine Research Similarities

"[Naturopathic medicine] is not defined by the substances used but rather by the principles that underlie and determine its practice, which include the following: the healing power of nature, find the cause, do no harm, treat the whole person, prevention, and doctor as teacher," write Jon Wardle, ND, MPH, and Erica B. Oberg, ND, MPH. Its holistic system of health promotion, grounded in patient education, makes it ideally suited for addressing the many chronic disorders, such as type 2 diabetes and cardiovascular disease, which respond to lifestyle behaviors. However, few research studies testing its effectiveness have been conducted. Naturopathic medicine's

pragmatic, holistic framework cannot fit into a blinded, randomized, controlled trial (RCT), a model that often fails to show real-world effects.

Instead of relying on biomedical research models, such as RCTs, Wardle and Oberg suggest using public health research models to study naturopathic medicine. Public health, like naturopathy, emphasizes health promotion and patient education. It uses multidisciplinary, multimethod, and whole-systems approaches to conduct research. Whole-systems research, including pragmatic RCTs and outcomes studies, uses actual patient populations and settings instead of the narrowed parameters typical of most RCTs. Whereas successful, blinded RCTs show that an intervention has greater effect than a placebo, whole systems research aims "to produce the largest clinical effect."

Outcomes studies are versatile. "Outcomes studies can be conducted as case-control studies matching patients receiving naturopathic care to conventional or usual-care controls," Wardle and Oberg state. Specific components of naturopathic care can be tested by comparing disease or risk outcomes in groups of patients receiving routine naturopathic care (NC) and those receiving NC minus a specified treatment. In addition to biomedical outcome measures (e.g., lipoproteins, glycemic levels), outcomes studies can be used to evaluate health behaviors, quality of life, the physician's role, care satisfaction, cost effectiveness, and other factors.

Although blinded RCTs are presently considered the "gold" standard, the establishment of the Patient-Centered Outcomes Research Institute (PCORI) indicates a growing acceptance for other research designs. As part of its mission, this federally-funded institute aims " ... to give appropriate weight to health services methods such as pragmatic trials and observations methods," according to Wardle and Oberg. Both naturopathic medicine and public health will benefit from an increased acceptance of whole-systems research.

Sutherland E. Naturopathic medicine and public health: teaming up for a transformative tomorrow. *J Altern Complement Med.* 2011;17(11):981–982. Available at EBSCO. Accessed November 18, 2014.

Wardle J, Oberg EB. The intersecting paradigms of naturopathic medicine and public health: opportunities for naturopathic medicine. *J Altern Complement Med.* 2011:17(11);1079–1084. Available at EBSCO database. Accessed November 18, 2014.

Whole-Systems Research Challenges

In 2009, an international roundtable panel consisting of six researchers discussed several challenges that they face as they apply whole-systems research concepts to the study of holistic CAM practices. First, they reported a need to collect more and diverse data than conventional research demands. Conventional biomedical studies focus solely on information that can be interpreted with conventional statistical analysis. Consequently, valuable information that does not fit the statistical model is ignored. German researcher Frauke Musial, PhD, said, "I believe that the most important thing we can do in training other people to conduct whole-systems research is to broaden the attention to cover points to which they were not trained to be attentive."

Second, panel members advocated for focusing more on individual differences and less on group averages. Each person is a complex dynamic system with individual variations underlying a disease label. Instead of studying a set number of variables at predetermined points in time, US researcher Mikel Aickin, PhD, would like medical research to emulate engineering research: " ... engineers examine all of the factors that exert forces and have influences on other components of the system and on the system as a whole."

Practitioners and medical researchers are also part of the dynamics. Norwegian Sameline Grimsgaard, MD, PhD, MPH, reported that individual acupuncturists had very different results in one study, even though the needling patterns they used were the same. Similarly, Cheryl Ritenbaugh, PhD (US), said a Women's Health Initiative study comparing hormone treatment and diet at 40 sites had different results that correlated to the principle investigator's interest: " ... the sites led by nutrition-oriented investigators tended to perform better in that aspect of the trial, and the sites led by hormone-oriented investigators performed better in that aspect. So research results are not just determined at the level of the providers and the patients ... "

Publishing these more complex studies is challenging. The panel suggested that print journals might publish the concept, design, methods, discussion, and most prominent results. Complete results would be available online.

Ritenbaugh C, Aickin M, Bradley R, Caspi O, Grimsgaard S, Musial F. Whole systems research becomes real: new results and next steps. *J Altern Complement Med.* 2010; 16(1):131–137. Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC3056386/pdf. Accessed November 18, 2014.

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Literature Review & Commentary

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

Probiotic for Diverticular Disease

Two hundred ten patients (median age, 62 years) with symptomatic, uncomplicated diverticular disease in remission were randomly assigned to receive, in double-blind fashion, 1600 mg per day of mesalazine, *Lactobacillus casei* subsp. DG (24 billion organisms per day), both treatments, or placebo. The treatments were administered the first 10 days of each month for 12 months. A recurrence was defined as the reappearance of abdominal pain with a rating of at least 5 on a scale of 10, with higher numbers indicating worse symptoms. The proportion of patients who had a recurrence was 0% with combination therapy, 13.7% with mesalazine, 14.5% with the probiotic, and 46% with placebo ($p < 0.001$ for probiotic vs. placebo; $p < 0.01$ for mesalazine plus probiotic vs. mesalazine alone). Acute diverticulitis occurred in 6 patients receiving placebo and in 1 patient receiving the probiotic ($p = 0.003$).

Comment: Patients with diverticular disease have been found to have a decrease in healthy colonic bacterial flora and an increase in the number of pathogenic bacteria. It has been suggested that these changes may promote inflammation and an increase in epithelial cell proliferation in the colonic mucosa. These results of the present study indicate that *L. casei* subsp. DG was effective for maintaining remission of symptomatic, uncomplicated diverticular disease, and that the combination of the probiotic and mesalazine was more effective than the probiotic by itself.

Tursi A et al. Randomised clinical trial: mesalazine and/or probiotics in maintaining remission of symptomatic uncomplicated diverticular disease – a double-blind, randomised, placebo-controlled study. *Aliment Pharmacol Ther.* 2013;38:741–751.

Probiotic Prevents Dental Caries and Gingivitis

One hundred thirteen mother-child pairs were randomly assigned to receive, in single-blind fashion, the probiotic *Lactobacillus reuteri* strain ATCC 55730 (derived from breast milk) or placebo. The mothers received 5 drops of oil daily (containing 10^8 colony-forming units) during the last month of gestation, and the children received the same daily dose during the first year of life. At 9 years of age, the proportion of children who were free of dental caries was significantly higher in the probiotic group than in the placebo group (82% vs. 58%; $p < 0.01$). In addition, there were fewer sites with gingivitis in the probiotic group than in the placebo group ($p < 0.05$). There was no difference between groups in the concentration of *Streptococcus mutans* (an organism that promotes the development of dental caries).

Comment: These results demonstrate that daily administration of *L. reuteri* strain ATCC 55730 during the last 4 weeks of pregnancy and the first year of the child's life resulted in a decrease in caries prevalence and less gingivitis at 9 years of age. The probiotic presumably worked by altering the oral flora, although it did not influence the concentration of *S. mutans*. Studies using xylitol gum have shown that the best results are obtained when treatment is begun before the child's teeth have erupted. If that is also the case with probiotics, then treatment should be started early in life, as was done in the present study.

Stensson M et al. Oral administration of Lactobacillus reuteri during the first year of life reduces caries prevalence in the primary dentition at 9 years of age. *Caries Res.* 2014;48:111–117.

Pantethine Lowers Serum Cholesterol

Thirty-two patients (mean age, 51 years) at low-to-moderate cardiovascular disease risk who were eligible for statin therapy according to the National Cholesterol Education Program guidelines were randomly assigned to receive, in double-blind fashion, pantethine (300 mg twice a day for 8 weeks, then 300 mg 3 times per day for 8

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weeks) or placebo. The mean serum LDL-cholesterol level decreased by 11% after 16 weeks in the pantethine group and increased by 3% in the placebo group ($p = 0.01$ for the difference in the change between groups). The decrease in LDL-cholesterol levels compared with placebo was also significant in the pantethine group after 8 weeks ($p < 0.03$).

Comment: Pantethine is the stable disulfide form of pantetheine, a biologically active form of pantothenic acid. As a precursor to coenzyme A, pantethine plays a role in fat metabolism. Pantethine also inhibited HMG-CoA reductase activity in isolated rat hepatocytes, an effect that mirrors that of statin drugs (Cighetti G et al. Effects of pantethine on cholesterol synthesis from mevalonate in isolated rat hepatocytes. *Atherosclerosis*. 1986;60:67–77). Several previous studies, mostly uncontrolled, have shown that pantethine supplementation can lower LDL-cholesterol levels, a finding that was confirmed in the present randomized controlled trial. Pantethine has also been reported previously to decrease triglyceride levels and to increase HDL-cholesterol levels. Pantethine is generally well tolerated and has not been reported to cause serious side effects. However, unlike with statin drugs, there have been no long-term studies to determine whether lowering lipid levels with pantethine decreases the incidence of cardiovascular disease. Pantothenic acid, despite being structurally similar to pantethine, has no effect on lipid levels.

Evans M et al. Pantethine, a derivative of vitamin B5, favorably alters total, LDL and non-HDL cholesterol in low to moderate cardiovascular risk subjects eligible for statin therapy: a triple-blinded placebo and diet-controlled investigation. *Vasc Health Risk Manag*. 2014;10:89–100.

Human Milk for Diaper Rash

One hundred forty-one Iranian infants (mean age, 4.6 months) with mild-to-moderate acute diaper dermatitis were randomly assigned to apply sparingly 1% hydrocortisone ointment or human breast milk twice a day for 7 days. The breast milk used was the hind milk (the milk at the end of the feed that is higher in fat content). Marked improvement was seen in both groups, and improvement was similar between groups.

Comment: This study demonstrates that topical application of human breast milk is as effective as topical hydrocortisone for the treatment for diaper rash in infants. The mechanism of action is not known.

Farahani LA et al. Comparison of the effect of human milk and topical hydrocortisone 1% on diaper dermatitis. *Pediatr Dermatol*. 2013;30:725–729.

N-Acetylcysteine Prevents Exacerbations in Chronic Obstructive Pulmonary Disease

One thousand and six Chinese patients (mean age, 66 years) with moderate-to-severe chronic obstructive pulmonary disease (COPD) were randomly assigned to receive, in double-blind fashion, 600 mg of N-acetylcysteine (NAC) twice a day or placebo for 1 year. The mean number of exacerbations per patient was significantly lower in the NAC group than in the placebo group (1.16 vs. vs. 1.49; 22% decrease; $p = 0.001$).

Comment: NAC is a precursor to glutathione, one of the major antioxidants in lung tissue. NAC also functions as a mucolytic agent when given by inhalation. The extent to which this effect occurs after oral administration is not clear, although orally administered NAC has been shown to enhance the clearance of mucus by the pulmonary cilia. The results of the present study demonstrate that treatment with NAC can prevent disease exacerbations in patients with moderate-to-severe COPD. Most, but not all, previous research has found a similar effect of NAC.

Zheng JP et al. Twice daily N-acetylcysteine 600 mg for exacerbations of chronic obstructive pulmonary disease (PANTHEON): a randomised, double-blind placebo-controlled trial. *Lancet Respir Med*. 2014;2:187–194.

Interpreting Negative Research

One hundred sixty adults with recurrent aphthous ulcers (canker sores) were randomly assigned to receive, in double-blind fashion, a daily multivitamin providing the US reference daily intake for vitamins A, B complex, C, D, and E or placebo for 1 year. The mean number of new episodes of aphthous ulcerations was nonsignificantly lower by 9% in the multivitamin group than in the placebo group (4.19 vs. 4.60 episodes; $p = 0.69$). The mean duration of new episodes was also nonsignificantly lower by 3.7% in the multivitamin group than in the placebo group (8.66 vs. 8.99 days; $p = 0.60$). The authors concluded that supplementation with a daily multivitamin did not decrease the number or duration of recurrent aphthous stomatitis episodes.

Comment: Many low-potency multivitamin supplements on the market contain artificial coloring agents and other additives to which some individuals are allergic or sensitive. I wrote to the author of this study, to ask what additives were present in the multivitamin used in the study. He replied that the multivitamin contained artificial coloring agents, whereas the placebo was pure lactose. According to some investigators and to my clinical experience, food allergy is one of the most common triggering factors for aphthous ulcers. The presence of allergens in the multivitamin may therefore have masked a beneficial effect of the vitamins. Previous research suggests that several different nutrients, including B vitamins and iron, can reduce the recurrence rate of aphthous ulcers.

Lalla RV et al. Multivitamin therapy for recurrent aphthous stomatitis: a randomized, double-masked, placebo-controlled trial. *J Am Dent Assoc*. 2012;143:370–376.

Iron Depletion Improves Nonalcoholic Fatty Liver Disease

Thirty-eight patients (mean age, 54 years) with severe nonalcoholic fatty liver disease and elevated serum ferritin levels (250 ng/ml or higher) were randomly assigned to lifestyle changes plus iron depletion by phlebotomy ($n = 21$) or to lifestyle changes alone (control group; $n = 17$). Iron depletion was achieved by removing 350 ml of blood every 10 to 15 days according to baseline hemoglobin values and venesection tolerance, until the ferritin level was less than 30 ng/ml and/or transferrin saturation was

less than 25%. Among the 21 patients who followed the program, the proportion of patients who had histological improvement was higher (67% vs. 22%; $p < 0.04$) and the degree of improvement in steatosis grade was greater ($p = 0.02$) in the iron-depletion group than in the control group. Among the 35 patients who were followed up at 2 years, serum levels of liver enzymes (alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transpeptidase) were lower in iron-depleted than in control patients ($p < 0.05$).

Comment: Elevated serum ferritin levels with mild hepatic iron accumulation is seen in 20% to 30% of patients with nonalcoholic fatty liver disease who are referred to specialty clinics. Iron overload directly induces liver damage and plays a role in the pathogenesis of metabolic syndrome by promoting insulin resistance. The results of the present study suggest that iron depletion by phlebotomy enhances the beneficial effects of lifestyle changes in patients with nonalcoholic fatty liver disease and iron overload (as indicated by elevated serum ferritin levels). Other, less invasive, ways to decrease iron overload are to avoid red meat and to consume foods and beverages that inhibit iron absorption (such as coffee, tea, and soy products).

Valenti L et al. A randomized trial of iron depletion in patients with nonalcoholic fatty liver disease and hyperferritinemia. *World J Gastroenterol.* 2014;20:3002–3010.

Another Benefit of Chewing Your Food

Forty-five volunteers (aged 18–45 years) were asked to attend 3 test sessions to eat pizza for lunch until comfortably full by chewing each portion of food either 100%, 150%, or 200% of their usual number of chews before swallowing. Food intake in the sessions with 150% and 200% of the usual number of chews was reduced significantly, by 9.5% and 14.8%, respectively, compared with the 100% session. Increasing the number of chews also prolonged meal duration and reduced the eating rate.

Comment: These results suggest that increasing the number of chews before swallowing may reduce food intake and potentially help prevent obesity. Chewing food thoroughly also stimulates the secretion of saliva, which contains factors that help prevent the development of dental caries and other factors that help protect the esophagus from the deleterious effects of acid reflux. There is truth to the old saying that "Nature will castigate those who do not masticate."

Zhu Y, Hollis JH. Increasing the number of chews before swallowing reduces meal size in normal-weight, overweight, and obese adults. *J Acad Nutr Diet.* 2014;114:926–931.

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F.A.C.T. – Just the Facts

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

Are Metal Toxicity, Metabolic, and Genomic Tests Key to Improving Health?

There are several saliva, urine, and blood provocation tests that I have utilized over the years to determine a patient's toxic body burden. All hold some value, but I believe that genetic testing is destined to dramatically change the way medicine is practiced today, and will soon become a routine part of personalized protocols in the prevention of chronic diseases.

Everyone today is heavy metal toxic and will benefit from a daily detoxification program, the more aggressive the better. My patients who complete a gene panel typically always show some type of genetic blocks to their detox pathways, whether you look at acetylation, sulfation, or methylation. This information helps motivate them to more consistently adhere to the protocols needed for detoxification and recommended supplementation.

Blood tests for heavy metals aren't always indicative of toxicity, however. Lead accumulates in bone, and is then slowly released back into the body for years and even decades, contributing to a host of health problems, according to a study conducted at the Harvard School of Public Health (HSPH). Howard Hu, an associate professor of occupational medicine at HSPH, and lead author of the study published in *JAMA*, reports for the first time that "bone lead is exerting a toxic effect even in the presence of low blood-lead levels."

To measure bone lead, the researchers developed a noninvasive method using X-ray fluorescence (XRF). Unfortunately, this method of in vivo testing is used only in about a dozen facilities in North America, and largely for research purposes, rather than routine diagnosis. Professor Hu is optimistic and believes that "Bone lead screening may become an important preconception clinical test, just like genetic screening."

Hair analysis is also useful in detecting increased exposure to toxic heavy metals, as well as helping to identify deficiencies of essential elements. A 2012 study in *Mædica – a Journal of Clinical Medicine* provided data showing that hair mineral analysis may be of use in diagnosing autism spectrum disorder (ASD). This is surprising, as although I have found hair mineral testing very useful in clinical practice to help motivate patients to identify and remove heavy metals, it often finds no mercury or lead in autistic children because standard tissue testing methods are often nonindicative of total body burden levels of toxicity, and essential bone mineral testing is not still not widely available. It has also been reported that there are much lower levels of heavy metals found in many autistic children due to their impaired ability to excrete heavy metals.

For instance, lead is excreted primarily through the feces, in urine, and to a very minor extent, in sweat and saliva. But because lead excretion is rather inefficient, most of an absorbed lead dose will ultimately be stored in the body. This is important to know, since IV chelation does not remove lead from bones, so patients feel better with their courses of IV EDTA, but will get ill again unless they are kept on some long-term detoxification program. This is why I use oral chelators such as CaEDTA and zeolite, on a daily basis for life, since bone takes 15 years to remodel, and while remodeling they are consistently releasing lead into soft tissues.

I personally benefited dramatically from IV chelation therapy many years ago, and at first I really thought I had found the answer to reversing arteriosclerosis. It turns out that things in medicine are not always that simple. At the time I was not fully able to imagine the cellular metabolic basis for the dramatic successes I had in documenting improved blood flow in my patients, even those with gangrene, memory or vision loss, or inoperable blockages in their coronary blood vessels. Today I know that a large part of the success of chelation-related blood flow improvement is attributable to "getting the lead out"!

As reported in a 2007 study in the *Journal of Nutrition*, toxic and heavy metal exposures early in life may promote disease later in life, via epigenetics. Most recently, in the September 22, 2014, issue of *New Scientist*, we learn how essential our mitochondria are for *all* life processes. Mitochondria are the "micromanagers of everything from memory and ageing to obesity." They are also especially vulnerable to heavy metals and environmental toxins, resulting in mitochondrial dysfunction, and decreased metabolism and energy production.

This is so important to understand, as we are all toxic, and so we are all suffering from power failure! On a chemical and physical level all disease is caused by a loss of organization – by entropy – or essentially a loss of energy. Dr. Douglas Wallace of the Center for Mitochondrial and Epigenomic Medicine in Philadelphia says, "Every one of the diseases we can't solve is absolutely logical if we put energy at the center." Mitochondria are the powerhouses in our cells that produce energy through two metabolic processes. One is the citric acid cycle, which converts fuel (food) into ATP and hydrogen, and the second is through oxidative phosphorylation, whereby hydrogen is combined with oxygen to generate ATP. Oxidative phosphorylation is the primary energy process for all aerobic organisms. Pollution and various toxins and poor food all contribute to the breakdown of this fundamental cycle. Mitochondria produce power for our cells, and also give out charged molecules called free radicals. Once thought to have only destructive effects, free radicals have been found to be essential signaling molecules needed to regulate critical cell processes that stimulate immune responses against viruses, assist in autophagy, and protect us against the ravages of time. This is also why consuming too many antioxidants can disrupt the precise balance of mitochondrial redox signaling, causing us harm.

Wallace feels a strong sense of mission to change the way people think about medicine because the resulting treatments for disease could be game changing for human health. He sees connections to mitochondria in everything from heart disease to obesity to diabetes to Alzheimer's disease. "We're on the verge of a major revolution of medicine," Wallace says. "We're going to change from an anatomically based medicine to an energetically based medicine, and more than half of all the complex diseases that we're worried about right now may be solved that way." A method that Wallace and his team are currently developing is a diagnostic test that will easily detect mitochondrial defects using a patient's exhaled breath, and practitioners may have access to this new technology using a smartphone app, rumored to be available as early as this year.

This is why I am an enthusiastic proponent of genomic testing. A couple of the more affordable gene panels available, which I have personally used, are provided by Fitgenes.com and SmartDNA.com. With 72-plus genes screened for, patients receive a detailed personal report of 60 to 80 pages, learning much about their possible gene-disease related susceptibilities and which diet and nutritional supplements are the best for them. However, in the near future gene tests will focus more on mitochondrial DNA, and not just nuclear DNA, as it is more indicative of mitochondrial reactive oxygen species (mROS) generation and regulation, which is the most critical for healthy cell function. At any rate, if we do too little testing and find nothing of consequence, patients may give up and never go back to delve deeper. Since my patients usually come to me after all else has not worked, I feel I need the broader test, and I usually uncover enough issues that patient compliance with my aggressive, intensive F.I.G.H.T. program is much improved. With improved compliance, my results get better and better and that makes it all seem worthwhile.

For instance, if patients find that they produce little or no glutathione, they are more willing to take recommended supplements, such as oral acetyl glutathione, NAC, or the even more powerful stabilized redox signaling molecules now available in supplement form such as ASEA. In clinical studies, ASEA has shown to naturally increase intracellular production of glutathione 500% to 800%. As patients more rapidly see and feel vast improvements in their health, they are more apt to follow the program for life. Otherwise, without knowing they have a gene related issue, sick patients hope for overnight results and often only plan to stay on their program religiously for 1 month or so. If they do not improve, they give up and if they are feeling better, without some gene testing that makes it clear why they need the extra support, they taper off supplements and go back to their prior lifestyle.

Just the Facts

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Meaningful answers are being found for complex conditions that, without gene testing, no one has been able to help. What we do to provide our cells with the optimal environment of necessary nutrients for energy production, repair and function, and the elimination of toxins and wastes, along with affordable and meaningful tests to help patients adhere to their programs for the long-term, are all key measures in achieving and maintaining health, happiness, and longevity.

Here are two Q&A examples on the subjects of metal provocation and genetic testing methods utilized by F.A.C.T. forum participants (names and responses redacted to protect member confidentiality).

Q: Can someone provide information on heavy metal testing in terms of provocation studies (i.e. what form and what dose – specifically for urine collection are you using). I have been unable to purchase oral DMPS for over one year. Thanks, ~MB

A1: Dear MB, We first draw blood for a random Lead, Mercury, Arsenic & Cadmium, level.

We collect a random urine for Lead, Mercury, Arsenic, & Cadmium. On the same day, we administer Calcium EDTA at 1/2 the calculated dose. 125 mg of DMPS and 1.4 mg of Glutathione are likewise administered. At the time the DMPS is administered, a 6 hour urine is collected and sent to Doctors Data. ~CA

A2: I've been using a combination of CaEDTA (1.5g) IVP + DMPS (500mg) PO. If not available then DMSA as a single bolus based upon taking half of the therapeutic dose (25mg/kg, so 70kg person takes 875mg). ~EA

A3: We use DMSA advanced protocol, 10mg per 10lbs body weight. ~WP

A4: Dear MB, Please see www.melisa.org on the testing of metal sensitivity rather than metal exposure (through the examination of the metal concentration in body fluids). Different people have different susceptibility to metals and therefore, some might tolerate a certain amount of heavy metals in the body. Usually the measured metal concentrations are below the risk limit which is determined under the occupational conditions. Hair analysis will tell you about the patient's excreting activity but not about the deposition of the metal in the body. It is well known that patients in danger for metal toxicity/allergy are those who are weak detoxifiers.

Kind regards. ~VS

A5: The simple answer? Galvanic skin response testing and the LED procedure developed by Dr. Lee Cowden. Some of the work I've done in the last years with autistic children has given me a new respect for the lack of sensitivity for urine challenge testing for heavy metals. I have had several children come in who had a binder of previous testing, including multiple pre- and post-urine challenge tests that showed no mercury or other significant heavy metal load. Challenge agent was usually DMPS oral.

In all of these children, we did EDS testing and based on this designed a LED protocol. In the children with multiple previous negative metal tests we repeated the urine test after about a week. The only challenge was the LED procedure itself, and in all of them the mercury and lead and cadmium were off the charts. The lab called back one child for a repeat sample, convinced the very high value was an error. (It was not). With the standard support we designed for all of these children, none were sick or compromised after the treatment. All showed significant clinical improvement in the following months.

If you are going to do a procedure with risk like intravenous chelation, then you need to cover your backside by having positive testing to prove the need for the procedure. If your treatment is something as safe as an LED treatment, then electrodermal screening is an adequate workup. Use clinical response to determine if you did something useful for your client. Even when planning more invasive therapies, be aware that the "gold standard" for lab testing may miss many patients who would benefit from treatment. ~DM

Q: Is any FACT member aware of scientific studies which clearly show that individualization of nutrient intake based on genetic testing leads to objective and positive results? ~FR

A1: Dear FR, There are definite genetic links to dysfunction of carnitine, vitamin E, and vitamin B12. Genetic problems with the ability to process Carnitine can lead to 'Familial heart failure' and other problems. It is called 'Primary Carnitine Deficiency' and is rarely suspected unless other children in the family have already died from heart failure. Here's a link: http://journals.lww.com/pedresearch/Abstract/1990/09000/Impaired_Skin_Fibroblast_Carnitine_Uptake_in.20.aspx

Defects in Vitamin E processing can lead to neurologic problems. These problems can start in childhood or come on even into late adulthood and are usually considered problems of 'old age' as it causes ataxia, memory loss, and neuropathy. There seems to be much research on several specific families with this disorder and many individual case studies.
http://www.nature.com/ng/journal/v9/n2/abs/ng0295-141.html
http://www3.interscience.wiley.com/journal/109681461/abstract

Methylenetetrahydrofolate Reductase Deficiency is a genetic inability to process Vitamin B12 and requires treatment with Betaine. There are variations in severity causing anything from profound mental retardation during infancy to familial hyperhomocysteinemia.

Giving dental nitrous oxide to undiagnosed cases can be deadly: http://journals.lww.com/anesthesiology/Abstract/2008/07000/Influence_of_Methylenetetrahydrofolate_Reductase.8.aspx

I could go on, but the following link http://www.ajcn.org/cgi/content/full/75/4/616 sums it up nicely, stating, "About 50 human genetic dis-eases due to defective enzymes can be remedied or ameliorated by the administration of high doses of the vitamin component of the corresponding coenzyme, which at least partially restores enzymatic activity. Several single-nucleotide polymorphisms, in which the variant amino acid reduces coenzyme binding and thus enzymatic activity, are likely to be remediable by raising cellular concentrations of the cofactor through high-dose vitamin therapy. Hope that this helps. ~KK

A2: A quick correction to the above response from KK: Methylenetetrahydrafolate reductase deficiency is NOT "a genetic inability to process B12" but a problem with folate metabolism. ~RL

A3: Interesting question FR. The fact is that the whole concept of genetic testing revealing nutrient need has hit quite a roadblock. The most important thing to know about your patients is if they

have the potential to methylate properly for gene expression. This data may be elucidated by drawing a lavender top tube of blood and sending it to a national lab such as Quest or LabCorp for a MTHFR where both A1298C and C677T will be assessed. Out of pocket this runs about $350, but if the patient is an adult and has an insurance plan that covers labs it may be covered completely. If there is a polymorphism then the POTENTIAL to have difficulty with methylation is there. Since 65% of the US population has a polymorphism on their MTHFR, especially those with neurological illness or cardio disease then there is a good chance that your patient with health difficulties will have a test result that is positive. You want to explain to your patient that if their test is positive that they can PREVENT difficulties that may occur by supplementing with methyl B12, Riboflavin (Vit B2) and Folinic acid (NOT folic acid) or Rx: Leucovorin.

I explain it this way to patients: We bring to "our genetic table" strengths and weaknesses in our genetics. Our genetic "glitches" or Achilles heel is not turned on UNTIL we have a toxic insult. THEN there is a problem. We can protect ourselves by taking B vitamins - folinic, methyl B12, riboflavin - and by AVOIDING toxins in our environment and food intake.

Should your patient do detailed genetic testing??? Overall it is a complete waste of money.

It may have no meaning whatsoever to the patient's present health problems.

But it does make sense to run a MTHFR if insurance covers it for the patient to have a view into their vulnerability to toxic insult and as a preventive measure towards cardio and neuro disease and the developmental health of their future children. ~PK

Just the Facts

The Gordon Research Institute's F.A.C.T. forum is a dynamic online community of practitioners that include physicians, dentists, chiropractors, nurses, dieticians, psychologists, physical therapists, and many others licensed within the health-care field. The F.A.C.T. group, or "Forum for Anti-aging and Chelation Therapies," originated as a way to help doctors learn about and facilitate the use of the latest alternative therapies and nutritional supplement protocols in managing their patients.

Over the years, F.A.C.T. has grown to a membership of over 4000 practitioners from 68 countries around the world. F.A.C.T. membership is free to qualified practitioners, and as members, they can discreetly consult on and discuss cases with one another, learn about new treatments and protocols, share their success stories, and gain access to an extensive catalog of information gathered from 55 years of ongoing research, conferences, and lectures on the latest developments in natural and alternative health therapies.

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Anti-Aging Medicine

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

The Harmony Between Naturopathic Medicine and Anti-Aging Medicine

Naturopathy is a form of health care that is time tested for safety and efficacy among two-thirds of the world's population. Natural medicine, including naturopathy, is the most democratic of all health-care approaches as it is widely accessible by the broadest population segments. Further, it is notable that almost all pharmaceutical products (drugs) owe their origins to natural medicine. Indeed, Carl C. Pfeiffer, MD, PhD, researcher, author, and founding director of the Brain Bio Center (Princeton, NJ), stated: "For every drug that benefits a patient, there is a natural substance that can achieve the same effect."

Natural medicine, including nutritional therapies and other nontoxic approaches such as that advanced by naturopathy, is a cornerstone of anti-aging medical therapeutics. Because these approaches have proved to be extremely effective and absent of significant contraindications or adverse effects that would justify further restrictions to their availability, natural medicine upholds the anti-aging medical commitment to safe and responsible patient-centric medical care.

In this column, we share some of the latest scientific data reaffirming the validity of natural medicine.

Mangos Moderate Blood Sugar

Abundant in the antioxidant vitamins C and A and folate, mangos are a good source of fiber, copper, and vitamin B6. Edralin Lucas and colleagues from Oklahoma State University (US) completed a 12-week study involving 20 adults, ages 20 to 50 years, with a body mass index (BMI) of 30 to 45 kg/m2. The study subjects were asked to maintain their usual diet, exercise habits, and regimen of regularly prescribed medications. Each day during the study period, participants consumed 10 grams of freeze-dried mango (*Mangifera indica* L.). Dietary intake was monitored at the study's start and after 6 and 12 weeks of mango supplementation. Anthropometric measurements (height, weight, and circumference of waist and hip) were measured at those same time points. Body composition and blood analyses of fasting blood triglyceride, HDL-cholesterol, glucose, hemoglobin A1c, and plasma insulin concentration were evaluated at baseline and at the end of 12 weeks of mango supplementation. The researchers found that after 12 weeks, participants had reduced blood glucose (−4.41 mg/dL). While no changes were observed in overall body weight, hip or waist circumference, waist to hip ratio, percent fat mass, and lean mass, hip circumference was significantly lower in males (−3.3 cm) but not females; BMI tended to be higher in females (+0.9 kg/m2) but not males after mango supplementation. The study authors report: "Our findings indicate that regular consumption of freeze-dried mango by obese individuals does not negatively impact body weight but provides a positive effect on fasting blood glucose."

Evans SF, Meister M, Mahmood M, et al. Mango supplementation improves blood glucose in obese individuals. *Nutr Metab Insights*. 28 Aug. 2014;7:77–84.

Honey Compounds as Antibiotic Alternative

Natural products such as honey have been applied against human infections and are a staple of folk medicine. Today, interest in honey as an alternative to antibiotics is peaking in both developing countries, where fresh honey is easily available, and Western countries, where antibiotic resistance is seriously increasing. Tobias C. Olofsson and colleagues from Lund University (Sweden) have identified a unique group of 13 lactic acid bacteria found in fresh honey, from the honey stomach of bees. The bacteria produce a myriad of active antimicrobial compounds. These lactic acid bacteria have now been tested on severe human wound pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, and vancomycin-resistant *Enterococcus* (VRE), among others. When the lactic acid bacteria were applied to the pathogens in the laboratory, they counteracted all of them. While the effect on human bacteria has only been tested in a lab environment thus far, the lactic acid bacteria have

been applied directly to horses with persistent wounds. The lactic acid bacteria were mixed with honey and applied to 10 horses whose owners had tried several other methods to no avail. All of the horses' wounds were healed by the mixture. Writing, "We demonstrate a strong antimicrobial activity from each symbiont and a synergistic effect, which counteracted all the tested pathogens," the study authors submit: "The mechanisms of action are partly shown by elucidating the production of active compounds such as proteins, fatty acids, anaesthetics, organic acids, volatiles and hydrogen peroxide. We show that the symbionts produce a myriad of active compounds that remain in variable amounts in mature honey."

Olofsson TC, Butler E, Markowicz P, Lindholm C, Larsson L, Vásquez A. Lactic acid bacterial symbionts in honeybees – an unknown key to honey's antimicrobial and therapeutic activities. *Intl Wound J.* 8 Sept. 2014.

Go Bananas

Potassium, found abundantly in bananas, is a mineral that previous studies suggest is effective at lowering blood pressure. The US Department of Agriculture recommends that women consume at least 4700 mg of potassium daily. Sylvia Wassertheil-Smoller and colleagues from Albert Einstein College of Medicine (New York) studied 90,137 postmenopausal women, aged 50 to 79 years, who did not have a history of stroke at the study's start, for an average 11 years. With subjects having an average dietary potassium intake of 2611 mg/day, the researchers tracked potassium consumption and incidence of strokes (ischemic and hemorrhagic) or mortality during the study period. Data analysis revealed that women who ate the most potassium were 12% less likely to suffer stroke in general and 16% less likely to suffer an ischemic stroke, as compared with those women who ate the least. Women who ate the most potassium were 10% less likely to die, as compared with those who ate the least. Among women who did not have hypertension, those who ate the most potassium had a 27% lower ischemic stroke risk and 21% reduced risk for all stroke types, compared with women who ate the least potassium in their daily diets. The study authors conclude: "High potassium intake is associated with a lower risk of all stroke and ischemic stroke, as well as all-cause mortality in older women, particularly those who are not hypertensive."

Seth A, Mossavar-Rahmani Y, Kamensky V, et al. Potassium intake and risk of stroke in women with hypertension and nonhypertension in the Women's Health Initiative. *Stroke.* September 4, 2014.

Flavanol-Rich Diet Deters Cancer

Oranges, grapefruits, lemons, and other citrus fruits are a good source of flavanols and related antioxidant compounds for which previous studies have suggested cancer–risk reductive effects. Aedín Cassidy and colleagues from the University of East Anglia (UK) followed 171,940 women, enrolled in the Nurses' Health Study and Nurses' Health Study II, to ascertain associations between intakes of total flavonoids and their subclasses, and the risk of ovarian cancer. Dietary intake was calculated from questionnaires collected every 4 years. During 16 to 22 years of follow-up, 723 cases of ovarian cancer were confirmed. Data analysis revealed that while total flavonoids were not statistically significantly associated with ovarian cancer risk, subjects in the highest quintiles of flavanol and flavanone intakes were at modestly lower risk of ovarian cancer. Specifically, dietary intakes of 75 mg/day of flavanols and flavanones were found to reduce the risk of ovarian cancer by 21%, especially in women ages 30 to 55 years. The study authors report: "Higher intakes of flavonols and flavanones ... may be associated with lower risk of ovarian cancer."

Cassidy A, Huang T, Rice MS, Rimm EB, Tworoger SS. Intake of dietary flavonoids and risk of epithelial ovarian cancer. *Am J Clin Nutr.* October 2014; ajcn.088708.

Omega-3s Enhance Brain Cell Structure

A growing number of studies suggest that consuming oils with high polyunsaturated fatty acid content, in particular those containing omega-3 fatty acids, exerts beneficial health effects. CNRS (France) researchers investigated the effect of lipids bearing polyunsaturated chains when they are integrated into cell

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membranes. Their work shows that the presence of these lipids makes the membranes more malleable and therefore more sensitive to deformation and fission by proteins. The study shows that cell or artificial membranes rich in polyunsaturated lipids are much more sensitive to the action of two proteins, dynamin and endophilin, which facilitate membrane deformation and fission. Other measurements in the study and in simulations suggest that these lipids also make the membranes more malleable. By facilitating the deformation and scission necessary for endocytosis, the presence of polyunsaturated lipids could explain rapid synaptic vesicle recycling. The abundance of these lipids in the brain could then represent a major advantage for cognitive function. The study authors submit: "By reducing the energetic cost of membrane bending and fission, polyunsaturated [phospholipids] may help to support rapid endocytosis."

Pinot M, Vanni S, Pagnotta S, et al. Lipid cell biology. Polyunsaturated phospholipids facilitate membrane deformation and fission by endocytic proteins. *Science*. 2014 Aug 8;345(6197):693–697.

Boost Fruits and Veggies to Lower Disease and Death Risks

Consume 5 servings of fruits and vegetables each day to reduce your chances of developing heart disease and dying from it. Frank B. Hu and colleagues from Harvard School of Public Health (Massachusetts, US) completed a meta-analysis of 16 published studies on all-cause, cardiovascular, and cancer mortality by levels of fruit and vegetable consumption, involving a total of 833,234 subjects. The researchers observed a dose-response relationship: the more fruits and veggies people ate, the less likely they were to have heart problems or die during the study period. The protective effects of fruits and veggies leveled out at 5 servings per day, consistent with current dietary recommendations. The study authors conclude: "This meta-analysis provides further evidence that a higher consumption of fruit and vegetables is associated with a lower risk of all cause mortality, particularly cardiovascular mortality."

Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. *BMJ*. 2014 Jul 29;349:g4490.

The A4M supports the practice of natural health therapeutics by licensed physicians of all medical specialties. At the A4M Congresses on Anti-Aging Medicine, the world's premier continuing medical education programming in advanced preventative medicine, many internationally renowned speakers have presented extensive data reaffirming the validity of natural medicine, including nutritional therapies and other nontoxic approaches such as those advanced by naturopathy. As such, our delegates embrace naturopathic therapies, and many of them return to their practices and engage these approaches safely and effectively, to the benefit of their patients.

To learn of the latest nutritional therapies and other nontoxic natural approaches that reflect the anti-aging philosophy, visit the World Health Network (www.worldhealth.net), the official educational website of the A4M and your one-stop resource for authoritative anti-aging information. Be sure to sign up for the free Longevity Magazine e-journal, your weekly health newsletter featuring wellness, prevention, and biotech advancements in longevity. ◆

Naturopathic Medicine People of 2015

by Jacob Schor, ND, FABNO

Not too long ago, while reading the Sunday paper, my wife Rena pointed out an article on human biome researcher Rob Knight and said, "Look, at Harvard they are giving people frozen poop pills instead of fecal transplants!"[1]

"Duh, that ND in Portland, Mark Davis, the poop guy, is already doing that in his practice," I said.

"That figures; Mark's one brilliant guy," she responded.

I count myself lucky to know Mark Davis. Actually I count myself lucky to know quite a few naturopathic doctors who are just as interesting, people who I hold in great affection as friends and in great esteem as colleagues.

This article is a short update on what several of these doctors have been up to.

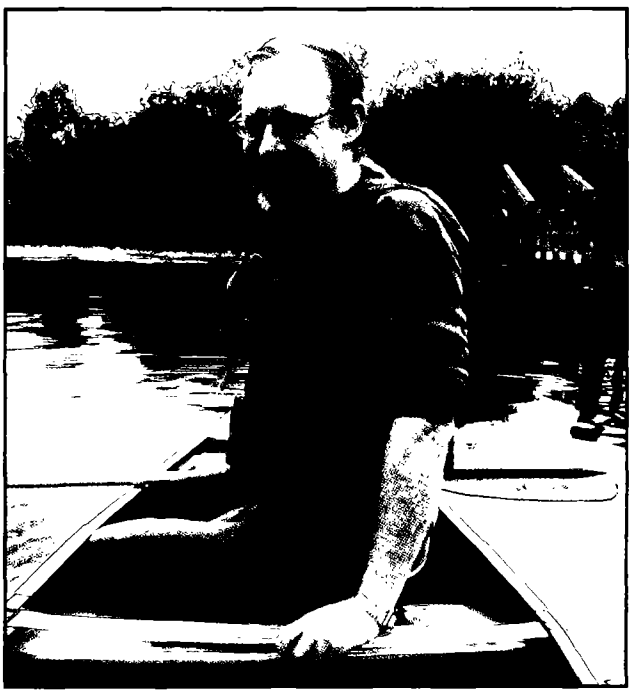
Eric Yarnell, ND

Our longtime friend Eric Yarnell, ND, who once upon a time considered joining our practice (but had the good sense not to), was on sabbatical this past year from his teaching job at Bastyr University. He made good use of the "free time." He is nearing completion of his next book, *The Natural Approach to Urology and Men's Health* (2nd edition), which he claims to have spent almost 15 years on and which will be similar in size and scope to his earlier massive two-volume set, *The Natural Approach to Gastroenterology*. Yarnell spent February at the Natural Doctors International (NDI) clinic in Ometepe, Nicaragua (http://www.ndimed.org). He helped in the clinic but also connected it with the Bonafide biodynamic farm and set it up so this farm will grow herbs for the clinic. The first crop is in the ground and should be available by the time he returns with a brigade of herbalists to harvest them in March 2015.

Yarnell completed a research project with the Institute for Preservation of Medical Traditions, housed at the Smithsonian Institute, looking at the herbs that the Roman physician Dioscorides wrote about in his 1st-century classic book, *De Materia Medica*, in particular the diuretics that Dioscorides described and whether they are still presently in use. Yarnell presented this research at the International Society for the History of Medicine conference in Tbilisi, Georgia, in September 2014.

Yarnell wrote me about his being awarded the "Vis Award" by the American Association of Naturopathic Physicians in August 2014, saying, "I was also shocked and humbled" to be selected for it, borrowing the words that I used when I received the same award years ago. In retrospect, I still feel the same way.

In September 2012, Yarnell and two other naturopathic doctors took a group of 14 students to Uganda to work with Reach Out Village Orphanages in Kampala (capital city) and Socolo (a village outside the capital). A student's husband knew the family who runs these orphanages. "We held four days of clinics (two days in each site) for the children and community members. We also taught classes on various subjects including hygiene and self-defense while people waited. We also worked with them to relearn their native medicinal plants and to encourage their growth as 'weeds' around the perimeter of their existing farmland to reduce dependence on difficult-to-obtain, expensive, potentially dangerous pharmaceutical medicines as much as possible."



Yarnell is now back to his usual routine as an associate professor in the botanical medicine department at Bastyr University, teaching gastroenterology, urology, men's health, nephrology, pharmacognosy, and herb–drug interactions, and coteaching the materia medica and formulation lab courses for the naturopathic students. He practices one day a week in a private practice specializing in urology and men's health, and gastroenterological and immune conditions; he supervises one student shift a week and continues to work as president of Heron Botanicals and chief financial and operations officer for Healing Mountain Publishing. He's working on several other books including a second edition of *Phytochemistry and Pharmacognosy for Practitioners of Botanical Medicine*, *Low-Dose Herbs*, *Natural Approaches to Nephrology*, and *Western Herbal Formulation* (a book that he began writing many years ago with his mentor, Silena Heron, ND).

Lise Alschuler, ND, FABNO

Eric isn't the only one on my list who received an award this year. In truth, if I make a list of all the awards that Lise Alschuler has received this year, I can't figure out when she found time to do anything else, especially time to consult with me about some particularly difficult patients. Alschuler received the AANP Physician of the Year Award in August 2014, an honorary doctorate from the Canadian College of Naturopathic Medicine earlier in the spring, and the Bastyr University Joseph Pizzorno Founder's Award this fall.

Alschuler is the executive director of TAP Integrative, a Web-based service providing clinically based and peer-reviewed expert opinions and research synopses on topics of integrative clinical practice (www.tapintegrative.org).

In August, to my great pleasure, she became the newest president of the Oncology Association of Naturopathic Physicians (www.oncanp.org), taking over the organization from this writer, who is ever so pleased with the way that she has taken control of the association and is steering it toward greater achievement.

Alschuler's second book, *Definitive Guide to Thriving After Cancer*, coauthored with our friend Karolyn Gazella, came out in September 2014 and is already a number 1 bestseller on Amazon! Alschuler is also involved in the launch of a family of nutritional supplements called Pro-Thrivers, targeted for cancer survivors, which she helped formulate. She seems to be on a nonstop road-trip promoting this product line in the company of Tina Kaczor for the past few months.

This past year, Alschuler joined the medical advisory board for Gaia Herbs while retaining her role on the advisory boards for Integrative Therapeutics and Emerson Ecologics. Despite all of these commitments, she continues seeing patients through Dan Rubin's practice Naturopathic Specialists in Arizona (www.ListenAndCare.com), work that she describes as "an incredible learning experience, a privilege and a honor to do."

Gosh, I feel that if I pause writing about Alschuler for even a moment I'll be drowned out by your applause. Applause that she deserves.

Gurdev Parmer, ND, FABNO

I always keep an eye out or an ear open for what Gurdev Parmer is up to. Gurdev and his wife, Karen Parmar, ND, employ a total of 45 people, including 9 naturopathic physicians, at their clinic in Fort Langley, B.C. Gurdev uses hyperthermia, along with nutrient supplementation and IV therapies integrated with standard of care, to treat his cancer patients. Parmer's research caught my attention at the 2013 Society of Integrative Oncology Conference. His reported 3-year survival statistics for glioblastoma patients are among the best that I have seen documented. Now with over 600 patients who have been treated with hyperthermia, both a 5-year retrospective study and also a prospective longitudinal study on cancer outcomes have been started.

Mark Davis, ND

Let's go back to Davis, the poop guy. He is a guy who keeps himself busy; he sits on the board of the Fecal Transplant Foundation (FTF), is the chair of the Fecal Microbiota Transplantation (FMT) committee for the C Diff Foundation (http://cdifffoundation.org), and has just recently been added to the editorial board of the *Natural Medicine Journal*.

Davis's clinic, the Good Life Medicine Center, is an integrative medicine clinic where NDs, acupuncturists, and others work together. The clinic has an herbal apothecary, a movement studio and classroom, a hydrotherapy suite, a lab, and a herbal café in the works. (Though given his fecal specialty, I question the wisdom of the last project, though the potential advertising slogans might make it hard to resist.)

For those new to FMT, it is literally the transplantation of fecal microbiota from one person to another. Microbes are sourced from the stool of a healthy person and transplanted into a sick person. Davis became fascinated with FMT while in naturopathic medical school, but no one in Oregon was using this process at that time. He had to seek guidance from world experts in FMT, including Tom Borody, MD; Alex Khoruts, MD; and Thomas Louie, MD.

FMT helps create a healthy gut ecosystem to properly regulate the immune system. Davis is confident that FMT offers benefit for people with infectious and autoimmune colitis, inflammatory bowel disease (IBD), and irritable bowel syndrome (IBS); evidence is emerging that FMT may benefit people with MS, diabetes, metabolic syndrome, and other conditions.

Davis is the first physician in North America (as far as he knows) to have run a donor-bank driven FMT program serving people with inflammatory bowel disease. He and a small group of clinicians are performing research advancing the use of FMT through using frozen material and centrifuged/encapsulated material. He's been preparing encapsulated FMT, and frozen FMT caps since early 2014.

To me, Davis is the quintessential Portland hipster. He's got four kids, Asher, 9; Jaia, 7; and twins Isaac and Daphne, almost 3 years old, and lives in what he describes as "a somewhat intentional community with the children, their mothers, wonderful neighbors, dogs, chickens, orchards and herbs."

Ruth Adele, ND

Over the last few days as I have collected these brief biographical tidbits, I confess to being the most moved by the simple recognition that our dear friend Ruth Adele has recently received. Adele practices about an hour south of us in Colorado Springs. Every year her local newspaper, the *Colorado Springs Independent*, confers a series of "Best Of" awards. Your local newspaper probably does something similar; awards go to the best Thai restaurant, dance club, or slice of pizza. Back in 2011, her newspaper started the category Best Naturopath. She won the "Best" award 3 years in a row, always competing with an unlicensed "traditional practitioner" or two who ended up in second and third place. This year the paper changed the award to "Best Holistic Practitioner." Adele still won it. That's 4 years running.

Adele is a 1983 graduate of Bastyr University, back an era when her main clinic doc was John Bastyr himself, and she preceptored with Bill Mitchell.

She practiced in Olympia, Washington, for 8 years, then in Colorado Springs for 23 years (we opened our practices within a few months of each other). She served on Bastyr's board of trustees for 3 years, on the Council for Naturopathic Medical Education (CNME) board that accredits naturopathic medical programs for 10 years, various committees of the AANP, and as vice president of Colorado's state naturopathic association. Mostly, though, she has practiced naturopathic medicine, seeing patients day in and day out for decade after decade.

For the past 10 years, Adele has also been deeply involved in animal rescue, including many years as president of her local dog rescue nonprofit organization, and 8 years in charge of all health-care decisions for 50 foster dogs at a time. She is proud to have saved many puppies infected with parvovirus and with pneumonia using naturopathic medicine. She currently lives with her own 3 dogs and 1 cat, and 1 foster dog and still finds time to hike the beautiful mountain trails several times a week around her home.

Dugald Seely, ND, FABNO

If Lise is receiving accolades in the front of the room at conferences, see Dugald Seely as the quiet guy lurking at the back of the room, eager to get back to his work. For an unassuming guy, he gets things done – actually, an amazing number of things done – with little fanfare. Both as a doctor and a researcher, he is playing a leading role in developing the fields of integrative and naturopathic oncology.

He is the founder and executive director of the Ottawa Integrative Cancer Center, an Affiliate Investigator with the Ottawa Hospital Research Institute, and director of Research & Clinical Epidemiology at the Canadian College of Naturopathic Medicine, Toronto. Seely may be best known to those of us south of the border for the dozens of synthesis reviews and meta-analyses related to naturopathic oncology that he has supervised over the years; he is the prime driver behind the growing body of evidence that supports integrating naturopathic medicine into medical oncology.

He is one of the most well-published authors in our profession, with 56 publications in the peer-reviewed Medline Indexed literature, and with 13 research projects currently in progress.

Seely completed his MSc in cancer research at the University of Toronto and is a Fellow of the American Board of Naturopathic Oncology (FABNO), a past board member of the Society of Integrative Oncology (http://www.integrativeonc.org), and has recently joined OncANP's board of directors. As a clinician scientist, Seely has been awarded numerous grants and funding over the years from groups including CIHR, CBCRA, the SickKids Foundation, the Lotte and John Hecht Memorial Foundation, the Ottawa Regional Cancer Foundation, and the Gateway for Cancer Research.

The biggest of these grants is a recent one for $3.85 million that will fund the largest clinical trial on integrative naturopathic cancer care ever conducted in North America. This study will follow 300 patients undergoing thoracic surgery for cancer and follow them for 11 years to see if a combination of naturopathic and conventional therapies will improve long-term outcomes.

It was a mistake to try writing something like this, as I've left out far too many people who deserve to be mentioned just as much as those I've included. At least it's a start. I am amazed at how many interesting and hard-working, devoted people this profession brings me in contact with.

Notes

1. Draper E. CU gut check: Humans' important relationships under the microscope. *Denver Post*. Nov. 9, 2014. Available at http://www.denverpost.com/news/ci_26899760/cu-gut-check-humans-important-relationships-under-microscope.

Naturopathic Colleges of 2015

National University of Health Sciences: Defining the Future of Integrated Health Care

Offering the only naturopathic medicine degree program in the Midwest, National University of Health Sciences has set standards of educational excellence in health career education since 1906.

The NUHS naturopathic medicine program offers a rigorous and academically challenging curriculum that blends a thorough scientific foundation with comprehensive training in naturopathic treatments. The program brings a strong emphasis on naturopathic principles and philosophy together with a thorough study of contemporary, evidence-based treatments.

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Naturopathic Colleges of 2015

National College of Natural Medicine

Since 1956, National College of Natural Medicine (NCNM) has a rich, long history filled with some of naturopathic medicine's most illustrious names: Bastyr, Spaulding, Farnsworth, Boucher, Pizzorno, Mitchell, Hudson, Traub, and Cronin. In recent years NCNM has experienced an exciting period of expansion in its campus, programs, clinics, and enrollment. Today NCNM offers three 4-year graduate medical degree programs in naturopathic and classical Chinese medicine, and four master's programs.

Research

NCNM's Helfgott Research Institute, established in 2003, is the recipient of numerous grants and NIH awards for its evidence-based studies in integrative medicine. In 2012, the college opened a dedicated facility to house the Helfgott Research Institute and Community Education Center, and the growing School of Research & Graduate Studies (SRGS) and its roster of master's programs in integrative medicine research, nutrition, global health, and mental health. The building features a large state-of-the art research and teaching kitchen for NCNM students – and for families in the Portland community interested in nutrition and whole-foods cooking classes.

At Helfgott, investigators with backgrounds in immunology, nutrition, and naturopathic and Chinese medicine study natural medicine modalities on a range of clinical diagnoses. Investigators supervise student-designed, hands-on research projects – which have been recognized with top awards at conferences throughout the world.

Currently numerous studies are under way, including a joint collaboration between Helfgott and Legacy Hospital in Portland to study whether a ketogenic diet can benefit patients with Parkinson's disease and a nutrition study to evaluate if whole-foods education courses result in decreased risk factors for diabetes and heart disease.

Clinics

In addition to the campus-based NCNM Clinic and the college's wide network of community clinics, NCNM opened the Beaverton Clinic in 2014, expanding its campus for the first time to the Portland suburbs. NCNM clinics utilize the Epic electronic health record system to better access and track data and outcomes for nearly 40,000 patient visits – and share patient information with hospitals and medical facilities. NCNM Clinic and its affiliated teaching clinic, the Center for Natural Medicine (CNM), have recently been credentialed by the Oregon Health Authority as Patient-Centered Primary Care Homes, a significant recognition. CNM supervises interns and residents in cardiology and pulmonary medicine.

In 2013, NCNM opened NCNM Clinic's SIBO Center, dedicated to the treatment of small intestine bacterial overgrowth (SIBO), irritable bowel syndrome, and associated gastrointestinal disorders. The new center has met with outstanding success in this emerging field. The SIBO Center cofounders, Steven Sandberg-Lewis, ND, DHABP, and Allison Siebecker, ND, LAc, won the 2013 *Townsend Letter's* Best of Naturopathic Medicine award for their article on SIBO.

➤ ***NUHS continued from page 45***

The one-year internship for ND students in the on-campus integrative medical clinic includes a rotation seeing homeless patients at a Salvation Army facility in downtown Chicago. Students can also choose an intensive rotation in homeopathic medicine during their internship to deepen their skills.

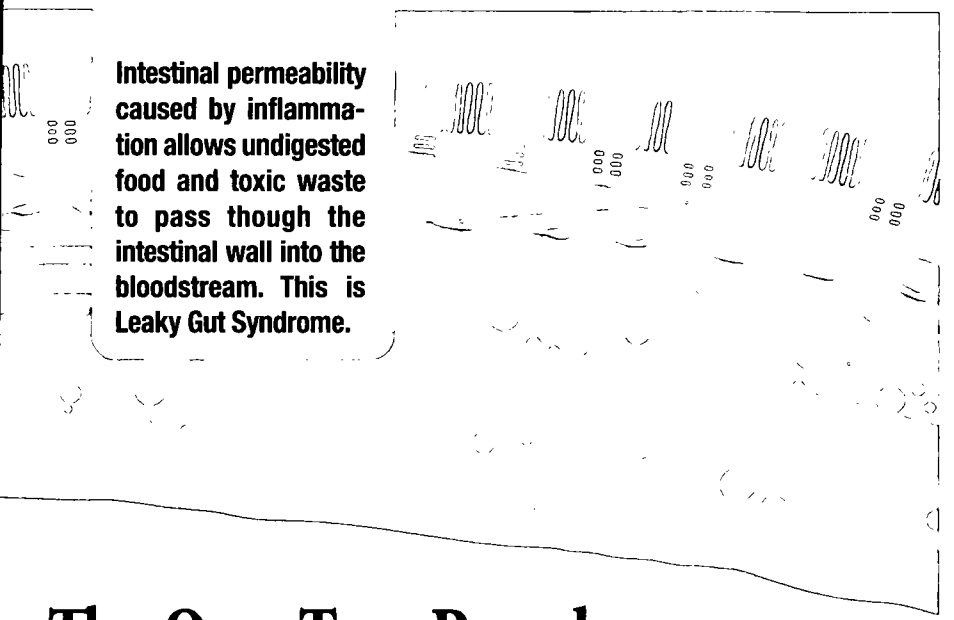
NUHS is one of only two schools in the US to offer degrees in naturopathic medicine, chiropractic medicine, acupuncture, Oriental medicine, and massage therapy on the same campus. This, plus the university's commitment to integrative medicine, provides a dynamic collaborative atmosphere where students and faculty of diverse medical specialties can work together as colleagues. It also offers advantages for students who are considering dual degree programs.

As the newest member of the American Association of Naturopathic Medical Colleges, NUHS may actually be one of the oldest naturopathic medicine schools in the country. In the early 1900s, National's founder had a strong relationship with Dr. Henry Lindlahr, a naturopathic medicine pioneer. The college also absorbed the Lindlahr College of Natural Therapeutics in 1926, and offered a degree in natural therapeutics (the forerunner of the ND degree) from 1927 to 1952. NUHS holds regional accreditation from the Higher Learning Commission of the North Central Association of Colleges and Schools and programmatic accreditation for the ND degree from the Council on Naturopathic Medical Education (CNME).

Located just 15 miles outside of Chicago, National's students easily access all of the cultural, entertainment, sports, and nightlife the city has to offer. Meanwhile, the quiet 35-acre suburban campus is within walking distance to grocery stores, restaurants, parks, and tree-lined streets of Lombard, a safe, family-oriented suburb. The university offers on-campus housing, and attracts a diverse population of ND students from both the US and abroad.

NUHS offers two unique campus visit day events each year, where participants can enjoy interactive classroom and clinic experiences, seeing what it's really like to be an ND student. Additionally, NUHS also offers multiple "student-for-a-day" events throughout the year. To learn more about National University of Health Sciences, visit www.nuhs.edu or call 800-826-6285.

Naturopathic Colleges continued on page 48 ➤



Intestinal permeability caused by inflammation allows undigested food and toxic waste to pass though the intestinal wall into the bloodstream. This is Leaky Gut Syndrome.

The One-Two Punch for Chronic Conditions

Colostrum is the only substance clinically proven to prevent and repair Leaky Gut Syndrome, and healing a patient's permeable gut halts disease progression and food allergies. But, that's only half the solution, and there's more work to be done. Existing cellular and tissue damage caused by Leaky Gut Syndrome still remains, and inflammation resulting from a hyped-up immune system must be attenuated if true healing is to occur.

A balanced, optimally functioning immune system is key to health and well-being, and once again, it's colostrum to the rescue. This time, it's the Proline-Rich Polypeptides (PRPs) in colostrum that balance the immune system. This collection of short chain peptides are powerful immune modulators that help regulate the thymus gland and stimulate the production of either helper or suppressor T lymphocytes, depending on the need to either stimulate or suppress immune system activity. PRPs also induce the growth and differentiation of B lymphocytes and stimulate cytokine production, particularly IL-10, an anti-inflammatory cytokine. The most active PRPs in colostrum are the PRP-2s whose mechanism is primarily antimicrobial, and the PRP-3s whose mechanism is primarily anti-inflammatory. PRPs are not species specific, which makes bovine colostrum an excellent and abundant source.

The Total Gut Solution

First, Colostrum-LD® heals gut lining inflammation, decreases permeability, and increases the surface area of the small intestine for improved absorption of beneficial and critical nutrition. Second, IRM (Immune Response Modulator)® with its concentrated PRP-2s and PRP-3s inhibits the initiation of inappropriate inflammatory cascades associated with allergy and autoimmune responses. IRM® helps stop the destruction of body tissue associated with improper immune response and inhibits viruses known to be associated with autoimmune response.

Sovereign Laboratories is on the forefront of colostrum research and processing to maximize bioavailability of active components. Liposomal Enhanced Delivery system, an applied coating, allows powdered colostrum to readily dissolve in liquids and ensures powdered colostrum and oral colostrum spray will bypass digestion; will be transported through the bowel wall; will circulate throughout the body; will reach the organs and cells; and will remain bioavailable at the cellular level. "Liposomal Delivery makes colostrum (and other nutrients) up to 1,500 % more bioavailable" (Robert R. Milne, MD). When used in combination, Colostrum-LD® and IRM® are clinically proven to provide the one-two punch for chronic conditions.

For more information, visit www.ColostrumTherapy.com (for professionals) or www.CenterForNutritionalResearch.org (for consumers).

"All Disease Begins in the [Leaky] Gut".

~ Hippocrates

Every patient who walks through your door with a chronic disease complaint or food allergies has Leaky Gut Syndrome.

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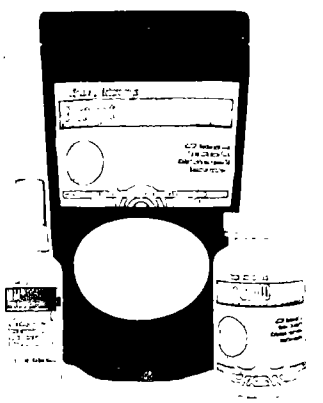

Medical professionals may receive professional pricing by registering on www.ColostrumTherapy.com or call Sovereign Laboratories at 928.282.9476.

Consumers may purchase at www.SovereignLaboratories.com

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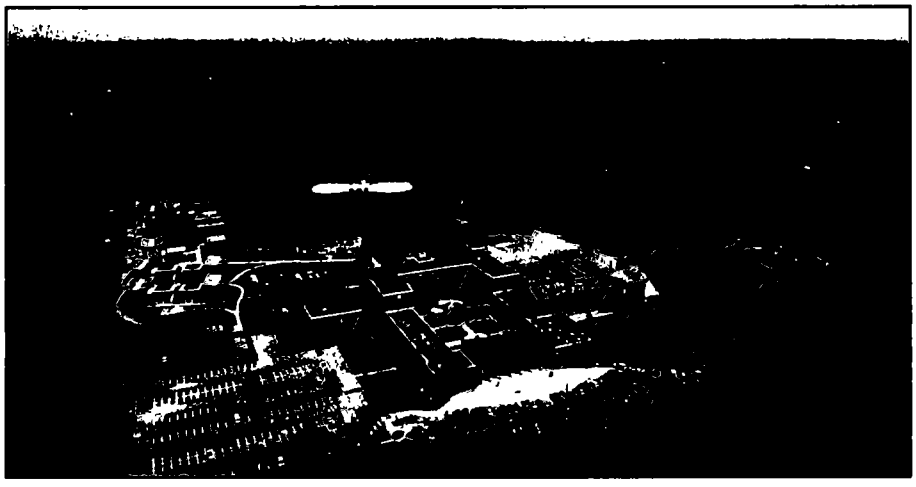
New Bastyr Public Health Degrees Promote Community-Level Wellness



For 36 years, Bastyr University has prepared health-care practitioners to treat patients one on one, training naturopathic doctors (NDs), acupuncturists, dietitians, midwives, psychologists, and others in globally recognized study programs.

But not all health issues arise at the level of individual patients. Not all cures happen in the examination room.

Three new degree programs reflect Bastyr's growing focus on serving the health of communities. In fall 2015, the university will launch a master of public health (MPH), a master of arts in maternal-child health systems and – in San Diego – a master of science in nutrition for wellness.

Each program recognizes the ways that health connects to broader issues of education, environment, culture, poverty, and race, preparing graduates to work across traditional boundaries in promoting wellness.

"These programs arose from our interest in having a broader impact on community wellness," says Lynelle Golden, PhD, dean of the School of Natural Health Arts and Sciences. "Most of the health conditions we are facing, such as diabetes and cardiovascular disease, have behavioral and cultural components. We need to provide ways for communities to improve their own health."

The programs reflect evolving demands on health leaders. For example, the key to improving health in some neighborhoods is not explaining the importance of exercise, it's improving traffic and crime to make it safe to exercise outside. That requires working with urban planners, politicians, and neighborhood leaders, says David Fleming, MD, who served for seven years as the director of Public Health for Seattle & King County, Washington.

"The skills that public health workers of the future need are going to be different than in the past," says Fleming. "Increasingly they will be skills needed to assist policymakers and communities to take the healthy actions that they themselves want to take."

Each of Bastyr's new programs addresses the changing picture of health in the 21st century. And each has innovative program designs to serve students at any point in their careers.

Master of Public Health

The two-year MPH program has a specialization in Community Health Education, preparing graduates to become certified as Community Health Education Specialists (CHES), a requirement for many jobs in the field. The evening-format program is also available as a dual-degree option for current Bastyr students.

The program offers career pathways to people who want to work in health but not as one-on-one practitioners, Golden says. People such as Ann Lanning, a senior in Bastyr's Bachelor of Science in Health Psychology program, who would like to work in corporate human resources developing workplace wellness programs. She is considering the Bastyr MPH to continue learning how to lead people toward healthful behavior changes.

"The MPH is a natural extension of what I've learned as an undergraduate student," says Lanning. "It would help me learn about how health and wellness apply to groups of people. I see corporate human resources as playing a big role in supporting broad health education and prevention-focused initiatives."

The program extends Bastyr's whole-person philosophy of individual health to the level of communities.

"A holistic perspective on communities fits the Bastyr philosophy of supporting health rather than just treating disease," says Golden.

The program also includes a focus on social justice, with seminars each quarter on issues such as access to medical care, access to healthy foods, and environmental health.

That approach appeals to Henry Appiah, a Bastyr student of naturopathic medicine and acupuncture who is considering the MPH program. Appiah has worked as a community organizer in Ghana, leading campaigns to drain stagnant urban waterways where disease-bearing mosquitoes bred. That work showed him the importance of community organizing for health – work he plans to continue in Ghana.

"Health comes not only from diagnosing and curing, but from prevention and education," he says. "So much disease can be avoided with education. I've seen it with my own eyes."

continued on page 50 ➤

Has Naturopathic Medicine Arrived? A Perspective from the Canadian College of Naturopathic Medicine

"Are we there yet?" The question that tires so many parents during long journeys with children also resonates among supporters of a profession that has waited far too long for the recognition that it deserves. However, as events at the Canadian College of Naturopathic Medicine (CCNM) demonstrate, times are changing and the level of acceptance of the medicine is rapidly advancing.

One of the members of CCNM's board of governors has started using the phrase "The time is now!" to emphasize the critical juncture that he sees the profession approaching. The readiness is there; the college must capitalize on the opportunities that are arising. In pursuit of this, CCNM has opened a naturopathic teaching clinic within a large Toronto-area hospital, opened an integrative cancer center in the nation's capital, secured more research funding in the last 6 months (over $7 million) than in the previous history of the college, signed a memorandum of understanding with Canada's largest and most prestigious university, and obtained degree-granting status in a province that has long sheltered that authority among the public universities.

One of the drivers of this change is the growing recognition that naturopathic medicine is very effective in the treatment of many chronic conditions. If we are to break the vicious escalation of health-care costs, we must adopt more effective approaches to treating common chronic conditions that are disabling so many. CCNM is working to build the evidence base attesting to the safety and effectiveness of naturopathic treatments, ensuring that the research results are published and accessible. Influential articles have been published on reducing cardiovascular risk (*Canadian Medical Association Journal*), chronic back pain (*PLoS ONE*), rotator cuff tendinitis (*Arthritis & Rheumatology*), and anxiety (*PLoS ONE*), to name a few. For two of these studies, there have been companion pieces on the economics of the care. (Details and references are available on the CCNM website, www.ccnm.edu.)

Bob Bernhardt, PhD

Doctors informed on naturopathic care will not be surprised at the role that naturopathic medicine can play in reducing or eliminating chronic conditions; the two most frequent therapies employed are lifestyle counseling and nutrition. Patients with chronic conditions cannot generally be "fixed"; they need to participate in improving their own health through the informed coaching of caring health-care providers.

Numerous other research projects are under way, particularly in the areas of cancer and diabetes, but describing them goes beyond the scope of this article. Have we arrived yet? No, but we are beginning to approach our destination.

Bob Bernhardt, PhD, President and CEO

Emerson Ecologics Launches 2015 Emerson Grant Program

Emerson Ecologics LLC, the leading distributor of over 275 brands of professional-quality vitamins, supplements, prescription medications, and natural health products, today announced that it is now accepting applications for the Emerson Grant. The Emerson Grant program supports the work of practitioners and promotes integrative medicine in the US.

In April 2015, Emerson Ecologics will award grants totaling $25,000 to support projects and initiatives designed to improve, expand, or support the practice of integrative medicine. The Emerson Grant is a competitive, discretionary award ranging from $500 to $10,000. Projects may include legislative efforts, public awareness campaigns, or enhancements to education or clinical training, but all projects are welcome.

The New York Association of Naturopathic Physicians, a winner of the Emerson Grant in 2014, used its grant to help further its efforts toward licensure for naturopathic doctors in New York. NYANP President Rick Brinkman, ND, said, "The Emerson grant was a blessing to the NYANP legislative efforts to gain licensure for NDs in New York. The grant revitalized our efforts at a crucial time when financial support was essential to forward progress. Thank you, Emerson!"

Emerson Ecologics is dedicated to the continued growth and awareness of integrative health care and wellness. The company recognizes that hundreds of volunteer-driven organizations work tirelessly to support integrative medicine. As the premier source of products and services for the integrative health-care community, Emerson wants to help these organizations achieve their vision. For more details on the Emerson Grant program or to download an application, visit emersonecologics.com/grant.

About Emerson Ecologics

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

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Naturopathic Colleges of 2015

➤ *continued from page 48*

Bastyr's MPH will prepare graduates to work in health departments, corporate settings, community organizations, assisted living facilities, and a variety of other workplaces, Golden says.

To learn more about the MPH program, go to www.bastyr.edu/academics/areas-study/master-public-health.

Master of Arts in Maternal-Child Health Systems

The master of arts in maternal-child health systems is designed for midwives and other maternal and infant care practitioners who want to shift their careers toward teaching, advocacy, research, and other ways of leading systemic change. The one-year program prepares graduates to promote the health of mothers and children at hospitals, medical centers, birth centers, public health departments, and elsewhere.

That can be an appealing change for midcareer midwives and doulas, says Suzy Myers, LM, CPM, MPH, chair of Bastyr's Department of Midwifery.

"There's only so long you can get up in the middle of the night and work crazy hours," says Myers. "There is a common need for midwives to shift their professional focus from the hard physical work of delivering babies to something that has a broader approach."

As midwives learn about structural barriers to providing effective birth care, many find themselves looking for ways to lead change in health systems, says Karen E. Hays, DNP, CNM, ARNP, an adjunct midwifery faculty member who helped develop the new program.

"You're out there practicing in the trenches and you realize all the frustrations and the obstacles to providing the kind of care you want to deliver," she says. "Things related to financing, insurance, cultural biases, and so on. The US health care system offers huge barriers to what we know is scientifically supported to empower women and improve their health outcomes and their lives. That's what this program addresses."

The program uses the hybrid-online model that Bastyr has developed for its midwifery program. Students attend classes on campus at the beginning and end of the year, with online modules in between. That allows them to stay involved in their home communities.

Audrey Levine, LM, CPM, a midwife in Olympia, Washington, practicing since 2001, has already begun a transition into full-time policy work. She is the legislative chair for the Midwives' Association of Washington State and serves on the board of the National Association of Certified Professional Midwives.

"As I embark on the next phase of my career, it seems like a master's degree in maternal-child health systems would give me a broader perspective as well as more credibility on the national scene," she says. "I already know a number of the prospective faculty members for the Bastyr program and am thrilled at the prospect of learning from all of them."

To learn more about the Maternal-Child Health Systems program, go to www.bastyr.edu/academics/areas-study/midwifery-degree-programs/master-arts-maternal-child-health.

Master of Science in Nutrition for Wellness (California Campus)

The master of science in nutrition for wellness rests on the whole-food philosophy that guides all of Bastyr's nutrition education, emphasizing eating a broad variety of foods in their least-processed forms. The two-year program offers a new focus on teaching nutrition to groups in a variety of settings and media.

That's an unfilled niche, says Debra A. Boutin, MS, RD, chair of Bastyr's Department of Nutrition and Exercise Science.

"We wanted to come at nutrition in a new way," says Boutin. "It's about training people at a graduate level to understand the science behind nutrition. That prepares them to share knowledge about whole foods in a way that has integrity and accuracy."

The program focuses on food for disease prevention, motivating behavior change, and developing nutrition education programs. Graduates will be qualified to lead the wellness programs that have risen in popularity at workplaces, health-care organizations, schools, and senior centers. They might develop nutrition programs for grocery store chains, produce cooking demonstrations, or lead grant-funded public health projects. Or they might become entrepreneurs, using video, writing, consulting, or other methods to bring nutrition information to others.

The common thread will be an ability to translate scientific research into accessible information that can change people's lives.

"We're looking for the same kind of passionate students who come to our Washington nutrition programs," Boutin says. "People who really want to work with groups and become comfortable with media and publicity."

To learn more about the Nutrition for Wellness program, go to www.bastyr.edu/california/academics/master-science-nutrition-for-wellness.

Changing Health Landscape

Students in each of the new programs will be preparing for a changing career landscape. Many of today's health problems in North America arose out of yesterday's health victories, according to Fleming of Public Health – Seattle & King County. People no longer die from infectious diseases such as tuberculosis at the rates that they did 100 years ago. Longer lives have created room for a new set of chronic health challenges – cardiovascular disease, cancer, diabetes, and others. Conditions more likely in old age, such as arthritis and lower back pain, have become more common. Mental illness and depression have also become leading health problems.

These changes create a need for new types of public health leaders who can collaborate on issues such as tobacco use, access to healthy food, and crime that keeps people from getting exercise outside, says Fleming.

"A public health worker is not going to be pouring cement for a bike path," says Fleming. "Instead, our work in the future is increasingly working with families and communities to enable them to make the changes they want."

With the Affordable Care Act ("Obamacare") placing an increased emphasis on preventive health, career opportunities will follow.

"We launched these programs because they prepare students to work in key fields," says Timothy C. Callahan, PhD, senior vice president and provost of Bastyr University. "Health care trends are increasingly moving toward preventive wellness. Bastyr's strength has always been the prevention-oriented focus of natural health. Graduates of these programs will have a lot to offer."

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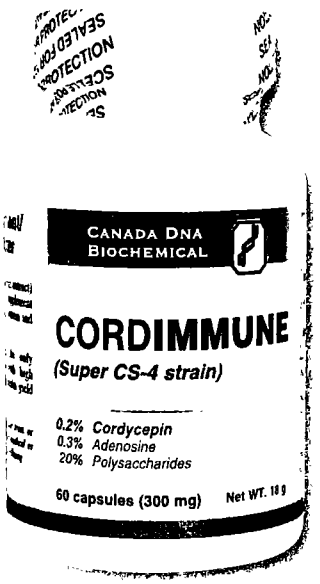

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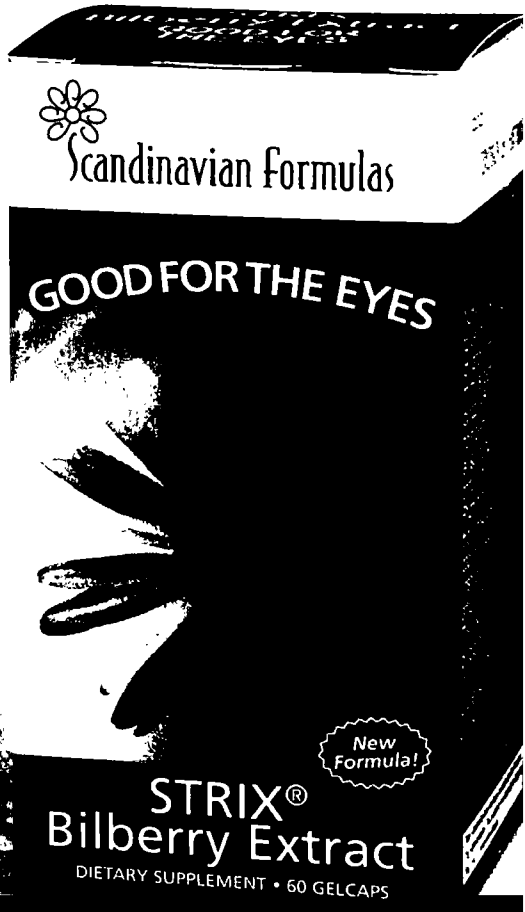

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Best of Naturopathic Medicine

Every two years, the *Townsend Letter* holds a competition for naturopathic students, faculty, clinicians, and practitioners to submit an article for our "Best of Naturopathic Medicine" competition. The first competition was held in 2003. Entries have been submitted by NDs and ND candidates from the National College of Natural Medicine, Canadian College of Naturopathic Medicine, Bastyr University, Southwest College of Naturopathic Medicine, Boucher Institute of Naturopathic Medicine, National University of Health Sciences, and University of Bridgeport College of Naturopathic Medicine. Since 2003 there has been more writing by naturopathic physicians in the *Townsend Letter*, reflecting the greater role that they are playing in proving functional, integrative, and complementary/alternative medicine.

The Best of Naturopathic Medicine articles from 2003 through 2013 are listed below. Each of these issues is available for ordering from the *Townsend Letter*.

February/March 2003 #235/236

The Role of Teaching in Naturopathic Medicine, by Greg Garcia, ND

A Position Paper on the Nature of the Counseling Relationship within the Philosophy of Naturopathic Medicine, by Hanna-Ian Faraclas, MS, CCE

The Healthy Side of Saturated Fats, by Teri Johnson, ND, and John Keoni Teta, ND

A Case Report on the Successful Use of Inositol Hexaniacinate for the Treatment of Achlorhydria: Its Possible Mechanism of Action Upon the Central Nervous System and Parietal Cell-Adenosine Triphosphate-Dependent K+/H+ Pump, by Jonathan E. Prousky, ND, FRSH, and Dugald Seely, BSc, ND

Ecological Perspectives on Naturopathic and Allopathic Medicine, by Jen Green, ND

Need of Frequent Repetition of the Remedy in High Potency in Chronic Cases with Causal Hypothesis, by Rajendra P. Upadhyay, MSc, PhD, DEHM, DIHom (UK)

The Future of Naturopathy is in Whole Systems Education and Research, by Dan Kenner, PhD, LAc

Whole Foods, Getting Back to the Basics: Our Foundation as Physicians, by Chris D. Meletis, ND, and Jason Barker, ND

February/March 2005 #259/260

Traditional Bone Broth in Modern Health and Disease, by Allison Siebecker, ND

Orthomolecular Treatment of Anxiety Disorder, by Jonathan E. Prousky, ND, FRSH

An In-Office Evaluation of Four Dietary Supplements on Natural Killer Cell Activity, by James Belanger, ND, MT

Melatonin, Menstruation, and the Moon, by Sari Cohen, ND

An Epistemology of Naturopathic Medicine: Toward a Model of Clinical Investigation Culminating in Transformative Experience, by Richard M. Krebs

Great Spirit Above, Hear My Prayer, by Lauren Russel, ND

February/March 2007 #283/284

The Art and Science of Naturopathic Medicine, by Rita Bettenburg, ND

A Vision for Naturopathic Medicine, by Paul Mittman, ND

Latent Autoimmune Diabetes of Adults (LADA): Diagnosis & Natural Approaches to an Often-Overlooked Presentation, by David Graves, ND

Hypothyroidism: Optimizing Medication with Slow-Release Compounded Thyroid Replacement, by Martin Milner, ND

The Orthomolecular Treatment of Schizophrenia: A Primer for Clinicians, by Jonathan E. Prousky, ND

Nutrigenomics and Nutrigenetics in Whole Food Nutritional Medicine, by Ani K. Hawkinson, ND

Parents' Reasons for Choosing Naturopathic Medicine for Their Children's Health Care, by Brenda Leung, ND

The Top Ten Challenges Facing Naturopathic Medical Education, by Greg Garcia, ND

February/March 2009 #307/308

Hiatal Hernia Syndrome, by Steven Sandberg-Lewis, ND

Homeopathy and Chinese Medicine: Uniting Two Forms of Energetic Medicine, by Mario Fontes, MSOM, and Stephanie Pina, ND

Links between ADHD and Environmental Pollutants: Implications for Preventative Naturopathic Clinical Practice, by Dugald Seely, ND, MSc; Kieran Cooley, ND, MSc (Cand.); and Heidi Fritz, ND, MA (Cand.)

Food for Thought: Review of Nutritional Modalities Used for the Treatment of Mental Illness, by Baljit K. Khamba Grewal, BSc, MPH, ND (Cand.)

February/March 2011 #332/332

Understanding the Serum Vitamin B12 Level and Its Implications for Treating Neuropsychiatric Conditions: An Orthomolecular Perspective, by Jonathan E. Prousky, ND, MSc

The *Merck Manual* Welcomes Alternative Medicine, by Stephanie Pina, ND, LAc, MSOM

A Case of Incipient Autism, by Artemis Celt, ND

Proton Pump Inhibitors: A Risky Experiment? by Steven Sandberg-Lewis, ND

Using the Feminine to Heal the Aggressive Masculine: Designing Acupuncture Protocols through Naturopathic Philosophy for the Treatment of Excess Yang Conditions, by Jennifer Coomes, BA, LMT, RYT

Caring for Chronic Hurt: Childhood Abuse and Holistic Treatment Perspectives, by Laura DeVincentis, ND, LAc, and E. Feigenbaum, PhD

February/March 2013 #355/356

How I Practice Now, by Jacob Schor, ND

Fatigue and Primary Hyperparathyroidism: A Case Report, by Karima Bassalé, ND, and Dohn Kruschwitz, MD, ND

What to Do When Patients Wish to Discontinue Their Psychotropic Medications? Effective Tapering Strategies to Limit Drug Withdrawal and Destabilization, by Jonathan E. Prousky, ND

Vitamin and Mineral Treatment in Asthma, by Aminder Singh, BSc, ND, and Lindsay Feuerstein, MSc

The Milner Acetylcholine Protocol (MAP) for Management of Cardiac Dysrhythmias, by Jeremy Mikolai, ND, and Martin Milner, ND

A Holistic Approach to Modern-Day Chronic Disease Management: Pharmacological Therapies, Lifestyle Choices, and Nitric Oxide Deficiency, by Nathan S. Bryan PhD

Small Intestine Bacterial Overgrowth: Often-Ignored Cause of Irritable Bowel Syndrome, by Allison Siebecker, ND, MSOM, LAc, and Steven Sandberg-Lewis, ND, DHANP

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Congratulations to all the participants in our Best of Naturopathic Medicine competititon. We thank you for your award-winning submissions. We invite the naturopathic physician community to send their entries next year for our 2017 competition.

The Manifestations and Triggers of Mental Breakdown, and Its Effective Treatment by Increasing Stress Resilience with Psychosocial Strategies, Therapeutic Lifestyle Changes, and Orthomolecular Interventions

by Jonathan E. Prousky, ND, MSc

Abstract

For more than 16 years, the author has focused his clinical practice on the evaluation and treatment of mental disorders. Here he presents two common patient scenarios, which are amalgams of many patient cases. He refers to these cases throughout this report to highlight specific themes, opinions, and/or observations about individuals having mental disorders. This article focuses on the psychological domain of chronic stress as resulting from allosteric overload, how it manifests, what factors exacerbate it, and how chronic stress can be managed effectively with a holistic plan that includes the appropriate use of psychosocial strategies, therapeutic lifestyle changes, and several "core" orthomolecular therapies.

Introduction

For more than 16 years, I have focused my clinical practice on the evaluation and treatment of mental disorders. This has afforded me a tremendous amount of education and clinical experience with this vulnerable group of patients. While I cannot speak of any particular patient as being "typical," since they are all individuals with their own unique histories and physical makeup, all such patients have presented with consistent commonalities (and themes). Here I present two common patient scenarios, which are amalgams of many patient cases. I will refer to these cases throughout this report to highlight specific themes, opinions, and/or observations about the evaluation and management of individuals having serious mental disorders.

Scenario 1: This patient, whom I will refer to as Mary, is a 32-year-old female with chief complaints of fatigue, insomnia, depression, and anxiety. The onset of her depression began 5 years ago following her marriage. She met her husband while in graduate school. After dating for 8 years, they decided to get married. Soon after their marriage, they started having difficulties getting along. Often they would not see each other for weeks at a time owing to their different work schedules. They have no children and are uncertain if their marriage should continue. They have not sought couples counseling.

Mary is tired for much of the day. If she is lucky, she may exercise once each week. She seldom eats breakfast, often rushing through lunch while working at her desk. Over the past year, her work performance has declined and people have noticed that she appears less sharp. She avoids most of her coworkers because she does not want to "waste" valuable time at work. Her boss has told her on numerous occasions that she needs to be more sociable because people often perceive her as cold, detached, and unfriendly. At dinnertime, Mary typically eats alone while watching television. Shortly after dinner, Mary will do some work and then watch more television. She tries to get to sleep by midnight. Her sleep is fragmented. She wakes up several times each night worrying about her marriage, her job, and how unwell she feels. She used to go to church on Sundays, but stopped since her husband finds that "religious" thing silly.

She saw her family doctor several times over the past 4 to 5 months. She was told that she has clinical depression and generalized anxiety disorder. At the first visit, she was prescribed sertraline hydrochloride (50 mg/day) and told that she has a biochemical imbalance that requires psychotropic medication. She is taking sertraline hydrochloride (150 mg/day), lorazepam (1 mg sublingually as needed), and zopiclone (7.5 mg at bedtime/day).

Scenario 2: This patient, whom I will refer to as Mark, is a 22-year-old male with a chief complaint of schizophrenia. He was diagnosed 4 years ago after being admitted to the hospital near the university that he attended. At the time of his first episode of psychosis, he had just ended a tumultuous relationship, and he had been smoking cannabis daily for months as well as occasionally using

amphetamines to improve his focus and get his homework done expeditiously. During his first episode of psychosis, he was in the hospital for 2 weeks, where his mental state normalized after he was administered a couple of haloperidol injections, followed by lorazepam as needed for acute anxiety (1 mg), and risperidone (5 mg) given nightly. At discharge, he was told to remain on the risperidone and lorazepam until he could be evaluated by a psychiatrist in the community.

About a month later, a community psychiatrist told Mark that he likely had schizophrenia and that he would need medication for the rest of his life. Mark left the psychiatrist's office irritated and thinking that the visit was a "complete waste of time." He took himself off his medications within a couple of weeks without any guidance. Several months later, another relationship went awry after he had fallen deeply in love with a different woman. Following this breakup, Mark began to use cannabis daily. After a few weeks he started isolating himself, stopped eating, became paranoid, and said bizarre things to people whom he knew and to complete strangers. Eventually, a concerned friend took Mark to the emergency room of a nearby hospital. While waiting, Mark became agitated. He was restrained forcefully, and given medication to quickly sedate him. He was kept for 2 weeks in a locked unit, where no visitors were allowed to see him. Then he was placed in a less strict mental health ward for approximately 2 months. He was discharged on the following medications: olanzapine (10 mg twice daily), paroxetine (30 mg/day), clonazepam (1 mg twice daily), and zopiclone (7.5 mg at bedtime).

When Mark was in my office for the first time, he was still taking these medications despite feeling that they were making him sick and progressively unwell. He weighed 230 pounds (his weight prior to medication was 170 pounds), felt tired most of the day, complained of an inability to concentrate (could not watch television or read without losing his focus), had no passion or enthusiasm for life, and felt "useless" as a person.

Mark has been away from university for 3 years and lost touch with most of his friends, all of whom have graduated. Mark normally goes to bed around 1 or 2 in the morning and sleeps until noon or later. He does nothing all day and feels bored most of the time unless he is smoking. He spends at least 4 to 6 hours on the Internet, much of that time on pornography websites. Mark was assigned to an assertive community treatment (ACT) team, but he feels that they care very little about his life and situation. Mark's case worker sees him once a week but only asks about the medications. That does little to promote Mark's well-being.

The psychiatrist told Mark on many occasions that he was a tremendous success since his psychotic symptoms have all but resolved. Mark felt awful and wanted to see if he could potentially get off his medications and return to university. His parents were unwilling to entertain the notion of Mark's discontinuing medication. They told him that he would need to remain on medication while living in the family home.

Mark and Mary's stories are similar in that both individuals found it progressively more difficult to moderate their stress levels amidst the storms of their lives. Both individuals succumbed to the effects of chronic stress, which has been defined as "ongoing demands that threaten to exceed the resources of an individual in areas of life such as family, marriage, parenting, work, health, housing, and finances."[1] When an individual is faced with chronic stress, it may seem enduring and without a clear ending. Somehow while unwell, the mentally ill individual has to manage his/her stress levels while moderating its problematic effects. The term *allostasis*, coined by Sterling and Eyer, defined as achieving "stability through change," was constructed to describe a process in which an individual adjusts to life's stresses over time.[2] While the specifics of these stabilizing adjustments (i.e., adaptive responses) are beyond the scope of this article, adaptation through change demands the synchronous activation of neural, neuroendocrine, and neuroendocrine-immune mechanisms.[3]

Mark and Mary experienced the effects of allosteric overload, which led to signs and symptoms of mental distress and/or physical dis-ease (denoting an imbalanced or disrupted physical state). This results when an allosteric system fails to habituate to the recurrence of the same stressor, fails to shut off following overwhelming stress, and/or whose response is deficient resulting in heightened activation of other, normal counter-regulatory systems.[3,4] Unmitigated chronic stress because of allosteric overload will typically cause psychological and physiological dysregulation, especially in people who are vulnerable to mental illness.

This article will focus on the psychological domain of chronic stress as resulting from allosteric overload, how it manifests, what factors exacerbate it, and how it can be managed effectively. Chronic stress is a systemic problem. Prolonged distress can damage the body and "mind," strain patients' adaptive capabilities, disrupt neurotransmitters, and deplete essential nutrients such as energy and enzyme cofactors. Vulnerable individuals can destabilize until they experience or relapse into episodes of mental illness.

Manifestations and Triggers of Mental Breakdown

1. *Mental Distress Signals of Inadequate Allostasis*

All individuals differ in their abilities to achieve adequate or productive allostasis when faced with an overload of life stresses. It is obvious that Mark and Mary displayed different observable signals of mental distress. Mary presented with constant worrying, insomnia, and depression, while Mark's signals of mental distress involved cannabis addiction, paranoia, and bizarre behavior. Though I have not statistically analyzed the different types of mental distress signals that my patients have displayed over the past 16 years, the most common ones that I've observed are listed in Table 1 (p. 56) in no particular order.

2. *Psychosocial Distress Signals and Triggers of Inadequate Allostasis*

Outside of the observable signals of mental distress that can be elucidated in the clinical encounter, patients will often report psychosocial distress signals that further damage the quality of their lives. Psychosocial distress signals refer to difficulties in maintaining productive

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relationships (i.e., at home, at work, or in other social settings). These typically lead to psychological difficulties or the exacerbation of existing psychological problems.

Mary's unhappiness was partly related to being disengaged from her husband and not being able to communicate effectively with him. Also, Mary was working too much, not meeting her deadlines, and perceived by her coworkers and boss as withdrawn and unapproachable. She ruminated excessively and worried about her job and her marriage. Generally she felt unwell.

Mark isolated himself from his peers during his second episode of psychosis, and this isolation continued following treatment. He lost contact with his university friends. Mark remarked on how bored he was, and stated that he didn't do much other than smoke and meet once each week with his ACT team case worker.

Patients with life situations and problems like those of Mark and Mary often report many psychosocial distress signals. The common ones that I've observed in clinical practice include: (1) frequent difficulties at work, problems completing projects on time, delays in getting things done, and so on; (2) boredom, often associated with persistent ruminations and negative thoughts; (3) isolation from others, commonly associated with loneliness; (4) lacking a sense of life purpose; (5) not having close or caring friends and/or a social support system; (6) poor relational skills accompanied by frequent interpersonal conflict and a lack of quality interpersonal connections; and (7) financial problems.

The overarching phenomenon that prevents patients from correcting their psychosocial problems is their inertia in confronting them. Psychosocial problems won't go away by ignoring them, yet patients often erroneously believe that their problems will eventually resolve on their own without any active work or consistent efforts to change things.

Table 1: Mental Distress Signals of Inadequate Allostasis

Anxiety, persistent or intense episodic
Depression
Despair
Helplessness
Insomnia
Lack of optimism (absence of a positive outlook)
Anger
Denial
Guilt
Hostility
Hyperactivity
Isolation
Restlessness
Shame
Addictive behaviors (e.g., using cannabis and alcohol) to anesthetize feelings
Inability to delay gratification
Not eating, undereating, or overeating
Habitual cutting or the desire to harm oneself
Suicidal thoughts
Homicidal thoughts
Delusions
Dissociation
Depersonalization
Grandiosity
Hallucinations
Hyperreligiosity or bizarre religious beliefs
Mania
Obsessions
Paranoia
Persecutory thoughts

Oppressive Forces That Promote Inadequate Allostasis

In addition to the mental and psychosocial distress signals just described, strong oppressive forces may undermine a patient's ability to achieve allostasis. This usually involves some combination of the following four interrelated domains: (1) the dominant mental health system; (2) psychotropic medication; (3) psychiatric diagnoses; and (4) family and friends.

This does not mean that all these domains are "bad" and unhelpful for every patient; rather, I am simply reporting observations and describing how these domains often operate oppressively to the detriment of patients under my care. These domains can weaken a patient's capacities for hope and enthusiasm, and undermine the belief that change is possible, thereby hampering the patient's efforts to reestablish allostasis.

1. The Dominant Mental Health System

I define the dominant mental health system as some combination of inpatient and outpatient medical services involving a psychiatrist, family physician, and other treatment members who have been charged with providing the majority of mental health care to an identified patient. If the dominant mental health system is needed (e.g., suicide prevention), it should only be a short-term commitment. I have concluded that the sooner a patient departs from the system, the better off he/she will be. When patients become more immersed in the dominant mental health system and get committed to it for an extended period, they are typically faced with increasing pushback, oppression, and an overall negativism about their recovery. This becomes particularly evident when patients question their current treatments, become empowered about self-care, seek providers outside the dominant system, and ask about "alternative" forms of treatment.

In Mark's case, he hated being on psychotropic medication and felt that it made him sick and progressively unwell. If Mark should voice his dissatisfaction to the clinicians overseeing his care, it has been my experience that such expressions of disappointment are usually met with oppressive and negative statements like:

"You need treatment for life."
"No other options can help you."
"This is the correct path and you should learn to accept it."

The after-effects of such statements often lead patients like Mark to become agitated, since their individual needs have not been validated, recognized, and/or handled empathetically. As a result, the prescribing clinician usually increases the dose of psychotropic medication or adds other psychotropic medication because he/she believes that Mark's behavior represents not only a lack of insight but also a need for more symptom-suppressive treatment (i.e., additional psychotropic medication).

Mark also participates in ACT, and should he question why he is being forced to take psychotropic medication, the pushback from the ACT team is something akin to: "You need medication for the rest of your life." While there are some very good ACT teams that do more than enforce psychotropic medication compliance and provide compassionate care, many of my patients have not been pleased with their ACT team experiences. Patients have repeatedly told me that their ACT team's focus has primarily been on medication compliance and not on their expressed individual needs. In one study, 4 in 10 patients with psychiatric disorders reported experiencing some form of leverage to adhere to treatment in the preceding 6 months. Medication compliance enforcement pressures may involve the criminal justice system, finances, housing, and outpatient commitment.[5] This study also found that patients exposed to the most coercion were more likely to take their medications as prescribed, but had less satisfaction with their treatment.

A more publicized study, the largest randomized trial to date on the subject of compulsory community treatment, compared community treatment orders (CTOs; same as ACT) and Section 17 among patients with psychosis in England.[6] The essential differences between patients on CTOs and Section 17 is that those on CTOs have longer periods of compulsory supervision. The results of this study did not show any differences in hospital readmission rates (36% for each group) despite the large differences in compulsory supervision (median 183 days for the CTO group compared with median 8 days for the Section 17 group). The authors of this study concluded: "The evidence is now strong that the use of CTOs does not confer early patient benefits despite substantial curtailment of individual freedoms."

Thus, it appears that forced outpatient treatment (as in CTOs or ACT teams) does little to improve outcomes and, more importantly, compromises patients' civil liberties. When patients like Mark become more unsettled and vocal about the way they wish to be treated, the dominant mental health system often becomes more controlling and oppressive to the point where, not uncommonly, patients lose hope and simply give up (i.e., after experiences that lead to "learned helplessness"). This typically happens over time as the patient's will and action to change are repeatedly ignored and disregarded, thus preventing the patient from receiving personalized care based on mutually respectful, nonjudgmental, and meaningful collaboration that considers each patient's individual symptoms, diagnoses, responses to treatments, and needs for support, encouragement, and competent care so that he/she can recover and live well.

The most egregious and dehumanizing form of oppression from the dominant mental health system results when a patient is involuntarily committed, forced to take psychotropic medication, isolated from family and friends, and kept in an unfamiliar environment for several days, weeks, or longer. Such violations of civil liberties can quash a patient's will to get better, or even impair a patient's will to live. Another unfortunate consequence of forced confinement and treatment is that emotional and physical trauma can be associated with such a harrowing experience.

Mental Breakdown

I was once asked by an intern at the college where I work if I would attend a Consent and Capacity Board meeting at a hospital on behalf of her sister, who was diagnosed with schizophrenia and had been held involuntarily in a hospital facility for months. The family and intern wanted me to speak about possible alternative forms of treatment for schizophrenia. The hearing attendees included a lawyer who also happened be a psychiatrist, the patient's treating psychiatrist, family members, me, and members of the hospital administration. The patient was committed and forced to receive psychiatric treatment despite the fact that she had deteriorated while under the care of the hospital. She was kept in a locked unit and had not seen any family members for 6 to 7 months. Her mother was a psychiatric nurse, and despite her pleas at the meeting that the hospitalization and psychotropic medications were making her daughter worse, she was denied any access to her daughter. The hearing determined that this patient needed to be in treatment for another few months despite these pleas. I was never granted the opportunity to speak about possible alternative treatments for schizophrenia. The patient was eventually discharged after having been kept in a locked ward with dangerous criminal justice offenders for about 12 months.

A few years ago, I had a conversation with this patient's sister (the former intern) and was told that the patient is now thriving without any medication, working, and living a normal life. Apparently, upon discharge, the patient's mother slowly tapered her off her psychotropic medications. This was done despite major pronouncements and decrees that her daughter would require psychotropic medication for life. The patient returned to Iran, where extended family could assist in her recovery without threats of hospitalization and forced involuntary commitment.

While this story eventually had a happy ending, many patients I work with feel completely helpless trying to understand and cope with the dominant mental health system that they have

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been forced to comply with. It takes time, but some of these patients can divorce themselves from this system. Many eventually become healthier and more productive. For some patients, the damage has been too much and continued for too long, making it unlikely that they will sever their connections with the dominant mental health system. For this group of patients, the oppressive forces of the dominant mental health system will always be an obstacle undermining their chances of experiencing meaningful recovery and achieving effectual allostasis.

2. Psychotropic Medication

Psychotropic medications are often touted as correcting some underlying defect or "broken" biology that is adversely affecting a patient's mental state. The most common example is the much-popularized belief that a serotonin deficiency is causal in depression and that augmenting serotonergic neurotransmission will "correct" this "broken" biological system and hasten recovery from depression. Truth be told, there are no convincing data to support this popular belief.[7] Psychotropic medications are not disease-modifying interventions when compared with other medications that conventional medicine prescribes for diagnosed diseases or pathologies. More appropriately, psychotropic medications are symptom-modifying interventions that "induce complex, varied, often unpredictable physical and mental states that patients typically experience as global, rather than distinct therapeutic effects and side effects."[8] These unpredictable global psychoactive effects (i.e., sedation, psychomotor slowing, activation, and altered sense perception) are often associated with negative outcomes.[9]

While the judicious use of psychotropic medication can benefit some patients (especially if the number of medications is minimized and treatment is restricted to short-term use only), this is not what I have commonly observed. I have seen numerous patients lose their drive and enthusiasm while on psychotropic medications. Drive and enthusiasm are essential "energetic" components in facilitating recovery. Patients like Mark often have their recoveries impeded by the resulting medication-induced psychoactive effects (e.g., alexithymia, anhedonia, cognitive dysfunction, inertia, and mental fatigue), which thwart their motivational systems. It was apparent that Mark's "energetic" capacities for change were severely limited due to the psychoactive effects of his taking four psychotropic medications daily.

In more extreme cases, patients can become so unaware of these adverse effects that they begin to think that they are functionally improved despite how impaired they have become. Dr. Peter Breggin has referred to this phenomenon as *intoxication anosognosia* (i.e., medication spellbinding), which has been explained as a failure to perceive that one's irrational, uncharacteristic, and/or dangerous behaviors are being caused by the brain-damaging effects of psychotropic medication, and believing that the medications are helping despite obvious mental deterioration.[10] I can recall a patient taking several psychotropic medications who deteriorated mentally over the course of 5 months under my care. She did nothing all day except watch television and listen to music. When I asked the patient about working, socializing, and exercising, she responded: "I am fine and feel well. I just like to relax all day. I like the way medications make me feel." I tried to help this patient for many months but could never provide any form of treatment that was capable of overcoming the demotivating and flattening psychoactive effects of the psychotropic medications that she was taking.

The example cited above demonstrates the ineffectiveness of psychotropic medication in facilitating recovery. When studies have evaluated patients more naturalistically (i.e., in a manner that is similar to office-based or outpatient medicine), the results have shown that the long-term use of psychotropic medication does not lead to recovery and is actually associated with worse outcomes for patients diagnosed with depression, bipolar disorder, and schizophrenia.[11-23] For a more thorough review of the literature on the poor long-term outcomes associated with psychotropic medication, the reader is urged to review the work of Whitaker.[24,25]

One study worth describing in greater detail, which illustrates these poor outcomes, involved patients with psychotic disorders.[26] This study included 64 schizophrenia patients, 12 schizophreniform patients, 81 other psychotic patients, and 117 nonpsychotic patients. All these patients were assessed as inpatients and then reassessed 5 times over the 15-year study period. At 15 years, the percent of schizophrenic patients in recovery while on antipsychotic medication was 5% compared with 40% of schizophrenic patients not on medication. In a more recent report by two of the same investigators, the schizophrenia patients in their sample who were treated continuously with antipsychotics over 15- and 20-year periods showed considerable psychopathology and few sustained periods of recovery.[27] They even noted that the sample of schizophrenia patients who were not treated with medication for many years fared significantly better and had much better outcomes than the sample of schizophrenic patients on antipsychotic medication.

While problematic medication-induced psychoactive effects cannot always be well demarcated in patients who have histories of poor lifestyle habits, problems with interpersonal relationships or social competence, difficulties in maintaining employment, and/or habitual substance use/abuse, the psychoactive effects of psychotropic medications in and of themselves add a significantly harmful "biological" burden that makes the capacity for change and recovery much more difficult. The most unsettling biological effects have to do with adverse brain changes (i.e., damage) that result from psychotropic medication. These have been well elucidated by many investigators. Examples include the extrapyramidal syndromes (i.e., akathisia, dystonia, parkinsonism, and tardive dyskinesia) associated with antipsychotic medication, psychomotor and cognitive impairment associated with long-term benzodiazepine medication, the depressogenic effects of antidepressant medication (especially long-term), and the cognitive deficits associated with

psychotropic medications used to treat bipolar disorders.[28–33]

Here is a case that demonstrates the damaging effects of psychiatric medication. The patient is a very pleasant 25-year old male with pronounced tardive dystonia. During his first year of college (sometime in 2004), the patient began to withdraw from life, slowly losing contact with his friends and family. He also became agitated, requiring little sleep, and his thoughts and therefore his behaviors became increasingly more bizarre to his fellow students and diminishing pool of friends. He was eventually admitted to a nearby hospital and given a diagnosis of schizoaffective disorder. He was prescribed 2 mg daily of risperidone to manage both the psychotic symptoms and agitation. Within about 10 days, his condition stabilized and he was discharged back into the community with a referral to an outpatient psychiatrist and instructions to attend an outpatient program for mental health patients. Within several weeks of taking risperidone, he developed frequent episodes of facial grimacing and painful upper-body contractures, characterized by having his shoulders being temporarily fixed into a shrugged position with concomitant tensing of the neck muscles. When I last saw this patient, the facial grimacing (tardive dyskinesia) had lessened, but his painful contractures (tardive dystonia) involving the upper trapezius and anterior cervical muscles were occurring constantly. The patient was having these dystonic episodes numerous times throughout the day. They became so bad that he had to leave his job because he was getting unwanted attention from his coworkers and clients, which resulted in shame, increased psychological distress, and embarrassment. When this patient questioned the value of this medication to several psychiatrists, each one told him that the medication was necessary for his ongoing stability, without any concern or compassion for resulting physical impairments. This is alarming, but not so surprising. The patient actually believes that the medication is necessary despite the fact that he has been neurologically damaged for life as a result.

The increasing medicalization of mental health makes patients believe that their human struggles can be remedied by taking prescribed psychotropic medication (i.e., "popping" pills) instead of committing to the very difficult task of identifying and solving problems, and thereby making their lives better and more fulfilling in spite of setbacks and learning to become more tolerant of emotional discomforts. Middleton and Moncrieff discussed this in their provocative article that questioned the merits of antidepressant medication. They noted the following: "Symbolically, medication suggests that the problem is within the brain and well-being is dependent upon maintaining 'chemical balance' by artificial means. This message encourages patients to view themselves as flawed and vulnerable and may explain the poor outcomes of treated depression in naturalistic studies."[34]

Another unfortunate consequence of psychotropic medication is that prescription drugs can be disempowering. Most clinicians providing care communicate to patients that the best thing they can do for themselves is to take psychotropic medication. This touted biological "fix" often makes patients believe that this is the most important component of their recovery. Too much emphasis has been placed on the essentialness and/or beneficial properties induced by psychotropic medication. This confuses patients and leads them to believe that other components (e.g., psychological and spiritual development, counseling, and regular exercise) designed to facilitate recovery are incapable of providing sufficient results over time. This often pushes patients in a "medication-only" direction and makes them less likely to use nonmedication resources that could be extremely beneficial. Thus, in many instances, the provision of psychotropic medication hinders recovery and undermines allostasis, particularly as a result of disabling psychoactive effects (especially, long-term), and by demotivating effects that result when medications are promoted as the most important elements involved in treating serious mental illness.

3. Psychiatric Diagnoses

What happens to patients when their signals of mental distress are labeled with psychiatric diagnoses? Some patients find comfort and solace in receiving a psychiatric diagnosis, since this legitimizes (in their minds) their suffering and provides succinct rational reasons for their misery. However, my clinical experiences have suggested quite the opposite. Patients often internalize their assigned psychiatric labels similar to patients who receive a diagnosis of diabetes or congestive heart failure. Typical doctor–patient interactions teach patients that their mental struggles are the result of some disease process requiring pharmacological treatment, or else the consequences will be disease progression, much like untreated diabetes. Patients learn to identify themselves with their psychiatric diagnoses, and their problems thereby become very specific, requiring precise psychotropic treatment.

When Mary went to her family doctor and received a psychotropic medication, she was told that her mental health struggles were the result of a biochemically "imbalanced" (i.e., diseased) brain. Instead of understanding Mary and her life problems, her family doctor disconnected Mary from them by assigning her psychiatric diagnoses and medicating her. Mary also became disconnected from her problems by believing in her psychiatric diagnoses with their assigned biological fix. The end result of this common clinical conundrum is that patients like Mary do little to enhance their lives beyond taking psychotropic medication, since the most valued and recognized approach to their treatment involves the "medicalization" of their human struggles.

Another unfortunate consequence involves the stigma associated with psychiatric diagnoses. When patients like Mary believe they have a psychiatric problem requiring a biological "fix" this implies an underlying defect. Stigmatizing patients only deepens their psychic injuries and makes them more recalcitrant to grow and change since their humanity and struggles become secondary consequences of their presumed mental defects. As a

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result, patients feel more vulnerable, experience more shame, and feel less tolerant of life stresses. This interferes with their motivation to solve problems and implement positive changes and reduces their capacity to stabilize (i.e., makes achieving allostasis more difficult to achieve).

4. Family and Friends

Having a good support system is a definite asset and an integral part of recovery. Many families and friends of mentally unwell patients provide loving support and helpful encouragement. However, it is not uncommon for families and friends to become obstinate when a patient exerts his/her own ideas about treatment. When Mark mentioned to his parents that he would like to eventually discontinue his psychotropic medications, they told him that he could only live with them as long as he remained on medication. This is a very common method by which families undermine progress in a loved one. When threats are used to manipulate a particular outcome, this usually results in more acting out (i.e., frustration and/or anger) or the opposite (the patient becomes more inward, depressed, and socially isolated). None of these outcomes are helpful, since they prevent an honest and frank negotiation about what the patient wants and how best to meet these expressed needs.

Another problem that patients experience is that family and friends become hypervigilant about the patient's day-to-day moods and behaviors. All people, not just patients, have normal ranges of emotional responses daily; these can vary from mild to very intense. Otherwise normal daily fluctuations by patients are often thought to signal mental distress and possibly destabilization. An angry patient with a diagnosis of schizophrenia is thought to be destabilizing and psychotic as opposed to being justifiably angry about something. The patient has to "walk on eggshells" and maintain, on a day-to-day basis, a very narrow range of emotional responses to life events. Inevitably, the patient cannot contain this narrow range (for such containment is abnormal) and will have moments where his/her emotional reactions can be sudden and even extreme when witnessed by family and friends. This often results in unnecessary pressures to take more psychotropic medication and/or to conform behaviorally in a manner that is unreasonable. Thus, threats and constant hypervigilance by family and friends do little to promote wellness or instill the confidence necessary to recover from struggles with mental illness. These factors undermine allostasis and deny patients the healing potentials and joys that loving and nurturing relationships can provide.

Psychosocial Strategies that Promote Allostasis and Functional Recovery

An individual's capacity to buffer the ill effects of allosteric overload arises from genetic endowment and life experiences.[3] Allostasis can be strengthened by psychosocial treatments aimed at increasing an individual's resilience to the stresses of life. Many resources can be utilized to strengthen a patient's circle of care, thus affording better outcomes and greater possibilities to live with satisfaction and purpose. This is all predicated, however, on the patient's ability to recognize value in such treatments despite the fact that they are given mere lip service by the majority of clinicians, who typically focus only on prescribing psychotropic medication.

1. Access to Proper Shelter and Regular Meals

Some patients live in inadequate environments where they do not feel safe or comfortable. If their living situations remain problematic, this will only trigger further mental distress. I had a patient who would dissociate when he felt physically threatened by the neighborhood surrounding his apartment. Only when he moved to a new apartment could he find solace and comfort in his living quarters. That moderated the frequency of his dissociation. It is important that patients have access to a residence that provides comfort, safety, and stability. As clinicians, we need to ask our patients about their living situations and get in touch with their case workers or social workers to see what opportunities exist when there are problems with their residences. This seems like a lot of work, but it becomes impossible to move treatment in a positive direction when patients' basic needs for shelter are compromised.

Additionally, patients need to eat regular meals and have access to nourishing food. I have a patient who often runs out of money and then ingests sugar packets instead of real food. Sometimes he consumes more than 50 sugar packets in a day. This patient does receive enough money for his basic needs, but due to compulsive spending he often runs out prior to the month's end. In supporting this patient, I have encouraged him to access free meals and food banks. All patients, despite their issues and obstacles (whether self-imposed or otherwise), need to eat regular meals and should be encouraged to use free resources. When patients cannot access regular meals, their treatment and progress are thwarted until they can eat normally.

2. Psychotherapeutic Service Referrals and Forming a Therapeutic Alliance

Patients should be referred for ongoing psychotherapy to better understand aspects of their lives that might be impeding their growth and/or to receive emotional support. The most integral aspect of successful psychotherapy happens to be the therapeutic alliance. It is vital to the patient–clinician relationship that the psychotherapeutic encounter offers understanding, acceptance, a safe space without judgment or threats of hospitalization, and well-articulated and negotiated care. These "alliance" factors facilitate healing and will impart feelings of wellness while also reducing or moderating symptoms of mental distress. Research across several studies and meta-analyses has consistently shown a strong relationship between the therapeutic alliance and outcome (for an example of this research see Horvath et al.).[35] In other words, the better the therapeutic alliance, the more likely that the patient will derive benefit from psychotherapy. These benefits are not just emotional but also physical, since structural brain changes have been associated with successful psychotherapy.[36] When people experience a sense of belonging and have the perception of feeling

supported and acknowledged, their brains will structurally change in a positive manner, rendering them less vulnerable to the stresses of life.

Among the many psychotherapeutic strategies available, I tend to refer patients to psychotherapists who also offer mindfulness-based approaches. Mindfulness practices teach patients to become more engaged in the moment while also allowing them to become more tolerant of emotional discomforts. Studies on mindfulness-based cognitive therapy have shown it to lessen excessive worry and emotionality.[37,38] For a thorough discussion on the beneficial neural or brain mechanisms implicated in mindfulness-based meditation, the reader is requested to review the paper by Zeidan et al.[39]

3. Building Social Competence and Interpersonal Connections

Many patients like Mark become increasingly isolated, even with the "gold" standard of modern psychiatric treatment. While Mark's friends have either remained in university or graduated and found regular employment, he spends most of the day alone without the usual social interactions that most people experience and take for granted. Mark's social network disintegrated as a result of his mental health struggles. Mark's only regular social interactions involve his parents and the weekly ACT team visits, during which his case worker seems more concerned about medication compliance than Mark's emotional and physical well-being. Mary, on the other hand, is not socially isolated, since she is married and has full-time work. Even though she is dreadfully unhappy, she derives benefits from full-time work and having regular interactions with people.

Spending too much time with oneself can escalate mental distress while also eroding important social skills. Some of the most common consequences of social isolation are loneliness and boredom. One study found loneliness to be associated with all mental disorders, particularly depression, phobia, and obsessive-compulsive disorder.[40] Recent research has shown that boredom is correlated to depression and likely manifests in two forms: apathetic boredom and agitated boredom.[41] I have observed in clinical practice the negative impact that loneliness and boredom have upon socially isolated patients, especially those who live on their own and receive disability support. Most of these patients lack a regular routine and a daily schedule. If social isolation is not managed aggressively, it can eventually lead to an early death when patients enter their fifth decade of life.[42] Only through interactions with other people can patients develop the necessary social competence and skills required to foster meaningful relationships. Social experiences teach patients about themselves through the implicit and explicit feedback that they receive to help them develop the necessary social skills and competence and maintain solid relationships over their lifetimes.

To assist patients in overcoming their social isolation, I work with them to develop a weekly routine that keeps them busy while also providing important social challenges. Patients should be encouraged to volunteer and participate in library groups, reading clubs, adult education, and regular physical activity (e.g., walking or running groups/clinics). Most patients live in a community with a library and a community center and thus they have easy access to regular social events in safe, nonthreatening settings. Those can help to build social competence and maintain interpersonal relationships.

Since many patients develop social anxiety disorder as a result of their isolation, I refer them to Toastmasters (www.toastmasters.org) when appropriate. It builds confidence in public speaking and helps patients become more socially competent while working through their social awkwardness. In an article discussing alternative psychotherapeutic approaches for social anxiety disorder, Toastmasters was highlighted as an alternative that provides positive social exposure while fostering confidence in public speaking.[43] Since many patients feel nervous being around other people, working on their public speaking skills in a no-pressure setting pays huge dividends with respect to their social competence and confidence over time. One of my patients with schizophrenia became so engrossed in the Toastmasters experience that he ascended the ranks and became the master host of his local group. The experience helped him make friends with other members and following the weekly meeting, he would often tell me in delight about the fun that he'd had at the local pub.

4. Getting Support

Patients need to feel supported by their peers and not just from clinicians providing care. Some of my favorite resources include 12-step groups (e.g., Alcoholics Anonymous and Emotions Anonymous), peer groups (e.g., Hearing Voices Network), and/or specific mental health support groups (e.g., Toronto Shyness and Social Anxiety Support Group). The majority of these resources are free and provide excellent support. They open up the possibility of creating lifelong friends or at least a consistent social network. Something extremely meaningful and therapeutic often happens when a person with lived experience connects to another person for similar reasons. This support reduces mental distress signals and helps patients remain focused on their wellness while also forging important social connections that provide a sense of belonging, the feeling of not being so alone, and community.

5. Engaging in Purposeful Work

For many patients, the idea of working has not been mentioned by their clinicians, since the visit focuses predominantly on their mental symptoms. Our patient Mark does nothing all day, and yet, with the right support, he is capable of securing regular work. He just needs someone to motivate him without focusing on his lack of self-worth and his mental distress. Mary, on the other hand, has a full-time job, but she is on thin ice since she has become impersonal and detached from her coworkers. With the right support, Mary could learn to socialize better at work. That might help her to relax and feel less anxious, and perhaps she might find work enjoyable again.

Like all people, patients need to feel productive through regular work and develop a sense that they are contributing to society. This work ➤

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does not need to involve money, but it needs to be regular and it needs to provide enough of a challenge that the job does not become mundane and boring. Regular work should not be overly stressful or too difficult; otherwise, it becomes another trigger of mental distress. In other words, work needs to strike a balance between something challenging (but not too onerous or stressful) and something achievable (but not overly boring or mundane). A life coach or career counselor can help patients figure out what work or volunteer positions are most suitable for their needs. Free career counseling is often available if patients are motivated. When patients secure the right type of part- or full-time employment and/or regular volunteer work, their symptoms improve and they feel an increased self-confidence and mastery over their problems.

6. *Developing a Self-Management Strategy*

Self-management denotes the ability of a patient to pursue an active wellness plan, to recognize his/her mental distress signals, and to have a plan in place when things begin to go awry. The best way in which patients can do this work is through a program called the Wellness Recovery Action Plan (WRAP; www.mentalhealthrecovery.com), designed by Mary Ellen Copeland, PhD, a Vermont psychologist who has lived with and recovered from mental illness herself. Copeland developed WRAP for patients with mental health issues. It has approximately 20 citations indexed in PubMed. When patients complete this self-management tool, they end up with a package of self-help planning and coping strategies, which include: (1) a wellness toolbox; (2) a daily maintenance plan; (3) the identification of triggers and an associated action plan; (4) the identification of early warning signs that things are breaking down and an associated plan; (5) crisis planning; and (6) postcrisis planning.[44]

Research unanimously supports this approach and found that when patients do this work, they learn more about recovery and develop improved self-awareness by integrating WRAP into their daily lives.[45] Engaging in WRAP leads to positive changes in patients' knowledge, skills, and attitudes toward recovery. This often inspires and empowers them and can even be life changing.[46] WRAP has been subjected to formal studies that have shown it to reduce symptoms of anxiety and depression, and psychiatric symptoms in general.[47,48] Even among patients with severe and persistent mental illness, WRAP was able to enhance hope, improve quality of life, and reduce psychiatric symptoms.[44]

Patients can pursue WRAP on their own by purchasing books and completing the required exercises individually and/or with the help of a social worker, case worker, friend, or family member. Patients can also enroll in a WRAP course, which is my preference, since it motivates them to take an active role in their recovery while also fostering social connections with people who have similar lived experiences.

Therapeutic Lifestyle Changes

Traditional therapeutic lifestyle changes (TLCs) need to be incorporated into an overall recovery plan because adequate physical activity, sufficient sleep, a healthy diet, and abstinence from smoking and other substances of abuse all buffer against allosteric load.[4] Dr. Roger Walsh has authored the most authoritative paper on this topic. He noted that the primary benefit from TLCs is that they reduce primary psychopathology, whereas the secondary benefits provide neuroprotection, reduce age-related cognitive decline, reduce neural shrinkage, and improve physical health, self-esteem and quality of life.[49] Walsh's review of the literature shows that TLCs can treat multiple psychopathologies while bolstering psychological and social well-being, and stabilizing and optimizing cognitive capacities and improving neural functions. Here I will summarize some of the key findings from Walsh's paper and explain why they need to be part of every patient's recovery plan.

1. *Regular Exercise*

Exercise favorably alters serotonin metabolism; improves sleep; increases endorphins (e.g., the "runner's high"); enhances self-efficacy and self-esteem; interrupts negative thoughts and ruminations; reduces psychosomatic muscle tension; increases cognition; increases brain volume (i.e., both grey and white matter); and improves vascularization, blood flow, and other functional measures.

If you recall, Mary only exercises once each week or less often, and Mark does not exercise. Both patients would find that exercise usually helps moderate symptoms while enhancing the quality of life. It appears that neither of these patients was encouraged to exercise by their conventional care providers, or exercise was not a focus of their treatment. It should be, since the positive effects of regular exercise cannot be disputed. In my clinical practice, I negotiate with patients on how often and how long they should exercise. Optimally, I would like them to exercise aerobically for 30 to 60 minutes every day or every other day, but for many this is not possible. It is important that exercise be presented like any symptom-moderating treatment. Patients need to be properly informed about the value of consistent exercise throughout their lifetimes. Some patients can only manage 10 to 15 minutes 3 times each week, while other patients can engage in lengthier and more frequent exercise. The goal is to motivate patients and encourage them to find joy in exercise and moving their bodies. I have found that something clearly shifts in a positive direction when patients become regular and avid about exercise.

2. *Diet Modifications*

Many patients do not understand the value of eating well and its potential symptom-moderating effects. The clinician should discuss diet and encourage patients to modify their eating to include: (1) lots of multicolored fruits and vegetables (a "rainbow diet"); (2) some fish, preferably cold deep-seawater fish that is low or without measurable levels of mercury (e.g., wild salmon); and (3) fewer excessive calories (i.e., eliminate or significantly reduce high-caloric nutrient-devoid foods such as processed foods and junk foods).

Research has shown that mood can be improved if diets are nutrient

rich, especially if supplemented with minerals.[50] A diet low in sodium and high in potassium was shown to improve overall mood, and to specifically improve depression, tension, and vigor.[51] Overall, an optimal diet should be as close to being pesco-vegetarian as possible, since this helps to prevent and possibly ameliorate psychopathologies across the lifespan. This type of diet is nutrient dense and contains lots of potassium.

3. *Connecting to Nature*

Patients need to be encouraged to spend more time outdoors and in natural settings. Spending too much time in cities and densely populated areas impairs the ability of the perigenual anterior cingulate cortex to inhibit activity in an overactive amygdala. An overactive amygdala contributes to increased stress and psychiatric symptoms.[52] Patients who only have limited access to nature risk developing disturbances of mood, sleep, and diurnal rhythms, as well as short-term impairment in attention and cognition. No pills can mimic the beauty and vastness of nature. Spending time in natural settings enhances cognitive, attentional, emotional, spiritual, and subjective well-being.

4. *Limit Media Immersion and Hyperreality*

Many of my socially isolated mentally unwell patients like Mark spend too much time on the Internet. Instead of interacting directly with people, they use the Internet as their only connection to people and the larger world. Mary has a different issue, but it is no less damaging to her psychiatric status. She does not stop working and she often uses her access to the Internet to continue her full-time job after dinner. Excessive media immersion is associated with psychological dysfunctions (i.e., "techno-stress") that include disorders of attention, cognition, overload, and addiction. Many of my socially isolated patients have unfortunately been "fueled" by the Internet and developed pathological gambling and/or pornography addictions. Clinicians need to discuss this with patients and educate them on the value of limiting Internet exposure, since this simulated reality can become more real to patients than actually living in the nondigital world. Patients need to understand the psychiatric implications of spending too much time on the Internet and not enough time with real people in real life.

5. *Religious and Spiritual Practice*

According to Walsh, approximately 90% of the world's population participates in religious or spiritual practices. For many individuals, having a religious or spiritual focus improves their ability to manage the stresses of life. When the focus of such practices centers on concepts like love and forgiveness, it can be very helpful, as opposed to notions of punishment and guilt that can undermine psychological well-being.

Numerous health indicators have been shown to benefit from spiritual practices. These include improved psychological, relational, and marital well-being, as well as lowered rates of anxiety, depression, substance abuse, and suicide. Attending a weekly religious service increases lifespan by approximately 7 years compared with individuals who do not commit to some type of weekly religious service.

Mary used to attend church on Sundays, but after her husband pronounced that type of involvement "silly," she stopped going. There is nothing silly about a person's religious or spiritual practice, especially since such practices can bolster resilience and facilitate a more positive psychological outlook. Mary would benefit from reengaging with her faith on a regular basis. I often discuss such ideas with patients despite that fact that, as Walsh points out, few professional do. It is important for clinicians to ask patients about their religious and spiritual practices. Simply reminding patients can be a powerful way to reinvigorate such practices and promote psychological well-being.

Even though this appears to be mostly positive, clinicians need to consider deeper issues when discussing religious and spiritual practices with patients. Only through lengthy discussions will clinicians begin to understand how a patient endorses the religious concepts and ideas that he/she was exposed to over time. These types of discussions affect a patient's development and psychological health, for they range from prepersonal notions (i.e., literal acceptances of how one should conduct his/her life) to personal ones, and even transpersonal beliefs and ideas. It is easy to imagine the types of psychological distress that can ensue if various life issues run counter to a patient's religious beliefs. For example, how would a person of strong Catholic faith deal with having had sex prior to marriage or an abortion? Along the same lines, what is someone of strong Catholic faith to do when he no longer wants children and yet wishes to have sexual relations with his wife? These situations can challenge a patient's prepersonal, personal, and even transpersonal religious notions; and, if not dealt with, they can be a constant source of psychological distress. Clinicians need to be aware that while religion and spiritual practices can be a tremendous source of psychological health, simply telling a patient to reconnect to his/her faith might not be complete advice unless a patient works through religious or spiritual issues that have been negatively affecting his/her state of mind.

6. *Getting Sufficient Sleep*

Patients do better when they can get at least 6 to 8 hours of minimally interrupted sleep. Many patients lack an adequate understanding of good sleep hygiene, so they should be educated and encouraged to develop good sleep habits. Some patients sleep during the day and are awake all hours of the night, which further isolates and impairs them from interacting with people. Some patients cannot quiet their minds due to continual ruminations, and feel so anxious that regular sleep becomes impossible. Some patients worry so much about sleeping that this anxiety undermines their capacity to fall and remain asleep during the night. Of course, many other mental incarnations can impair sleep or cause disrupted sleep patterns. Nevertheless, it is essential that sleep be improved, since prolonged impaired sleep will undermine anyone's mental state.

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If a patient's mental state does not improve despite a sound holistic sleep plan, the patient may have an undiagnosed sleep disorder. For example, obstructive sleep apnea is commonly comorbid with psychiatric disorders, especially depression and anxiety.[53] Also, having a psychiatric illness and/or taking psychotropic medication typically increases a patient's susceptibility to sleep disorders such as insomnia, obstructive sleep apnea, and REM sleep disorders.[54] While a thorough discussion of sleep architecture and its proper assessment is beyond the scope of this article, it is important that sleep issues are addressed when managing patients who have mental health challenges. Patients should be referred to a sleep clinic when treatment progress is slow or uneventful, or when it appears that an underlying sleep issue is present or probable.

Orthomolecular Interventions

The body (which includes the brain) demands a constant supply of micronutrients found in foods and through supplementation. If the body's needs are not met, then the individual will suffer from the consequences of micronutrient insufficiency and, in more extreme cases, malnutrition. Based on these known facts, the body is physiologically dependent on receiving a complete "sum" of around 40 micronutrients on a daily basis; otherwise, signs and symptoms of nutritional inadequacy will manifest and can be responsible for a myriad of physical and psychological perturbations.

In addition to micronutrient insufficiencies, our bodies have their own unique biochemical needs that cannot be met from diet alone and demand the proper provision of micronutrient supplementation. This is where orthomolecular therapies (i.e., combinations of diet modifications and/or supplementing vitamins, minerals, amino acids, and/or essential fatty acids) can have a tremendous impact, since they can moderate symptoms of mental distress and improve a patient's capacity to emotionally (i.e., affectively) regulate.[55–66]

Many orthomolecular clinicians have witnessed the beneficial effects of optimal orthomolecular therapies. Patients often return weeks or months later feeling much better, attributing much of their progress to the prescribed orthomolecular regimens. Putting together the proper orthomolecular regimen requires a comprehensive history, physical examination, laboratory testing (when indicated), and meticulous trial and error. Patients need to understand implicitly and explicitly that finding the "right" mix of orthomolecules takes time and can only be achieved through an effective collaborative process with their treating clinicians.

Here I will reference select publications which show benefits from single or combination orthomolecules upon general stress and/or extreme psychological stress (i.e., suicidality and subthreshold psychosis). Even though each treating clinician will prescribe specific orthomolecular therapies according to the process described above, these select publications support the use of several "core" orthomolecules either alone or in combination with other orthomolecules and should form the backbone of any individualized patient plan.

1. Vitamin C

When 3 grams of timed-release vitamin C was given in divided doses throughout the day to 60 healthy adults for 14 days, blood pressure, cortisol, and subjective response to acute psychological stress were all palliated.[67] In another study, when 500 mg of vitamin C was included in a multiple vitamin/mineral preparation (i.e., Berocca) that also included modest amounts of B-complex vitamins, 100 mg of both calcium and magnesium, and 10 mg of zinc, at the end of the trial the 40 men randomly assigned to take the nutrients for 28 days demonstrated statistically significant reductions in perceived stress.[68] Even though the latter study did not rely on vitamin C exclusively, preliminary human research has shown this vitamin to moderate stress both physiologically and subjectively. Basic animal research has shown that the adrenal cortex and the adrenal medulla both accumulate high levels of vitamin C, and that vitamin functions as a crucial cofactor in catecholamine biosynthesis and adrenal steroidogenesis.[69]

Based on these data, it appears that 500 to 3000 mg/day of vitamin C should be prescribed as a treatment to attenuate stress. Timed- or sustained-release vitamin C might be preferable, since it is retained longer within the body, even though research has shown considerable intersubject variation in vitamin C absorption from different formulations.[70–72]

2. B-Complex Vitamins with a Broad-Spectrum Multiple Vitamin/Mineral Supplement

Optimum doses of B vitamins should be prescribed (in combination with a multiple vitamin/mineral supplement), since these essential nutrients are particularly susceptible to cortisol mobilization that results in their depletion, and they also possess stress-moderating effects.[68,73–75] At the end of a 12-week study, during which 42 adults were randomized to the nutritional treatments (B-complex vitamins plus modest amounts of vitamin C, vitamin E, calcium, magnesium, potassium, lecithin, choline bitartrate, inositol, and the botanical medicines *Avena sativa* and *Passiflora incarnata*), there were significant reductions in personal strain, confusion and depressed/dejected mood.[74]

Another of these studies evaluated the effects of a B-complex supplement (i.e., a whole nutrient natural source extract from probiotic colonies containing vitamins B1–12, folate, PABA, biotin, and inositol) on depressive and anxiety symptoms among adults diagnosed with major depression or other forms of depressive disorders.[75] The 30 study participants taking the B-complex vitamins had notable continuous improvements in depressive and anxiety symptoms compared with the participants in the placebo group. The B-complex group also showed significant improvements on the mental health scale of the Study Short Form 36 (i.e., SF-36).

Another study involving micronutrients is worth mentioning, since it dealt with the effects of a broad-spectrum multiple vitamin/mineral

supplementation combined with herbal extracts (i.e., B-complex vitamins, lysine, antioxidants, minerals, and some herbal extracts) upon mood and stress levels.[76] In this study, 25 men randomized to the nutritional-herbal treatment for 8 weeks showed a significant reduction in their overall score on a depression anxiety stress scale (i.e., DASS), as well as improvements in their alertness and general daily functioning.

To combat stress, it appears that optimum doses of a well-rounded B-complex supplement should be combined with a daily broad-spectrum multiple vitamin/mineral supplement to support patients' psychological well-being.

3. Omega-3 Essential Fatty Acids

When patients feel suicidal, they typically experience acute distress and discomfort. No matter how well clinicians monitor patients for suicidal ideation, there are no reliable ways to be certain that patients won't attempt suicide. In a study that evaluated 33 medication-free depressed subjects over a 2-year period, 7 of the subjects attempted suicide.[77] Testing showed that their lower docosahexaenoic acid (DHA) percentage of total plasma polyunsaturated fatty acids and higher omega-6-to-omega-3 ratio predicted suicide attempts among the depressed patients over the 2-year study period. Even though these results are preliminary, there is no reason to wait for larger trials, since this data might suggest the need to moderate suicide risk among psychologically distressed patients. It makes sense to ensure that all patients' diets are modified to minimize levels of omega-6 fatty acids and maximize foods high in omega-3 essential fatty acids, and take a daily omega-3 essential fatty acid supplement (i.e., providing ample amounts of DHA such as 500 mg or more).

Outside of suicidality, patients can experience other distressing symptoms, including psychosis. A trial investigated the impact of an omega-3 essential fatty acid supplement among subjects who were having psychotic symptoms (i.e. subthreshold psychosis), but had yet to progress to having a primary psychotic disorder (e.g., schizophrenia, schizophreniform, bipolar, and schizoaffective disorders).[78] The subjects were randomized to receive a daily dose of 700 mg of EPA, 480 mg of DHA, and 7.6 mg of mixed tocopherol for 12 weeks, and then monitored for 40 weeks. The total study period was 12 months. At the conclusion of the trial, 2 of 41 subjects in the treatment group transitioned to psychotic disorder compared with 11 of 40 subjects in the placebo group (4.9% versus 27.5% respectively; $p = 0.007$). Compared with the placebo group, the use of omega-3 essential fatty acids reduced positive symptoms ($p = 0.01$), negative symptoms ($p = 0.02$), and general symptoms ($p = 0.002$), and enhanced general functioning ($p = 0.002$).

Given how important it is to moderate suicidality and/or symptoms of subthreshold psychosis, it behooves orthomolecular clinicians to prescribe an omega-3 essential fatty acid with at least a 2-to-1 ratio of EPA to DHA (e.g., 1000 mg of EPA and 500 mg of DHA).

Conclusion

There are many reasons why patients struggle to cope when they experience medical, metabolic, and psychological issues that negatively affect their mental health. Many patients have difficulty achieving adequate allostasis after traumatic experiences or prolonged distress. It is imperative that we upgrade our current standard of care by assessing, monitoring, and providing ongoing encouragement and support to complement the provision of orthomolecular medicines. We must be mindful and sensitive to patients' unique life experiences and consider whether oppressive forces may undermine their quality of life. We must engage our patients to develop holistic recovery plans that include the appropriate use of psychosocial strategies and TLCs as well as "core" orthomolecular therapies.

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Mental Breakdown

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SIBO: Dysbiosis Has A New Name

by Steven Sandberg-Lewis, ND, DHANP and Allison Siebecker, ND, MSOM

Many patients with bloating, abdominal pain, constipation, or diarrhea are diagnosed with irritable bowel syndrome and never get adequate responses to treatment. Others are given no diagnosis at all for their suffering, which leads to even less chance of recovery. Our experience is that many of these perplexing patients have commensal microbial overgrowth. This article details the complex issue of small intestine bacterial overgrowth (SIBO)

SIBO is a condition in which abnormally large numbers of commensal bacteria (or other microorganisms) are present in the small intestine. SIBO is a common cause of IBS – in fact it is involved in over half the cases of IBS and as high as 84% in one study using breath testing as the diagnostic marker.[2] It accounts for 37% of cases when endoscopic cultures of aerobic bacteria are used for diagnosis.[3] Eradication of this overgrowth leads to a 75% reduction in IBS symptoms.[4] Either bacterial overgrowth or the overgrowth of methanogenic archaea leads to impairment of digestion and absorption and produces excess quantities of hydrogen, hydrogen sulfide, or methane gas. Hydrogen and methane are not produced by human cells but are the metabolic products of fermentation of carbohydrates by intestinal organisms. When commensals (oral, small intestine, or large intestine flora) multiply in the small intestine to excessive numbers, IBS is likely. Hydrogen/methane breath testing is the most widely used diagnostic method for this condition. *Stool analysis has no value in diagnosing SIBO.*

Symptoms of SIBO include:

- bloating/abdominal gas
- flatulence, belching
- abdominal pain, discomfort, or cramps
- constipation, diarrhea, or a mixture of the two
- heartburn
- nausea
- malabsorption: steatorrhea; iron, vitamin D, vitamin K; or B12 deficiency with or without anemia; and osteoporosis[5]
- systemic symptoms: headache, fatigue, joint/muscle pain, and certain dermatology conditions

Other diseases associated with SIBO include hypothyroidism, lactose intolerance, gallstones, Crohn's disease, systemic sclerosis, celiac disease, chronic pancreatitis, diverticulitis, diabetes with autonomic neuropathy, fibromyalgia and chronic regional pain syndrome, hepatic encephalopathy, non-alcoholic steatohepatitis, interstitial cystitis, restless leg syndrome, acne rosacea, and erosive esophagitis.[6-21] Based on clinical experience, we suspect that biliary dyskinesia and lymphocytic colitis may also be associated with SIBO.

In our practices we have found that the following indicators increase the chances that a patient's IBS is caused by SIBO:

- when a patient develops IBS following a bout of acute gastroenteritis (postinfectious IBS);
- when a patient reports dramatic transient improvement in IBS symptoms after antibiotic treatment;
- when a patient reports worsening of IBS symptoms from ingesting probiotic supplements that also contain *pre*biotics;
- when a patient reports that eating more fiber increases constipation and other IBS symptoms;
- when a celiac patient reports insufficient improvement in digestive symptoms even when carefully following a gluten-free diet;
- when a patient develops constipation type IBS (IBS-C) after taking opiates;
- when a patient has a chronic low ferritin level with no other apparent cause;
- when abdominal imaging reveals a large gas accumulation obscuring the pancreas
- when small bowel follow-through imaging reveals areas of "flocculation."[22]

Mechanisms by Which Overgrowth Is Prevented

An important protective mechanism against SIBO is proper small intestine motility via the migrating motor complex because stasis promotes bacterial growth.[23] Also key in prevention are gastric, pancreatic,

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and gall bladder secretions, since hydrochloric acid, enzymes, and bile are bactericidal/static.[24] Conditions that disrupt the glycocalyx and microvillus portions of the brush border may fuel overgrowth. The pathophysiology involved is the loss of disaccharidases in these areas and the resulting carbohydrate malabsorption which provides excess substrate for microbial growth. The role of proper ileocecal valve function in preventing cecoileal reflux of colonic bacteria into the small intestine may also be important.[25,26] Surprisingly, a recent study suggests that surgical removal of the gall bladder reduces the risk as well.[27] Mucosal biofilms may be preventive or may be a risk.[28,29] Heavy drinking, as well as moderate use of alcohol, is significantly associated with increased SIBO risk.[30] The use of proton pump inhibitors encourages overgrowth, especially of the hydrogen-producing type.[31,32]

Definition

Traditionally, $\geq 10^5$ colony-forming units (CFU) per mL of proximal jejunal aspiration has been the definition of SIBO in culturing studies. $\geq 10^3$ CFU is now the suggested definition from more recent studies revealing that $\leq 10^3$ CFU is the normal level in healthy controls.[33,34] The bacteria which are most commonly overgrown are both commensal anaerobes – *Bacteroides* 39%, *Lactobacillus* 25%, *Clostridium* 20% – and commensal aerobes – *Streptococcus* 60%, *Escherichia coli* 36%, *Staphylococcus* 13%, *Klebsiella* 11%.[35] A more recent study found the aerobes to be *Escherichia coli* 37%, *Enterococcus* spp 32%, *Klebsiella pneumonia* 24%, and *Proteus mirabilis* 6.5%.[36] Colonic hydrogen production is believed to be anti-inflammatory and antineoplastic, whereas excessive small intestine hydrogen causes the symptoms and signs of diarrhea-type irritable bowel syndrome (IBS-D).[37] In addition to bacteria, the source of methane generation in SIBO is the archaeon *Methanobrevibacter smithii*. This organism has been linked to obesity in humans.[38] In addition, sulfate-reducing bacteria, such as *Desulfovibrio* species, are anaerobes that reduce sulfate to hydrogen sulfide (H2S). In addition to its role in SIBO, H2S is being studied as a possible etiologic factor in ulcerative colitis and colonic carcinogenesis.[39] In normal low levels H2S has GI protective activity.[40]

Pathophysiology of SIBO: Autoimmunity

Postinfectious IBS (PI-IBS) has been shown to have an autoimmune etiology in both murine and human studies (see figure 1). Infectious gastroenteritis is the most significant environmental risk factor for IBS.[41] Organisms that trigger PI-IBS include *Campylobacter, Salmonella, Shigella, E. coli*, viruses, and *Giardia*.[42–45]

Cytolethal distending toxin (CDT) is produced by enteric pathogens that cause PI-IBS. *Campylobacter jejuni* is the prototypical bacterium that produces CDT.[46] Other bacteria that produce CDT include *Haemophilus ducreyi* (chancroid), *Aggregatibacter actinomycetemcomitans* (periodontitis), *Escherichia coli* (traveler's diarrhea), *Shigella dysenteriae* (dysentery), *Salmonella enterica* (typhoid fever), and *Campylobacter upsaliensis* (enterocolitis).

The interstitial cells of Cajal (ICC) are fibroblast-like cells that act as pacemakers for the migrating motor complex (MMC). A key underlying cause of SIBO is thought to be deficiency of the MMC, which moves debris and bacteria down into the large intestine during fasting at night and between meals.[47] The number of ICC is reduced in post-*Campylobacter jejuni* gastroenteritis infected rats that eventually develop SIBO.[48] Three months after *C. jejuni* gastroenteritis, 27% of rats had SIBO. These rats had a lower number of ICC than controls in the jejunum and ileum (0.12 ICC/villus was the threshold for developing SIBO).

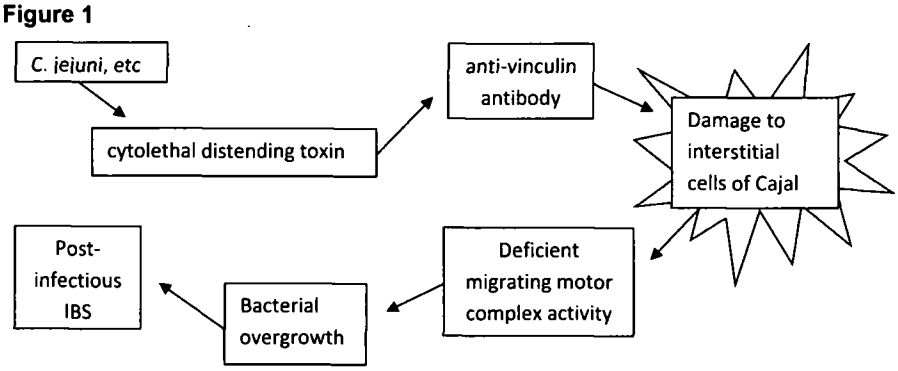
CDT toxin may destroy the interstitial cell of Cajal by stimulating the production of autoantibodies against a cytoskeletal protein known as vinculin. The antigen-antibody complexes between antivinculin antibodies and cytolytic distending toxin lead to autoimmune destruction of ICC.[49,50]

How SIBO Causes the Symptoms of IBS

There are two main pathophysiological issues involved in SIBO. First, bacteria can ferment carbohydrates and consume other nutrients ingested by the host simply by their inappropriate location in the small intestine. This allows them premature exposure to host nutrition before there is time for absorption. Bacterial fermentation produces hydrogen and/or hydrogen sulfide gas. In addition *M. smithii* produces methane.[51] *M. smithii* may be present in the intestinal tracts of up to 95.7% of humans.[52] Microbial gas leads to the IBS symptoms of bloating, pain, altered bowel movements, eructation, and flatulence (Figure 2).

The quantity of gas may be extensive, causing severe bloating and distention.[53] It is estimated that with normal levels of enteric flora, the quantity of lactose in an ounce of milk fuels the production of 50 cc of gas. With microbial overgrowth, gas levels produced from 1 ounce of milk may approach 5000 cc.[54] Excess gas can then exit the body as flatulence or eructation. A portion is also absorbed into the blood and eventually filters through the pulmonary alveolus to exit on exhalation. The intestines are sensitive to pressure, and therefore the pressure of distention can lead to abdominal pain. In addition, visceral hypersensitivity, a feature of IBS, may

Figure 1



create a lower threshold for pain/discomfort and a hyperresponsiveness of muscular contraction in response to the gas, leading to cramps.[55,56] The gases also affect bowel motility. Hydrogen has a greater association with diarrhea, and methane has an almost exclusive association with constipation.[57,58] Methane has been shown to slow gastrointestinal motility by 59% in animal studies, and the volume of methane overproduction correlates with the severity of constipation.[59,60] Therefore when both hydrogen and methane are present, diarrhea, constipation, or a mixture of both can be present based on the relative amounts of these gases.[61] It appears that the pressure created by either gas or the decreased gastric motility may lead to gastric distention resulting in gastroesophageal reflux (GERD).[62] The bacterial consumption and uptake of host nutrients, such as B12 and iron, can lead to macrocytic and/or microcytic anemia or chronic low ferritin levels in addition to general malabsorption and malnutrition in more severe cases.[63,64] The increased motility of diarrhea may also induce malabsorption. Finally, continuous fermentation of host nutrition by repeated exposure to daily meals perpetuates bacterial overgrowth and IBS symptoms, creating a vicious cycle (Figure 2).

The second mechanism is microbial damage to the digestive and absorptive function of the small intestine. Unlike the colon, the small intestine is not designed for heavy bacterial colonization. Commensal organisms may synthesize glycosidase, leading to damage of glycocalyx or disaccharidases. The gastrointestinal and systemic symptoms induced by these changes are listed in Figure 3. Key factors include bacterial deconjugation of bile, which induces fat malabsorption, steatorrhea, and fat–soluble vitamin deficiencies; bacterial digestion of disaccharidase enzymes, which furthers carbohydrate malabsorption, fermentation, and gas; and increased intestinal permeability (leaky gut), which often leads to systemic symptoms.[65–68]

Diagnosis of SIBO

As mentioned above, hydrogen/methane breath testing is the most common method of assessing SIBO. Instrumentation is available from Quintron Instrument Company in Milwaukee, Wisconsin. It builds and distributes the Breathtracker, which is used to measure these gases following a 24- to 48-hour prep diet and an overnight fast. After collection of the fasting baseline specimen, a solution of lactulose – an unabsorbable synthetic sugar – is ingested as the substrate for bacterial fermentation. Lactulose is nonabsorbable because only bacteria, not humans, produce the enzymes to digest it. Lactulose is a disaccharide solution of galactose and fructose in a base which also contains a minute quantity of lactose and epilactose.[69] Transit time for lactulose through the stomach and small bowel is approximately 120 minutes. Glucose may also be used as a test substance, but because of its rapid absorption in the proximal small intestine, it may fail to identify more distal SIBO.[70] Serial breath specimens are taken every 20 minutes during this time and for a third hour as well. Breath may be sampled and immediately analyzed at a lab, or these samples may be acquired at home using a series of tubes and a transfer device for later analysis. Home breath samples are exhaled into special vials similar to a Vacutainer tube, which store the labeled sample until it can be delivered to the lab. Not all labs have the equipment to test for methane, and the methodology for hydrogen sulfide is currently being perfected and is therefore not yet available. Testing for methane in addition to hydrogen is important because treatment varies based on the type of gas. The unique symptom of H2S production is "rotten egg" odor to the belching or flatus.

Preparation for the test varies from lab to lab, but a typical prep diet is limited to white rice, fish/poultry/meat, eggs, hard cheeses, clear beef or chicken broth (not bone broth or bouillon), oil, salt, and pepper. The purpose of the prep diet is to get a clear reaction to the lactulose solution by eliminating fermentable foods the day prior to testing. In cases of constipation, 2 days of prep diet may be needed to reduce baseline gases to negative. Antibiotics should not be used for at least 2 weeks prior to an initial test, although some sources recommend 4 weeks.[71] If symptoms allow, proton pump inhibitors should also be eliminated for at least seven days before testing.[72]

Interpretation of the test varies among practitioners. The criteria provided by Quintron for a positive test are as follows:

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Figure 2

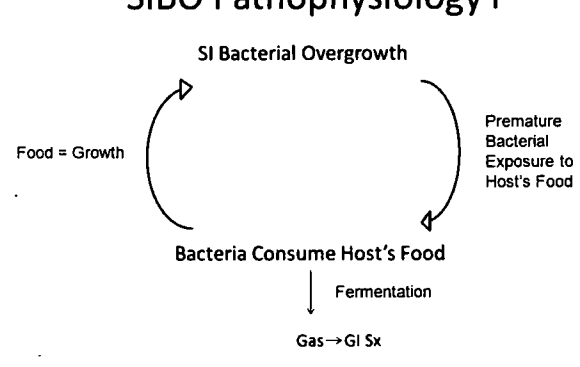
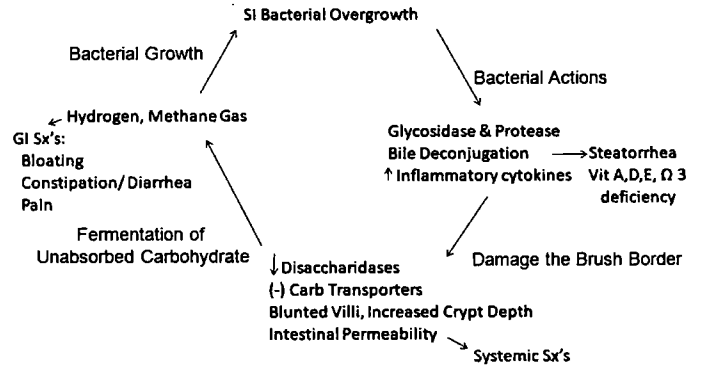


Figure 3



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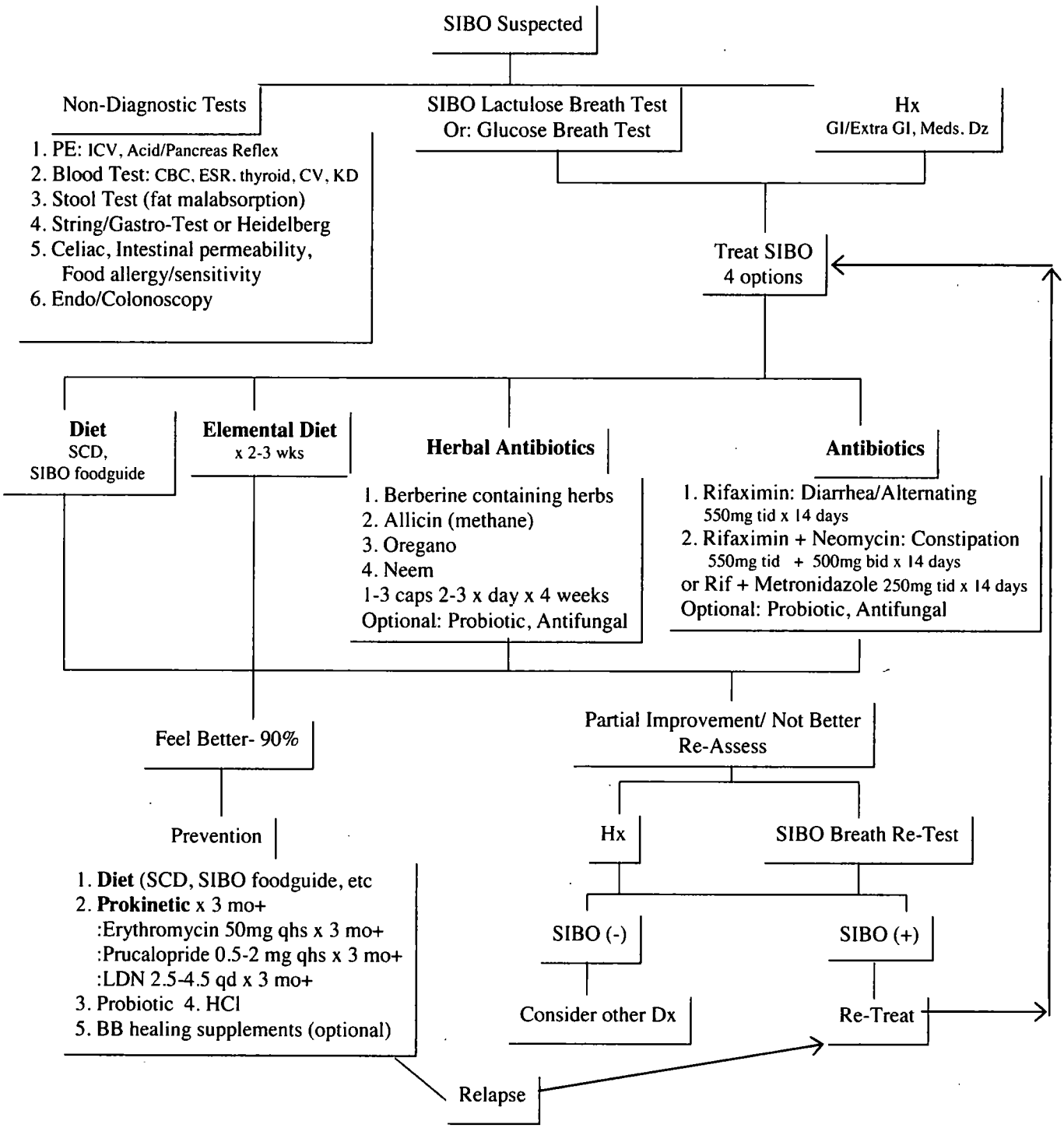
- a rise over baseline in hydrogen production of 20 parts per million (PPM) or greater within 120 minutes after ingesting the test substrate;
- a rise over baseline in methane production of 12 ppm or greater within 120 minutes after ingesting the test substrate;
- a rise over baseline in the sum of hydrogen and methane production of 15 ppm or greater within 120 minutes after ingesting the test substrate.

Additional testing and interpretation parameters:

- Hydrogen sulfide SIBO may be suspected when the typical symptoms are present but the breath test shows "flat-line" hydrogen and methane levels.[73]

Figure 4: SIBO Treatment Protocol
Variation of the Cedars-Sinai Protocol (Pimentel 2006)
Siebecker & Sandberg-Lewis (2014)



- Modest levels of methane gas at any level equal or greater than 3 ppm at any sample on a 3-hour lactulose breath test may be a cause of methane-induced constipation.[74]
- A "spot methane" level may be used for follow-up testing in methane-positive individuals. When testing methane alone, there is no need for a preparatory diet or fasting prior to this single breath sample.

IBS subjects who have elevated breath methane are constipated in most cases. In murine studies, methane infusion prolonged intestinal transit time.[75]

We have found that an absolute level of gases, without a rise over baseline, correlates well with clinical SIBO. This is especially true for methane gas, which can have a pattern of elevated baseline which remains elevated for the duration of the test. In cases such as these, methane may only rise a few ppm over baseline, but the level is consistently above positive. Interpretation of elevated hydrogen or methane on the baseline specimen (pre-lactulose ingestion) is controversial, but at the SIBO Center we prefer to consider a high baseline methane to be a positive test.[76]

The classic positive for SIBO has been considered to be a double peak, with the first peak representing the small intestine and the second peak representing the normal large intestine bacteria. It is not essential to have a second peak in order to have an accurate test. We find that a single peak which rises highest in the third hour may also represent distal SIBO followed by the normal colonic gas levels.

Breath testing may be used in pediatric cases, so long as the child can follow instructions to collect the samples. For those under 3 years old, testing is best done on site at a lab due to differences in collection methods versus at-home kits. Pediatric lactulose dosing is 1 g/kg body weight with a maximum of 10 g (22 pounds and above receive the max/adult dose of 10 g).[77] Lactulose is available only by prescription.

Treatment of SIBO

In 2006, Pimentel shared his treatment algorithm for SIBO, which included the use of antibiotics, elemental diet or both.[78] Our approach offers two additional options: diet and herbal antibiotics (Figure 4).

Diet

We advise the use of the Specific Carbohydrate Diet or the SIBO Specific Diet.[79,80] The latter (see www.siboinfo.com/diet.html) is a combination of the Specific Carbohydrate Diet, the low-FODMAP diet, and the clinical experience of Siebecker in the treatment of SIBO with diet. Bacteria use carbohydrates as their energy source and ferment them to gases; therefore, a low-carbohydrate diet can directly reduce symptoms by decreasing the amount of gas produced.[81] Reducing carbohydrates may also decrease the overall microbial load, though formal studies to validate this are lacking. The Specific Carbohydrate Diet and the SIBO Specific Diet greatly reduce the intake of polysaccharides, oligosaccharides, and disaccharides by eliminating all grains, starchy vegetables, lactose, and sweeteners other than honey or dextrose. Legumes are often avoided in initial phases of these diets. Many patients experience a rapid and significant decrease in symptoms after starting a SIBO diet. The Specific Carbohydrate Diet has been reported to have an 84% success rate for inflammatory bowel disease, a condition commonly associated with SIBO.[82,83] Patients who find the Specific Carbohydrate Diet or SIBO Specific Diet approach too restrictive can follow the Cedars-Sinai diet as described at www.gidoctor.net/diet-ibs-sibo.php.

The low-FODMAP diet is a nutritional plan that greatly reduces the fermentable levels of carbohydrate-containing foods and has a success rate of 76% in IBS.[84, 85] The low-FODMAP diet is not specifically designed for SIBO and therefore does not eliminate polysaccharide and disaccharide sources such as grains, starch, starchy vegetables, and sucrose. Eliminating these poly- and disaccharides is helpful in SIBO because these carbohydrates – which normally feed the host – also feed the increased numbers of microflora in the small intestine (Figure 2).

Diet alone has proved successful for infants and younger children, but for older children and adults, one or more of several treatment options are often needed to reduce bacteria quickly, particularly in cases in which the patient's diet becomes excessively limited in an attempt to obtain symptomatic relief. Additionally, any of the diets discussed above need to be customized to the individual by trial and error over time.

Low-carbohydrate diets often induce weight loss. Particular attention must be paid to underweight patients. Increased intake of winter squash, glucose, or honey may be recommended in these circumstances. White rice (jasmine/sticky variety is best) or white potato may also be needed to maintain weight along with medium-chain triglyceride sources such as coconut and other oils.

Diet is also essential for prevention of relapse following successful SIBO eradication. Pimentel recommends postponing any dietary changes until after the effective treatment of the microbial overgrowth, rather than during the treatment phase.[86] Our clinical experience with the SIBO Specific Diet is that it is beneficial for both the treatment and prevention phases.

Elemental Diet

An elemental diet can be used in place of antibiotics or herbal antibiotics to rapidly decrease bacteria. In the treatment of SIBO, elemental diet is used to the exclusion of all other food sources. These products are a powdered mix of free-form amino acids, fat, vitamins, and minerals as well as rapidly absorbed carbohydrates. The concept behind this treatment is that the nutrients will be absorbed before reaching the involved organisms, thus feeding the patient but starving the flora. It is used in place of all meals, for 2 to 3 weeks, and has a success rate of 80% to 85% using the Nestlé product Vivonex Plus.[87] Two versions of a homemade recipe for elemental diet can be found at www.siboinfo.com/elemental-formula.html. Elemental diets are not protein powders or typical detoxification formulas. They are available over the counter and are not reimbursed by most insurance coverage, which can make this treatment costly. Patients should be warned that Vivonex Plus or homemade

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elemental diets are very bitter tasting. Elemental diets may not be suitable to underweight patients who cannot afford to lose weight.

Herbal Antibiotics

While there have only been two published reports of herbal antibiotics in the treatment of SIBO, our experience is that they have similar effectiveness to antibiotics.[88,89] Chedid et al. studied patients with SIBO based on a positive lactulose breath test. A negative breath test after treatment was seen in 34% of the rifaximin- or triple-antibiotic-treated group vs. 46% of the herbal-treated group.

The study employed a pair of herbal formulas. The dosage was 2 capsules of each b.i.d. for 30 days. The two different paired formulas are listed in Table 1 below (FC-Cidal plus Dysbiocide or Candibactin-AR plus Candibactin-BR):

Table 1: Herbal Preparations for the Treatment of Small Intestine Bacterial Overgrowth

FC-Cidal	**Dysbiocide**	**Candibactin-AR**	**Candibactin-BR**
Proprietary blend, 500 mg: 1 capsule	Proprietary blend, 950 mg per 2 capsules	1 capsule, 408 mg contains:	1 capsule, 400 mg contains:
Tinospora cordifolia	*Antheum graveolens*	*Thymus vulgaris*	*Coptis chinensis*
Equisetum arvense	*Stemona sessilifolia*	*Origanum vulgare*	*Berberis aquifolium*
		Salvia officinalis	
Pau d'arco	*Artemisia absinthium*	*Melissa officinalis*	Berberine HCl
Thymus vulgaris	*Brucea javanica*		*Scutellaria baicalensis*
Urtica dioica	*Pulsatilla chinensis*		*Phellodendron chinense*
Artemisia dracunculus	*Hedyotis diffusa*		*Zingiber officinale*
Olea europaea	*Picrasma excelsa*		*Glycyrrhiza uralensis*
	Acacia catechu		*Rheum officinale*
	Achillea millefolium		

Antibiotics

The most studied and successful prescription antibiotic for SIBO is rifaximin (brand name Xifaxan). It has a broad spectrum of activity and is nonabsorbable. Its luminal status allows it to act locally, and it is therefore less likely to cause systemic side effects common to other antibiotics.[90] Rifaximin has up to a 91% success rate and is given at 550 mg t.i.d. × 14 days.[91,92] Many physicians continue to prescribe a lower dosage of 1200 mg b.i.d. × 10 days, although research shows a 22% increase in breath test normalization with the higher dosage. Suggested pediatric dosages are 200 mg t.i.d. × 7 days for ages 3 to 15 or 10 to 30 mg/kg.[93,94]

Additionally, rifaximin has several unique benefits: it purportedly does not cause yeast overgrowth and it decreases antibiotic resistance in bacteria by reducing plasmids.[95,96] Antibiotic resistance does not develop to rifaximin, making it effective for retreatments, and it has anti-inflammatory properties, decreasing intestinal inflammatory cytokines and inhibiting NF-κβ via the PXR gene.[97,98] Rifaximin as a solo antibiotic is best used for SIBO when only the hydrogen levels are elevated. When methane gas is also increased, double therapy of rifaximin plus neomycin (500 mg b.i.d. × 14 days) is more effective.[99] Many gastroenterologists use metronidazole (250 mg t.i.d. × 14 days) as an alternative to neomycin (unpublished). Since different antibiotic regimens are recommended based on the gas type, breath testing is necessitated when considering this treatment.

Furnari et al. compared the percentage of breath test normalization using rifaximin 1200 mg q.d. vs. rifaximin 1200 mg q.d. plus partially hydrolysed guar gum (5 g q.d.) for 10 days. The combination treatment was proved to be 23% more effective than rifaximin monotherapy.[100]

If hydrogen sulfide SIBO is suspected the same treatments as those used for methanogen overgrowth are indicated.

Biofilm Disruptors

Mucosal methanogenic organisms can elaborate biofilms.[101] The use of N-acetylcysteine, nattokinase, serrapeptase, or lumbrokinase may be considered in addition to herbal or prescription antibiotic treatment to provide mucolytic and biofilm disruption effects. As mentioned earlier in this article, there is evidence both for and against enteric mucosal biofilms and SIBO.

At our center we have used the following botanicals: *Allium sativum* (garlic), *Hydrastis canadensis* and other berberine-containing herbs, *Origanum vulgare* (oregano), and *Azadirachta indica* (neem). We have used these as both single agents and in various combinations at dosages that are at the upper end of label suggestions × 30 days. Specific single dosages that we have used include allicin extract of garlic: 450 mg b.i.d.-t.i.d., goldenseal/berberine: 5 g q.d. in divided dosage, emulsified oregano: 100 mg b.i.d. and a formula that contains 300 mg of neem plus a proprietary blend containing a total of 200 mg of the following: *Emblica officinalis, Terminalia chebula, Terminalia belerica, Tinospora cordifolia,* and *Rubia cordifolia*. The latter formula is dosed at 1 capsule t.i.d. Researchers at Johns Hopkins have studied other herbal combinations that are listed in Table 1. Our breath testing has validated the need for the longer treatment period of 30 days for herbal antibiotics compared with 14 days for prescription antibiotics. Note that although whole garlic is a high-FODMAP food, we do not observe purified allicin to provoke symptoms in our patients. Allicin is the only herb which we have noted so far that can reduce breath methane levels. We have also observed that some patients experience prolonged die-off reactions with herbal treatment that can last for the duration of the treatment course. More studies on herbal antibiotics for SIBO are needed, particularly to identify botanicals effective in reducing methane.

Prevention

SIBO is a disease that relapses because eradication itself does not always correct the underlying cause.[102,103] Pimentel's 2006 treatment algorithm includes 2 essential preventions: diet and a prokinetic (motility agent). Our approach offers additional options: hydrochloric acid, probiotics, and brush border healing supplements. Also worth consideration are physical exercises, breathing techniques, acetylcholine precursors and modulators of neural inflammation.

Prokinetics

A key underlying cause of SIBO is thought to be deficient activity of the migrating motor complex (MMC). An intact MMC moves debris and bacteria down into the large intestine during fasting at night and between meals.[104] Prokinetics stimulate the MMC, symptomatically correcting this underlying cause. Iberogast is a German compound botanical tincture with possible prokinetic action.[105] This formula includes alcoholic extracts of *Iberis amara totalis recens, Angelicae radix, Cardui mariae fructus, Chelidonii herba, Liquiritiae radix, Matricariae flos, Melissae folium, Carvi fructus,* and *Menthae piperitae folium*. It has been used to treat functional dyspepsia and IBS since the 1960s. One study found symptom improvement, but no increase in gastric emptying, which suggests that if this formula is prokinetic, it is likely not the only mechanism underlying its action in IBS.[106] A double-blind controlled trial compared Iberogast with cisapride (a prescription prokinetic with limited special use in the US due to cardiovascular side effects). The herbal formula performed as well as the prokinetic drug for functional dyspepsia and was superior to metoclopramide in a retrospective cohort study of 961 patients.[107,108] It has also been shown to be effective for IBS in children.[109,110]

Prescription prokinetics studied for SIBO include low dose naltrexone 2.5 mg q.h.s. for IBS-D or 2.5 mg b.i.d. for IBS-C, low-dose erythromycin 50 mg q.h.s., and tegaserod 2 to 6 mg q.h.s.[112,111] Tegaserod has a higher success rate for SIBO prevention versus erythromycin but has been withdrawn from the US for safety reasons.[113] Prucalopride (Resolor), 0.5 to 2 mg q.h.s., is not yet available in the US but is a safer alternative to tegaserod.[114] It is presently available in Canada and Europe. A trial removal of a prokinetic at ≥3 months is suggested but continued long term use may be needed for some patients.[115]

Diet

A lower-carbohydrate diet is used in combination with a prokinetic to discourage a return of bacterial overgrowth. Once the breath test has normalized and small intestine damage has healed, the diet can be expanded beyond the strictness of the Specific Carbohydrate and SIBO Specific diets. The time frame for this is uncertain. Two studies have examined the rate of healing post SIBO and found that intestinal permeability normalized 4 weeks after successful SIBO eradication in 75% to 100% of patients.[116,117] While these reports are very encouraging, they may or may not reflect the other repair needed post SIBO. Therefore, we currently suggest continuing a SIBO diet for 1 to 3 months post successful eradication. At this point, the Cedars-Sinai Diet, low-FODMAP Diet, or a similar diet may be adopted long term, as the patient tolerates.[118,119] These diets allow more carbohydrates in the form of grains, gluten-free grains, cane sugar, and soy, though they still limit overall carbohydrate load.

Spacing meals 4 to 5 hours apart, with nothing ingested but water, allows for activity of the MMC.[120] We have found this to be very helpful clinically. If a low-carbohydrate SIBO diet does not correct hypoglycemia, this strategy will need to be altered to allow for more frequent meals.

Optional Supplements

Hydrochloric acid or herbal bitter supplements, which encourage hydrochloric acid (HCl) secretion, may be used to decrease the load of incoming bacteria.[121] When considering HCl supplementation, Heidelberg testing for HCl levels and response to treatments is the gold standard. Heidelberg testing reveals achlorhydria, frank hypochlorhydria, and hidden hypochlorhydria and allows individualization of dosing.

Probiotics are a controversial intervention in SIBO because lactobacilli have been cultured in SIBO and there is also concern about adding to the bacterial overload.[122] Despite this, the few studies that have focused directly on probiotics for treatment of SIBO have shown good results. *Bacillus clausii* as a sole treatment normalized the breath test in 47% of cases.[123] An 82% clinical improvement in SIBO was found using a combination of *Lactobacillus casei* and *plantarum, Streptococcus faecalis,* and *Bifidobacterium brevis* (Bioflora).[124] Probiotic yogurt containing *Lactobacillus johnsonii* normalized cytokine responses, thereby reducing the low-grade chronic inflammation found in SIBO after 4 weeks.[125] We have used various multistrain and single probiotics as well as yogurt and cultured vegetables with our SIBO patients with good results. A key point for the use of probiotic supplements in SIBO is to avoid *pre*biotics as main ingredients. Prebiotics are fermentable food for bacteria that can exacerbate symptoms during active SIBO and encourage bacterial growth post SIBO. Common prebiotics found in probiotic supplements include FOS (fructooligosaccharide), inulin, arabinogalactan, MOS (mannose-oligosaccharide), and GOS (galactooligosaccharide). Prebiotics may be tolerated in small amounts used as base ingredients, but this depends on the individual.

Brush border healing supplements may be given to assist the repair of small intestine tissue. While mucilaginous herbs are traditionally employed for this purpose (licorice, slippery elm, aloe vera, marshmallow), their use is controversial post SIBO, due to their high level of mucopolysaccharides, which are fermentable and could encourage bacterial regrowth. Specific nutrients we have used include lactose-free colostrum, 2 to 6 g q.d.; L-glutamine, 375 mg to 1500 mg q.d.; zinc carnosine, 75 mg b.i.d.; vitamins A and D, often given as cod liver oil, 1 tbsp q.d.; curcumin, 400 mg to 3 g q.d.; resveratrol, 250 mg to 2 g q.d. glutathione (oral liposomal), 50 to 425 mg q.d.; or glutathione precursor N-acetylcysteine 200 to 600 mg q.d.,

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Supplements are given for 1 to 3 months, though may be continued long term for general benefit if desired. Higher dosages of curcumin and resveratrol are given for 2 weeks for the purpose of downregulating NF-κβ, a mediator of increased intestinal permeability, and then reduced to maintenance levels.[126-128] Herbal cholinergic support may include phosphatidyl choline, pantothenic acid, huperzine A (from *Huperzia serrata*), and N-aceytl-L-carnitine.[129] Pranayama (yogic alternate nostril breathing) has been shown to have benefits in IBS-D by normalizing parasympathetic tone.[130]

If dampening of CNS inflammation is indicated, consider the use of green tea catechins, *Curcuma longa*, bioflavonoids, *Scutellaria*, resveratrol, *Chrysanthemum morifolium* leaf, and *Matricaria chamomilla*.[131]

In our practices we have found that the following circumstances increase the chances for an unsatisfactory patient outcome:

- *Failure to continue treatment courses until SIBO is eradicated (negative breath test or patient ≥90% better).* This crucial process of successive treatment is indicated by the long go-back arrow on the right side of our algorithm (Figure 4, p. 70).
- *Failure to use double antibiotic therapy for methane producers.* Methanogenic flora need different antibiotic treatment than hydrogen-producing bacteria.
- *Failure to utilize breath testing to identify if patients have SIBO, the type of gas that they produce, and the overall level of gas.* This information is necessary for diagnosis, treatment choice/duration, and prognosis.
- *Failure to use a prokinetic immediately following treatment.* Prokinetics along with diet are needed to prevent relapse of this commonly recurring condition. Antibiotic treatment as a sole therapy typically leads to recurrence of hydrogen SIBO within 3 months and methane SIBO within 1 month.[127]
- *Failure to use a low-carb preventative diet following treatment.* Diet along with prokinetics is needed to prevent relapse of this commonly recurring condition.
- *Failure to tailor diet to individual tolerances with personal experimentation.* No fixed diet can predict an individual's complex bacterial, digestive, absorptive, immunological, and genetic circumstances; therefore customizing is necessary.
- *Failure to identify underlying causative conditions.* One report found that the following conditions led to a poor response to antibiotics: anatomical abnormalities (adhesions, blind loops, diverticuli, superior mesenteric artery syndrome, etc.), chronic narcotic use, Addison's disease, scleroderma, colonic inertia, inflammatory bowel disease, and NSAID-induced intestinal ulceration.[128] Some of these patients will need long term cyclical rotation of herbal treatments or, very rarely, a 550 mg single dose of rifaximin every other day in order to stay asymptomatic.
- Failure to find the underlying causes to allow for repair or modulation of the MMC will lead to a less desirable outcome.

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In 2013 he was listed among "Top Docs" in *Portland Magazine*. His articles on hiatal hernia and SIBO won first prize in the *Townsend Letter's* Best of Naturopathic Medicine in 2009 and 2013. His piece on proton pump inhibitors was an honorable mention in 2011.

As cofounder of the SIBO Center for Digestive Health at NCNM, Dr. Sandberg-Lewis often treats patients whose health conditions have defied diagnosis despite exhaustive medical testing. Restoring ideal digestive function and normalizing the gut microflora have earned the center a reputation for success in helping many who previously suffered digestive diseases without hope of cure.

Sandberg-Lewis is the author of the textbook *Functional Gastroenterology: Assessing and Addressing the Causes of Functional GI Disorders* (NCNM Press; 2009). He and his wife and son have also written a comic book explanation of SIBO for patients. The textbook and comic are both available at www.ncnm.edu/bookstore.

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What Potentially Evil Molecule Is Actually Lurking In Your Dairy Products?

by Jim Cross, LAc, ND

"Every body needs milk" – or does it? Or are some types of milk more favorable than others for specific people? I tend to favor the latter statement after research that I have uncovered. I am not going to reconstruct the original research of the beta-casomorphin-7 (BCM-7) molecule. This is the result of tireless work by many scientists. I am just going to try to bring their hard work together and illuminate the big clinical picture.

The key information stems from published scientific papers that will be listed. Some dairy people are not interested in having this information disseminated. They think that it will damage their industry. I think that this information can help more people become tolerant of ingesting dairy products, which in the long run will only benefit their industry. Anyway, integrity in research requires that we need to follow whatever path the evidence leads to. I call this the scientific attitude. Unfortunately, this isn't always the case in real life. Ask Nancy Wertheimer, who died in 2008 and initially linked electromagnetic fields to cancer, about that sad state of affairs.[1] She was vilified as a bad scientist (even though she was just asking a question that came about because of research she had conducted) or a woman cursed with PMS.

Milk Basics

First, let's begin with some Milk 101 basics.[2] Cow's milk can be broken down into 7 basic ingredients (Figure 1).[3] The most prolific is plain old water at approximately 88%. Next is protein at about 3% to 4%, of which 80% or so is casein and 20% or so is whey and can vary from breed to breed. Milk proteins also contain all 8 essential amino acids required by humans. Depending on the type of milk, the fat content varies from 3% to 6%. In around 5% of milk lurks the potentially evil carbohydrate lactose. Next, milk contains a fair amount of the water-soluble B vitamins and vitamin C, a large portion of which are destroyed during pasteurization. Cow's milk also contains vitamins A, D, E, and a small amount of K, which are mostly removed in our society's quest to consume lower-fat or nonfat products. Finally, there are minerals in milk, primarily calcium and phosphorus. Unfortunately, soluble and assimilable calcium in milk is reduced again via that unnecessary step of pasteurization.

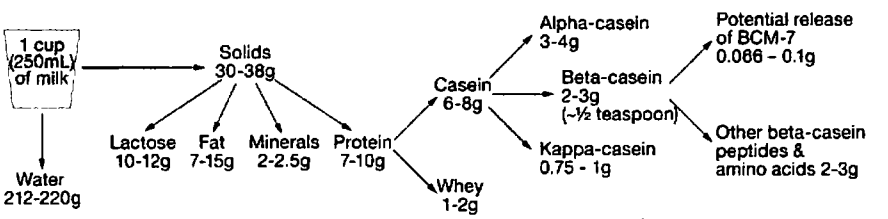
The serum (whey) protein family consists of approximately 50% ß-lactoglobulin, 20% α-lactalbumin, and a smattering of less prevalent molecules: blood serum albumin, immunoglobulins, lactoferrin, transferrin, and many minor proteins and enzymes. Each whey protein has its own characteristic composition and variations. Whey proteins do not contain phosphorus. They do contain many amino acids that have sulfur, which form disulfide bonds within the protein. Denaturation can break the disulfide bonds and is an advantage in yogurt production because it increases the amount of water that the proteins can bind, which improves the texture of the yogurt.

The casein family of protein consists of several types of caseins: alpha (α), beta (β), and kappa (κ) caseins. The high phosphate content of the casein family allows it to associate with calcium and form calcium phosphate salts. The abundance of phosphate allows milk to contain much more calcium than would be possible if all the calcium were dissolved in solution. Casein proteins provide a good source of calcium for milk consumers if the milk is not pasteurized.

Also, as a result of where caseins reside in milk, they will only be present in the milk-solid portion of cow's milk. They are not present in the fat portion and will, as a result, not be present in butter. In addition, caseins are not present in the liquid portion or the whey. Butter and whey products will not have beta-caseins and thus will not cause problems in individuals who have problems with A1 milk. ➤

Figure 1: Beta-casein content and potential BCM-7 release per 250 ml of milk.

Milk and Beta-casein



Evil Molecule

➤

A2 versus A1 Milk and Beta-Casomorphin-7

Numerous references have begun to reveal how diseases, such as type 1 diabetes and cardiovascular disease, are linked to a tiny protein fragment that is formed during the digestion of the A1 beta-casein, BCM-7. This milk protein fragment is produced by cows in the US, New Zealand, Australia, and many other Western countries. Milk that contains A1 beta-casein is known as A1 milk, whereas milk that does not is called A2 milk. Originally all milk was A2 until a mutation affecting Holstein cattle occurred some 8000 years ago.[4] This mutation has been passed on to many other breeds, because Holsteins have been used to genetically improve the production of most other breeds. Herds in much of Asia, Africa, and parts of southern Europe remain naturally high in A2 cows. Also, interestingly, the human beta-casein molecule consists only of the A2 type, which means that breast milk releases no BCM-7. In addition, human milk contains primarily whey proteins, whereas cow's milk has about 80% of its protein as casein. Finally, goats and yaks only produce A2 caseins, and most sheep milk is A2.

A2 beta-casein is found in all types of bovine animals, including all Western, African, and Indian cattle and water buffalo. A1 beta-casein is carried by some cows of European breeds, all of which belong to the subspecies *Bos taurus*.[5] African and Asian cattle belong to the *Bos indicus* subspecies. However, the prevalence of the A2 and A1 beta-casein allele varies between cow herds and also between countries. For instance, a recent study on the beta-casein allele frequency in indigenous Indian cattle (*Bos indicus*) and river buffalo breeds reported 99% to 100% presence of the A2/A2 genotype in its indigenous cow and buffalo breeds.[6] The same study also reported an absence of the A1/A1 genotype in indigenous Indian cow and buffalo breeds. Turning to European breeds, the Holstein, the most common dairy cow breed in Australia, Northern Europe, and the US, carries the A1 and A2 beta-casein alleles in approximately equal distribution. Jersey herds typically have an A2 allele frequency somewhat higher than this, but with considerable between-herd variation. The Guernsey breed has an A2 beta-casein allele frequency of more than 90%.[7]

The difference between the A1 and A2 type beta-casein variants is a single amino acid substitution at the 67th residue of the 209-amino acid beta casein protein chain (Figure 2).[8] This difference in structure results in A1 beta-casein. The beta-casein protein consists of 209 amino acids strung together. The sole difference between A1 and A2 amazingly takes place at amino acid position 67, where histidine is substituted for proline. The proline forms a tight bond with amino acids on either side of it, but histidine does not. In our digestive tracts, because of the weakness of the peptide bonds with histidine, a peptide consisting of 7 amino acids breaks off. This peptide is BCM-7 and is also an opioid peptide.[9]

A recent study in humans has confirmed that BCM-7 is produced in the digestive system following the intake of milk casein protein.[10] This study found detectable bovine BCM-7 in the small intestinal effluents of adults fed 30 grams of milk casein protein. BCM-7 has the demonstrated potential to elicit opioid activity via its affinity to mu-opioid receptors on a range of tissues and systems including the digestive tract, neurological system, and immune system.[11-15] Giving naloxone with A1 milk will neutralize those opioid properties.[16] BCM-7 can also be hydrolyzed further to produce the shorter exorphin with greater opioid receptor binding affinity, beta-casomorphin-5 (BCM-5).[17]

Due to the large size, it should be difficult for BCM-7 to pass through the gastrointestinal mucosal barrier.[18] Many Americans suffer from leaky gut syndrome, which unfortunately facilitates the entry of BCM-7 into their bloodstreams. To possibly confirm this association, BCM-7 has been found in the urine of some people diagnosed with leaky gut. BCM-7 is also released when milk is pasteurized before it can be digestively produced in our guts. The vast majority of milk in the US is pasteurized.

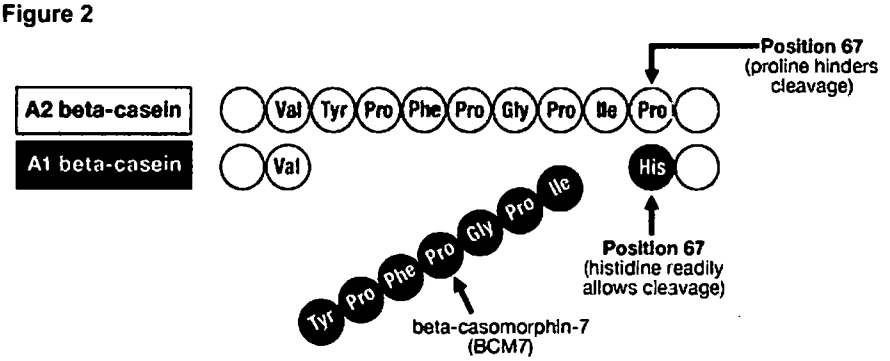
Ischemic Heart Disease

There is epidemiological evidence that links A1 beta-casein and ischemic heart disease (IHD) and also pharmacological evidence linking A1 beta-casein to oxidation of LDL. Let us look at epidemiology first.

Corran McLachlan discovered some very interesting information on the epidemiological connection between A1 milk and IHD. In Figures 3 and 4, WHO 1990 IHD death rate data for males over 65 years old and females over 65 years old are presented against A1 consumption (excluding cheese).[19] The results were remarkable. The correlation between IHD and A1 beta-casein consumption was very high, at 0.84 for men and 0.73 for women. The statistical probability here is less than 1 in a 1000.

The rationale behind the exclusion of cheese is that the subsequent enzymatic action that takes place as cheese ages causes alterations in the casein structure. This leads to chemical changes in individual casein molecules, which decreases the amount of BCM-7 available to be absorbed. Several people have confirmed the absence of BCM-7 in a variety of cheeses.[20,21] Thus, the release of BCM-7 is much lower from cheese than from fresh milk.

Figure 2



There also exists a significant correlation for A1 beta-casein consumption and IHD mortality in 8 states of the former West Germany (Figure 5).[22] Regional variations in β-casein A1 consumption may be estimated in West Germany, where cattle breed distribution data by state have been recorded since the 1950s, and breed distribution remained constant from 1951 to 1984.[23,24] The daily consumption of the β-casein A1 allele was calculated using 1965 breed distributions and the FAO consumption data. They show a statistically relevant relationship between the amount of A1 casein consumed and the IHD death rate/100,000 people from 1977 to 1979 in males of all ages.

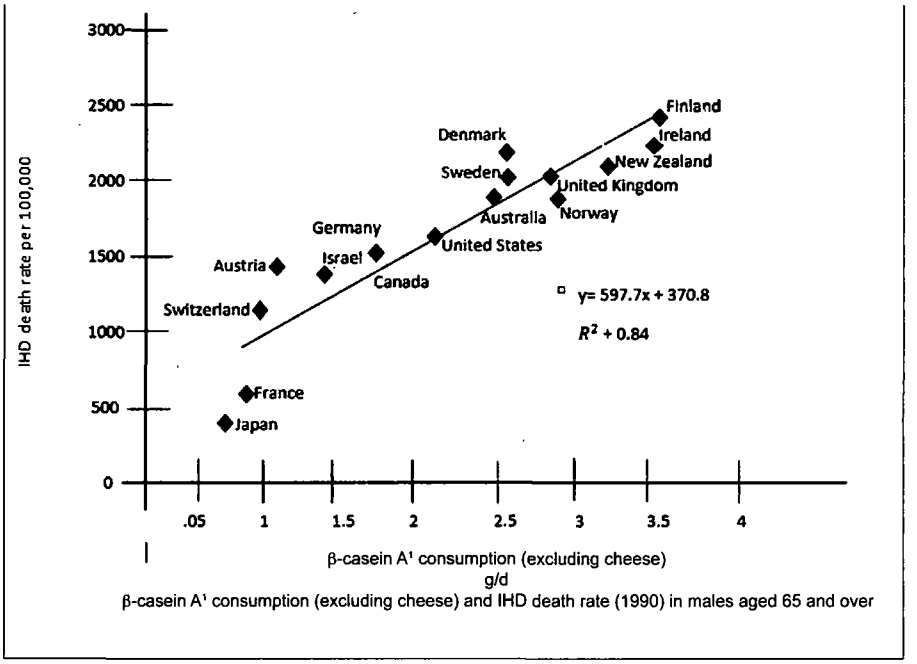
A research program called Prime investigated the relationship of several risk factors to IHD incidence and mortality rates in Northern Ireland and France.[25] Data showed that cardiovascular event rates were 2.3 to 2.5 times more frequent in Belfast than in Lille or Strasbourg and 3.3 times more frequent in Belfast than in Toulouse.[26] There were no important differences in macronutrient intake, although saturated fat intake was significantly higher in Belfast and dietary cholesterol was significantly higher in Toulouse. IHD mortality rate in Northern Ireland was about 3 times higher than in France without major differences in classical risk factors. The A1 beta-casein consumption in Northern Ireland is also about 3-fold higher than the cities in France (excluding cheese).

Around the world, there are also communities who are recorded as having extremely low rates of IHD but who drink milk, such as the Masai and Samburu in Kenya. They obtain their milk from Zebu cattle, which all contain the A2 beta-casein allele. Tibetan highlanders' source of milk, the yak, also does not have the beta-casein A1 allele and they share similarly low rates of IHD.[27]

With regard to pharmacological evidence, BCM-7 has also been shown to catalyze the oxidation of low density lipoprotein.[28] Oxidized LDL (oxLDL) is considered a useful marker of heart disease, according to many cardiologists who consider it the main molecule responsible for initial injury to the cardiac endothelium.[20] LDL oxidation is also considered to be one of the initiators of endothelial damage. In addition, oxLDL is associated with cholesterol accumulation in vascular walls, and elevated plasma oxLDL has been found in patients with arteriosclerosis.[30,31] The tyrosine amino acid on the end of BCM-7 gives it strong oxidative capability, especially since the tyrosine radical has been found in atherosclerotic lesions.[32] Torreilles and Guerin found that peptides from casein-derived peptides could act as a catalyst for the oxidation of human LDLs.[33]

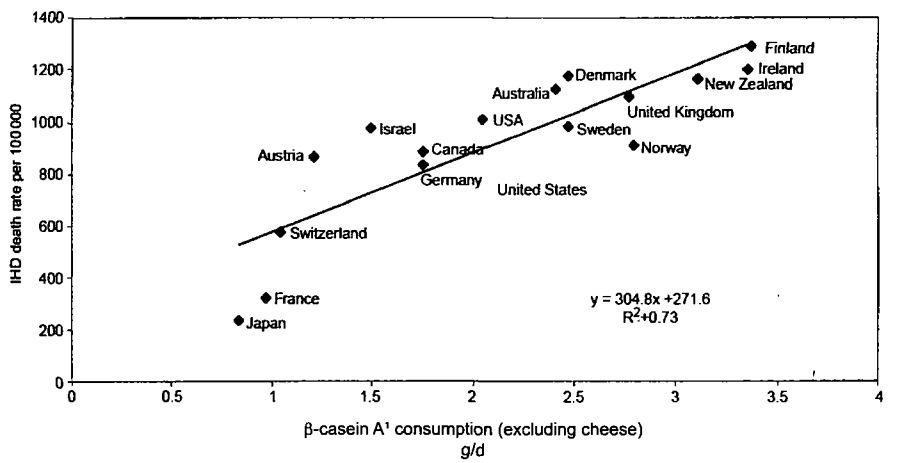
A study in formula-fed human infants found elevated serum levels of antibodies to oxLDL relative to breast-fed babies.[34] The formula contained A1 milk. Since BCM-7 has already been shown (above) to oxidize LDL, it is possible that the BCM-7 present in the formula caused the oxidation of the LDL molecules. Although the researchers in this study did not assess serum BCM-7 levels in these infants, they suggested, "As human milk does not contain beta-casein A1 and infant formulas are based on bovine milk, we can express a hypothesis that beta-casein A1 is the substance, which caused increased production of IgoxLDL."[35]

Figure 3



β-casein A¹ consumption (excluding cheese) and IHD death rate (1990) in males aged 65 and over

Figure 4



β-casein A¹ consumption (excluding cheese) and IHD death rate (1990) in females aged 65 and over

Annand has pointed out that the introduction of pasteurization in the UK around the early 1920s coincided with a near doubling of heart disease mortality.[36] Holder pasteurization, which caused milk to develop a slightly cooked flavor, was generally replaced by the high-temperature short-time (HTST) pasteurization process in the late 1940s to mid 1960s, depending on the country. HTST pasteurization was almost universally adopted by 1980.[37] The US was the first country to introduce pasteurization of milk, around 1900. Ostler in 1910 reported an increased heart disease prevalence that had been observed in the US.[38] It is unknown which of these two possible effects of HTST, whether the heat treatment of milk prior to consumption affects the transmission of β-casein through the gut wall or whether it contributes to greater production of specific casein fragments, is the main culprit and this remains to be established. However, the two factors, changes in pasteurization and differing β-casein allele frequencies between areas, in conjunction with changes in traditional risk factors, may provide an explanation for the historical changes in IHD and regional variations in the disease.

Type 1 Diabetes

Ecological evidence across 20 developed nations show strong correlations between the consumption of A1 beta-casein and the incidence of DM-1.[39–42] Figure 6 shows this nicely.[43] In addition, a recent study reported that A1 beta-casein consumption during early childhood may be more important than during adolescence for DM-1 development. Birgisdottir et al. (2006) compared A1 beta-casein consumption among 2-year-olds and among 11- to 14-year olds in Iceland and Scandinavia (i.e., Norway, Denmark, Sweden, and Finland) and evaluated this against the incidence of DM-1.[44] For the 2-year-olds, but not the 11- to 14-year olds, A1 beta-casein consumption correlated strongly with DM-1 incidence ($r = 0.9$; $p = 0.037$). They raise the possibility that intensive dairy cattle breeding may have emphasized a genetic variant in milk with adverse effects in humans. Further animal research and clinical trials would be needed to compare disease risks of A1-free versus "ordinary" milk.

A limited number of human trials also suggest that beta-casein may stimulate a T-cell immune response or an antibody immune response in the development of DM-1.[45–48] For instance, Monetini et al. (2001) showed significantly higher levels of antibodies to beta-casein in bottle-fed infants under 4 months of age compared with exclusively breast-fed infants ($p <$ 000.1) and significantly higher levels of antibodies in prepubertal children with DM-1 compared with age-matched controls ($p = 0.03$).[49] How this should be interpreted is open to debate. It is possible that this is a manifestation of those with DM-1 being particularly sensitive to antibody reactions. However, in one of the only human studies to investigate differences in antibody response to A1 and A2 beta-casein, Padberg et al. (1999) showed that the ratio of A1 to A2 beta-casein antibodies was higher in those with DM-1 compared with case controls ($p < 0.001$).[50] These results suggest that A1 beta-casein may be a modifier in the development of DM-1 in "at risk" individuals.

One mechanism by which A1 beta-casein may contribute to the development of DM-1 relates to the potential molecular mimicry (or cross-reactivity) between beta-casein and an epitope of the pancreatic beta-cell glucose transporter GLUT2, as autoantibodies to GLUT2 have been described in patients with recent-onset DM-1.[51–53]

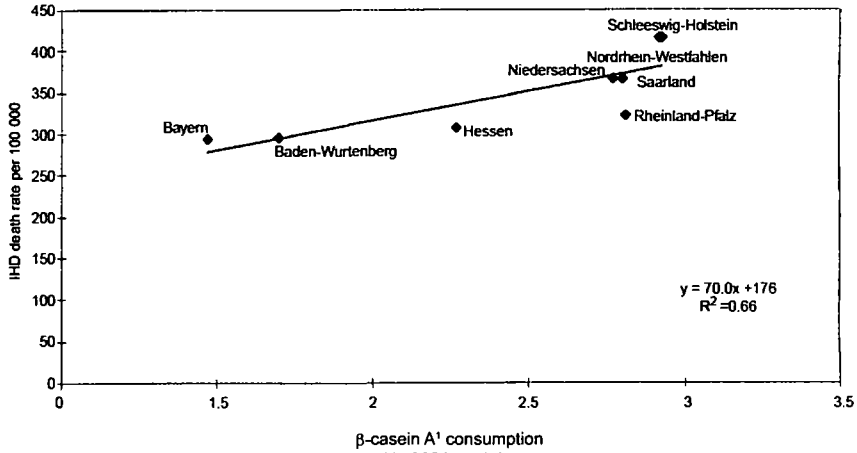
A second mechanism involves the potential antigenic determination characteristic of beta-casein, which may lead to the autoimmune destruction of pancreatic beta-cells.[54] More specifically, Cavallo et al. (1996) have suggested that there may be molecular mimicry between a sequence of the beta-casein protein and an epitope of the GLUT2 transporter, which may give rise to autoantibodies capable of targeting pancreatic beta-cells.[55]

Currently, the role of *bovine* BCM-7 in the health and development of human infants is the topic of extensive scientific debate. Such debate was stimulated recently with the publication by Russian scientists, Kost et al. (2009), who found that BCM-7 could be measured in the blood of infants fed cow's milk formula.[56] The higher blood levels of bovine BCM-7 found in some infants correlated with delays in psychomotor development.[57]

Clinical Stories

I have personally seen some people (not all!) who switched from A1 to A2 milk and had their milk intolerance disappear. One patient was a Czech who had escaped in 1962 from Czechoslovakia, was raised in Switzerland, and came to the US as an adult. He could not tolerate any dairy products here. He went to a farmers' market in Portland, Oregon, where he saw advertised that they only sold milk from A2 cows. He decided to try their

Figure 5



β-casein A¹ consumption and IHD death rate, West Germany (1977–79) in males of all ages.

cheese and milk and, voilà, his milk intolerance was gone, as long as he only drank the A2 milk.

Another patient has found that his severe chronic lower back and morning stiffness has almost completely disappeared after he switched to only A2 milk. These symptoms had been present almost continuously for 20 years. He feels as if a miracle has happened.

Another patient said she used to avoid drinking milk in the evenings because it would make her legs jerky. She has now consumed A2 milk in the evening several times and that has not happened. On a recent night she had symptoms again and thought that maybe it was not the A1 after all. Then she remembered that she had eaten a salad with feta cheese that was made from A1 milk.

Potential Genetic Solution

The solution to the problem is both simple and unbelievably cheap. All that is required is for farmers to ensure that their cows are inseminated, naturally or artificially, with semen from A2/A2 bulls. In New Zealand, some of the smaller groups of dairy farmers, predicting the increase in consumer demand for A2 milk, have already converted their herds to A2 cows.

The A1 gene can be bred out of a herd in about 10 to 15 years simply by choosing what are called A2/A2 sires. This means that neither the dam or sire carries the A1 gene.[58] Unfortunately, until the consumer is educated and begins to request A2 milk, the motive will not be there for the selective breeding in most dairies. Interestingly, New Zealand labels A2 milk in its grocery stores.

What can you do? You can ask your providers of local milk if they are breeding for A2/A2 milk. If they do not understand it, you can refer them to this article. You could also consider purchasing your own milk goats (they do not carry the A1 gene), buy a cow with A2 genetics, or buy a cow with the plan to breed A2 genetics and select future heifers.

Notes

1. Nancy Wertheimer, who linked magnetic fields to childhood leukemia, dies [online article]. Microwave News. http://microwavenews.com/news-center/nancy-wertheimer-who-linked-magnetic-fields-childhood-leukemia-dies.

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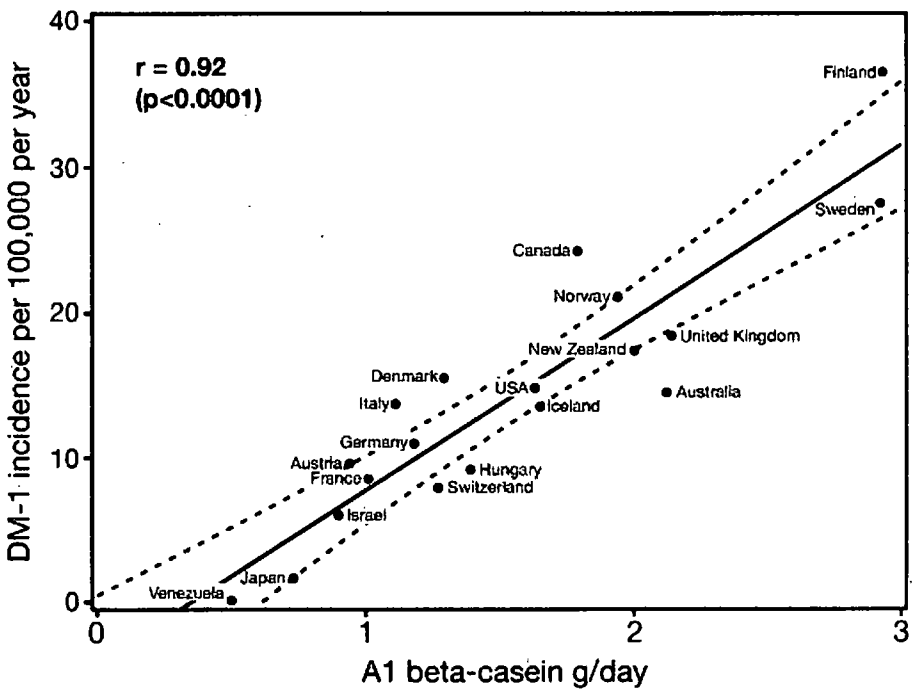
Figure 6: Correlation of A1/capita (A1 b-casein in the per capita milk and cream supply) with the incidence of diabetes mellitus type 1 at 0–14 years of age, 1990–1994, 19 countries; r = 0.92 (95% CI 0.72 to 0.97); p <0.0001; dotted lines = 95% confidence limits of the regression line.



Evil Molecule

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Jim Cross graduated with a degree in biology from the University of California at Davis in 1975 and with a secondary teaching credential in life science from California State University, Sacramento, in 1976. Wanting to initially see more of the world and expand his knowledge of different regions and their people, he traveled and worked in Germany, Switzerland, Holland, Taiwan, and Alaska. Having been helped by a naturopath, he became part of the first-year class at Pacific College of Naturopathic Medicine in little Monte Rio on the Russian River in Sonoma County, California. After PCNM folded, he finished his naturopathic studies at National College of Natural Medicine in Portland, Oregon, in 1984. He later earned his LAc at San Francisco College of Acupuncture in 1989. He has practiced acupuncture and naturopathy in the tiny Northern Sierra town of Quincy since 1990. He has also taught anatomy and physiology at tiny Feather River College in Quincy since moving there. He and his family are extremely lucky to live in a beautiful area where there are more trees than people and that also allows him to practice the hydrotherapy that he learned in naturopathic school from Wade Boyle, ND, by jumping in the local creek one or two times each week all winter. He also wishes that his mother had lived to see him become a doctor, because she was an RN and his first medical teacher. As a child, whenever he was sick, he was made to fast on ginger ale until his symptoms abated. She also taught him, being the good German that she was, to alternate hot and cold in injuries that he incurred playing basketball in high school and college. His true passion is to open an in-patient medical facility in the Sierra Nevada for people with chronic disease.

Dr. Cross also taught at American College of Traditional Chinese Medicine in San Francisco from 1999 to 2005. He has taught ad currently teaches continuing education classes for professionals focusing primarily on nutrition and its relation to optimal health and treatment of chronic disease. He has taught weekend seminars utilizing nutrition to normalize neurotransmitter function and treat addiction, obesity, and cardiovascular disease. He can be reached at thias1020@yahoo.com to schedule speaking engagements.

I would sincerely like to thank Dr. Keith Woodford. I conceived the idea of writing this article after reading his brilliant book about A1/A2 milk, *Devil In the Milk*. He is a truly independent thinker and researcher who truly follows what I call the scientific attitude: follow the evidence unbiasedly, no matter where it leads.

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The Medicine of the Microbiome

by Mark Davis, ND

The Story

I can still remember where I was standing when I first heard of fecal transplants. It was the fall of 2009, and I was in my fourth year in the naturopathic medicine program at National College of Natural Medicine (NCNM) in Portland, Oregon. As a student, I interned with Dr. Steven Sandberg-Lewis, a naturopathic doctor with over 30 years of experience treating patients with inflammatory bowel disease (IBD). His patients were often very sick people who had failed many or all pharmaceutical interventions, or were only stable on strong doses of prednisone, and I helped manage their care.

We used diet, herbs, nutritional supplements, and other interventions, and many of our IBD patients improved, some quite dramatically. For those who continued to suffer, I scoured the literature, researching everything from traditional world medicines to cutting-edge discoveries, and one day, standing in the hallway at a computer kiosk at NCNM, I came across Thomas Borody's 2003 paper "Treatment of Ulcerative Colitis Using Fecal Bacteriotherapy."[1]

Borody is an Australian gastroenterologist who has been using fecal transplants for patients with IBD since 1989, when his Centre for Digestive Diseases reported on using the technique with 55 patients with irritable bowel syndrome (IBS) or IBD.[2] His paper took my breath away. The six ulcerative colitis (UC) patients whom the 2003 paper described reminded me of my own UC patients: frequent bloody stools, pain, weight loss, anemia, and, most importantly, nonresponsive to most or all other therapies.

His patients became asymptomatic, they came off medications, their lab values normalized, and eventually colonoscopy revealed normal tissues with all traces of inflammation gone. He followed one patient as long as 13 years, and at his last colonoscopy there was no sign that the patient had ever had UC. Borody called the process "human probiotic infusions," a name that I love, but since then the name fecal microbiota transplantation (FMT) has become more standard.[3]

The treatment seemed simple enough – dilute fresh stool (from a screened donor) with normal saline, filter, and administer the liquid, teeming with healthy bacteria, as a retention enema. Borody applied "anticlostridial" antibiotics and oral bowel lavage beforehand to reduce the endogenous bacterial population, and suggested a high-fiber diet afterwards, to feed the new bacteria.

Standing there in that hallway, it felt like I had found a silver bullet. I remember thinking, "This could be so powerful, and it sounds so simple!" As I reflect on FMT now, 5 years later, I continue to be floored by what a powerful tool it has been, but it is not always simple, and it certainly isn't a silver bullet for everyone with UC.

History

FMT is the process of administering microorganisms from the stool of a healthy donor to a patient's GI tract. Coprophagy is an important biological

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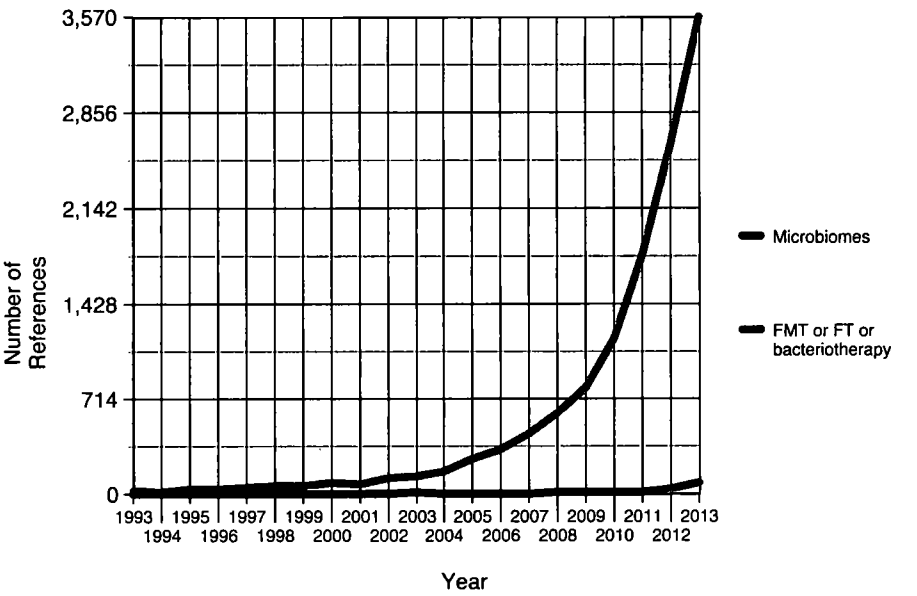
Figure 1

Medscape references to "microbiome" and "fecal microbiota transplantation" OR "fecal transplant" OR bacteriotherapy1993-2013



http://dan.corlan.net/medline-trend.html accessed 8/15/14

trait in some animal species, and the oral administration of stool from healthy human donors to human patients with intractable diarrhea has been reported since the 4th century in China, through the 16th century in China and Europe and in modern times.[4-7] FMT was first documented in modern medical literature by Eiseman et al. in 1958, who reported using FMT retention enemas with four patients with infectious colitis, three of whom were very close to death.[8] All four recovered completely within 48 hours following FMT retention enemas. After Eiseman, there are sporadic reports of FMT for pseudomembranous colitis and other forms of *Clostridium difficile* infection (CDI) for a few decades, and then, in 1989, two reports of FMT for IBD. One is the report by Borody, in which he describes treating 55 patients with IBD and IBS. The other is a letter from American physician J. D. Bennet, whose own UC had been steroid dependent for 6 years until a series of FMT retention enemas reversed his disease.[9]

Over the past 5 years, interest in the microbiome, and in fecal transplant in particular, has skyrocketed (see Figure 1, p. 83). FMT continues to appear safe and quickly curative for adults, children, and immunocompromised individuals with refractory CDI.[10-12] There have been no serious side effects conclusively associated with FMT in hundreds of published case reports. FMT also appears to be safe, and effective to varying degrees for children and adults with IBD.[13,14]

Mechanisms

How does FMT accomplish all this? Analysis of patient fecal microbiomes after FMT shows that they more closely resemble the donor's microbiome than the patient's own pre-FMT microbiome.[15] Unlike aerobic *Lactobacillus* and *Bifidobacterium* probiotics, which are typically transient organisms, the anaerobic colon organisms of FMT appear to effectively colonize and inhabit the colon. They may help banish *C. difficile* by taking over the same niche and simply outcompeting it. Or, it may be that antibiotics produced by the donor colon microbes are sufficiently lethal to the *C. difficile* organism.

Theories abound as to how FMT benefits patients with IBD, some of whom may get durable benefit from a single or limited series of infusions, some of whom may need "top-off"

A Good Joke Changes the Human Intestinal Biome

by Jacob Schor, ND, FABNO

Before asking patients to ingest someone's feces, there is an easier intervention that you might want them to try.

Back in 2010, Hajime Kimata reported that gut flora can undergo a rapid and dramatic shift in people who view humorous films.

Kimata is a Japanese allergist who first came to our attention in 2001 when he reported that watching a Charlie Chaplin movie (*Modern Times*) significantly decreased the size of skin wheals caused by allergen provocation. In that trial, he studied 26 patients with atopic dermatitis who all had significant allergies. They underwent skin-prick tests before and after viewing the movie. The size of the resulting wheal was measured. A similar procedure was repeated before and after an 87-minute video of weather information. The wheal responses to allergens were significantly reduced after patients' laughing at Charlie Chaplin; the effect lasted for hours. Watching the weather had no effect.[1]

In his 2010 "poop study," Kimata recruited 24 healthy people and another 24 with atopic dermatitis. As is often the case, those with atopic dermatitis had significantly fewer *Lactobacilli* or *Bifidobacterium* in their stools and instead had larger populations of *Staphylococcus aureus* or *Enterobacteria* than the healthy study participants. Fecal levels of bacterial metabolites (polyamines) were also reduced. These participants were split into two groups; one group watched a humorous movie each and every day for a week. The "control group" watched nonhumorous movies instead. Sample of feces were obtained before and after the week of movies. Fecal flora and fecal polyamine levels were determined.

The intestinal flora in the healthy people were unaffected by watching either type of movie, funny or not funny. In contrast, the patients with atopic dermatitis who watched the humorous movies had significant changes in gut flora; watching the nonhumorous movies had no effect. Stool testing of the atopic dermatitis patients who watched the humorous movies showed increased levels of *Lactobacilli* and *Bifidobacterium*, decreased colonization with *S. aureus* and *Enterobacteria*, and increased fecal levels of polyamines.[2]

These changes occurred in a week.

Laughter has the power to quickly change the gut biome. With this in mind, I sometimes send patients home with a curious prescription that reads: "Every evening for the next 7 days, watch something on Netflix that makes you laugh out loud for a minimum of 120 minutes." Many people already know what they can watch that will make them laugh. I often suggest *The IT Crowd* or *The Vicar of Dibley* (which probably says more about me than I should admit). A week of regular laughter may shift their symptoms for the better. It certainly can't hurt.

Could Davis use this idea in his FMT protocol? Would having people watch humorous movies in the days leading up to and following his procedure elicit better results? Davis likes people to retain the FMT enema for hours. Laughing hard might make this part of the treatment more challenging.

Notes

1. Kimata H. Effect of humor on allergen-induced wheal reactions. *JAMA*. 2001 Feb 14;285(6):738.
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infusions to stay well, and some of whom to do not appear to respond at all. It may be that IBD is triggered or aggravated by the lack of important immunomodulating organisms such as *Faecalibacterium prauznitzii* that FMT replaces.[16] It could be that FMT is outcompeting or killing bad actors in the native microbiome as we suspect it does with *C. difficile*. It could be that FMT simply restores a ratio, or triggers immunomodulating reactions in the same way that even heat-killed *Lactobacillus* and *Bifidobacterium* probiotics can.

More of the Story

The first patient whom I pitched FMT to was a 14-year-old male with a 6-month history of ulcerative colitis. The conversation went something like this:

Me: So, there's another therapy I'd like you to consider. It's called human probiotic infusion.

14-year-old: What is it?

Me: Well, the idea is that you might have some bacteria in your colon that are causing your immune system to react, or you might be missing some bacteria that normally quell inflammation. The bacteria in someone else's colon might be a better fit for you, so we collect stool from a healthy person, strain it, and give the part with the bacteria to you as an enema.

14-year-old: The therapy is giving me poop?

Me: Yes.

14-year-old: Well, that doesn't sound too bad. I guess I'll think about it. What's an enema?

Me: It's a tube that's lubricated and inserted through the anus into the rectum, then the HPI flows through the tube into the rectum.

14-year-old: Anus? Butt? My butt? You stick something into my butt? No way. Can't you just inject it into my veins or something?

Dr. Sandberg-Lewis: Actually, that would kill you.

That first patient did not take me up on my suggestion, in part because he was a 14-year-old boy, but also because he hadn't been living with ulcerative colitis for very long. When researchers at the University of Chicago asked a series of focus groups consisting of patients with UC and parents of children with UC how desperate they'd have to be to consider FMT as a therapy, they were nearly unanimous: not only would they be interested in trying it, they'd like to have it available as a first-line therapy, before they tried immunosuppressants.[17] As one patient in my practice says, "People who don't have inflammatory bowel talk about 'the yuck factor' of FMT. They have no idea – the yuck of FMT pales in comparison to the yuck of living with this disease every day."

Before I started my private practice in 2011, I had worked with exactly one patient with FMT. Laurie was 37 years old at the time, with a 4-year history of UC, and mother of twin toddlers. Her first round of five FMT retention enemas didn't benefit her at all. Two months later, she wanted to try again, so we tweaked everything: different donor, different timing, and a different support system that helped her retain the infusions for longer. This time, her UC improved – she described herself as 90% better. I was hooked.

The Question of Antibiotics

In 2011, there was, as far as I could tell, no one in the US offering FMT for inflammatory bowel disease and offering a donor bank, although there were a few medical doctors around the US and Canada regularly using it for CDI. I decided to make that my niche. I bought the website fecalmicrobiotatransplantation.com, and started spreading the word. I wrote articles, and gave talks for IBD support groups and CE talks for professionals.[18-20] The FDA had not yet regulated FMT, so I was treating patients with CDI, IBS, chronic constipation, microscopic colitis, ulcerative colitis, Crohn's disease, and occasionally other autoimmune or inflammatory diseases.

Early in my career, I had the opportunity to ask Borody some questions about FMT. He told me at that time that he had never had a patient decline the antibiotic pretreatment part of his protocol. Without any comparative data on the topic, I tell my patients that they can choose whether to use Borody's protocol or try FMT without antibiotic pretreatment. I work with patients who choose some combination of pharmaceutical and/or herbal antimicrobials and biofilm busters, and some who choose no pretreatment at all. Oral bowel lavage can leave patients with too much bowel laxity to retain the fecal slurry enema for the 6 hours that I recommend, so I often use large-volume water cleansing enemas about an hour before FMT instead. I'm often using other interventions alongside FMT, offering guidance on diet, and supplements tailored to the individual.

My favorite quote about medicine is from Hippocrates: "Life is short, and the art is long. Opportunity is fleeting, experimenting is dangerous, and deciding is difficult." It can be hard, as a clinician, to feel confident about which interventions have made a difference for your patient. That being said, my experience leads me to believe that some people with IBD can have near-miraculous benefit from FMT without any antibiotics involved. I also suspect that there are some people with IBD who will not see any benefit from FMT unless there are antibiotics on board beforehand.

Several of my IBD patients have not benefited from an initial round of FMT, then completed a course of Borody-style antibiotics followed by a second round of FMT and then benefitted. However, in the spirit of avoiding the *post hoc, ergo propter hoc* fallacy, let me return to Laurie, the 37-year-old with UC and twins. Her first round of FMT did not benefit her, but a second round of FMT, also without antibiotics, benefited her substantially. Perhaps my other patients who did a second round of FMT with antibiotics may have just been benefiting from a second round of FMT.

Conventional Medicine vs. Alternative Medicine and the FDA

An advantage of conventional medicine is its consistency. Conventional docs generally follow professional society recommendations, and have a similar standard of care,

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which values the known over the unknown. At least in theory, they use therapies whose risks and benefits have been evaluated. The drawback of this approach is that many patients have a medical aesthetic which favors the potential benefits (and concomitant risks) of therapies that have not yet been examined in trials, and MDs often won't consider discussing those therapies since they can't weigh the risks and benefits in the same way, and they could be legally responsible if a patient suffers an adverse event from an untested therapy.[21]

People often come to naturopathic doctors because the bedrock of our therapeutic armamentarium is made up of interventions that have not been evaluated using rigorous science. We use herbs, diet, exercise, hydrotherapy, and other traditional interventions and are comfortable operating outside the known evidence base.

With that in mind, I spent 2 years using FMT to treat patients with a variety of conditions before a letter from the American Gastroenterological Association to the FDA prompted the FDA to classify FMT as a drug and a biological agent.[22] In April 2013 the FDA limited the use of FMT to clinical trials, but after objection from clinicians around the country who were seeing FMT save the lives of their refractory CDI patients, the FDA agreed to provide discretionary enforcement for clinicians preparing and administering FMT to treat refractory CDI.[23] Many of my patients with IBD are determined to do home FMT, so I counsel them in what I believe to be best practice, in the interest of harm reduction and with hope for benefit. I believe that some of my patients still have their colons because of their use of home FMT.

The Fecal Transplant Foundation (whose board of directors I'm honored to serve on) now lists over 75 practices or physicians in the US offering FMT for patients with refractory CDI, including the Mayo and Cleveland Clinics.[24]

Safety and Efficacy

Clinicians who use FMT have had a growing sense for years now that FMT is very safe in the short term, massively effective for CDI, and perhaps helpful for IBD, IBS, and more.

Is it really effective? The one randomized, controlled trial published so far weighed a standard treatment for recurrent CDI (500 mg vancomycin 4×/d for 14 days) vs. an abbreviated course (500 mg vancomycin 4×/d for 4 or 5 days) followed by FMT nasoduodenal administration.[25] They unblinded the study halfway through, and had to stop the study because the difference in the groups was so dramatic – only 25% of the treatment-as-usual group was cured, while all but 1 of the 16 FMT patients (94%) were cured after no more than two FMT infusions. This small study supports the 92% cure rate generally reported in case series.

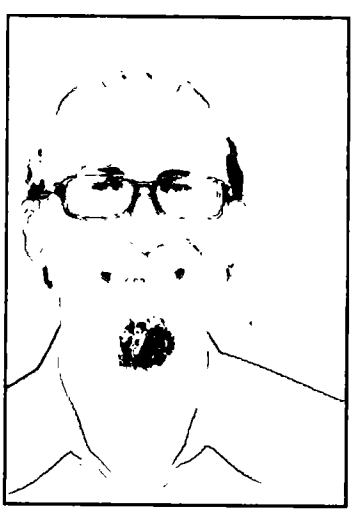
Case series have indicated enough benefit for IBD.[13,14] that randomized controlled trials are warranted – at the time of this writing, 14 of the 35 FMT trials listed on clinicaltrials.gov are studying FMT for IBD.

Occasionally fascinating cases pop up, such as Borody's patient with Parkinson's whose symptoms completely resolved after FMT.[26] Borody also reports a case of idiopathic thrombocytopenic purpura (an autoimmune condition) that resolved after FMT, and he reports three people with diagnoses of multiple sclerosis (MS) whose symptoms reversed after FMT, including one who had an indwelling catheter and was confined to a wheelchair, who then regained the ability to walk and urinate unassisted.[27,28]

I've used FMT with two patients with multiple sclerosis. They were both early in their diagnoses, and hadn't progressed very much. Following a series of FMT retention enemas, they remained quite stable, and one reported a side benefit. A type 1 diabetic for 20 years, he reported a distinct 20% to 30% drop in his postprandial insulin needs after FMT. He recently told me that at his last appointment, his neurologist told him "You have the brain of a healthy person." "Like a healthy person with MS?" he asked. "No," said the neurologist, "like a healthy person." It is important to note that he had also made dietary changes and undergone chelation and other interventions.

Is it really safe? There are still no serious adverse events clearly attributed to FMT, although there was a report of a 1-year-old with UC who had self-resolving ananaphylactoid responses to two out of seven FMT infusions. The infusions appeared to put her colitis into remission.[29] There have been minor adverse events in my practice and the literature, such as gas, cramping, stool changes, increased flatulence, and borborygmi. In the short term it appears quite safe. One of my colleagues in the Fecal Transplant Foundation, gastroenterologist Colleen Kelly, is spearheading a plan to institute an FMT patient registry, where people will be able to report beneficial and adverse effects for years and decades after receiving FMT – that kind of data gathering might reveal long-term sequelae that we hadn't anticipated.

Are capsules safe? As of this writing I've administered FMT capsules (spun down at about 5000 G in a centrifuge) to



Mark Davis, ND, is the medical director of Good Life Medicine Center, an integrative medicine center in Portland, Oregon. His naturopathic practice, Bright Medicine Clinic, focuses on gastroenterological health. Dr. Davis is one of a handful of physicians in North America with clinical expertise in fecal microbiota transplantation (FMT), which he offers via retention enema and capsule.

Dr. Davis sits on the board of directors of the Fecal Transplant Foundation and is on the editorial board of the *Natural Medicine Journal*. He received his ND with honors in research from the National College of Natural Medicine.

You can find more information about Dr. Davis's practice and FMT at brightmedicineclinic.com

eight patients with CDI, seven of whom have been quickly cured. Many people have asked about the safety of upper GI FMT, concerned that it could bring on small intestine bacterial overgrowth. Before I started administering capsules, I was relieved to see a Dutch group who'd given FMT to CDI patients through a duodenal tube; they biopsied the duodenum before FMT and 6 weeks afterwards, and did not find any difference in small intestine bacterial abundances before or after FMT.[30]

The Future ...

Several groups are working to culture groups of fecal-derived microflora, lyophilize them, and encapsulate them. There is likely to be an FDA-approved lab-grown microbial product to treat CDI sometime in the next few years. Will those products be useful to treat IBD or other indications? Will other products be developed to treat those conditions? The products may be expensive, and perhaps limited in use (since they are extracts, not whole stool).

Other groups, including my own practice in Portland, are spinning their fecal slurries in large centrifuges, collecting the bacterial pellet, and triple encapsulating the whole-stool extract.

There will always be patients who want to try home FMT, and clinicians will serve their patients well by being knowledgeable about FMT best practice. In my practice, I'll continue to prepare FMT enemas and capsules for my refractory CDI patients. I'll continue to guide patients with IBD and other conditions in home FMT, and I'll continue to observe and collect data. I'm excited to see the science of microbial medicine grow, and happy to be one clinician quietly feeding its growth.

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Dr. Graves, We Can Heal Your Disease: A Love Letter to Naturopathic Doctors

by Heather Herington, BSc (Biol), ND, DHANP

There's nothing like having a disease considered incurable to sense the impact that naturopathic medicine might have. Especially when you, a naturopathic doctor, are the patient and have been diagnosed with a serious disorder, one that you have been taught not to treat. And you figure that there has to be more to that story.

It took me two bouts of Graves' disease 5 years apart to really understand what this autoimmune hyperthyroidism is all about. I say this in all humility, because my intention in writing this article is to generate interest in bona fide research from the perspective of naturopathic medicine. I believe that this will verify the positive effect of a holistic approach, demonstrate that our medicine can do much to alleviate suffering from this poorly understood disease, and in fact must be engaged to help reverse the allopathic practice of "slash and burn" that continues to be the norm in 2015.

The literature cites Graves' disease as a consequence of a faulty immune system; antibodies treat thyroid tissue as foreign and attack. No different than any autoimmune disease except that this one strikes the thyroid, generating increased thyroid hormone that produces serious results.

Yet the thyroid gland is no shrinking violet in its healthy state. It is the master regulator of the body, the "queen bee," so to speak. Every cell and organ in the body takes direction from it, both physical and mental. It affects not only protein and carbohydrate metabolism, body weight, heart rate, blood pressure, sleep, and sexual response but also mental well-being, particularly cognitive ability and mood stability.

After my own diagnosis, I wanted to know what factors might cause a thyroid to succumb to a spinning of hormone that in its most severe complications, without treatment, could lead to disfigurement, even death. What were the roots of this inflammatory process? I had to know. Was there a link to food, minerals, environmental toxicity, exhausted adrenal glands, and/or unfettered emotion, as is the cause of much of what we treat?

"Thyroid gland function is one of the most misunderstood systems by conventional medical doctors," write Erin Lommen, ND, and Jay Mead, MD, in *Slim, Sane and Sexy*. "Regaining full thyroid function requires a willingness to strive for optimal hormone levels rather than normal levels."

A willingness to strive for optimal health, I translated. By necessity a whole-person approach, the kind that takes all aspects of health into account to manifest a positive outcome. How could I do this with a diagnosis of Graves' disease?

The bottom line of the physical manifestation of autoimmune hyperthyroidism is clear. The "queen bee," in its hyper state, means an acceleration of the metabolic rate and subsequent pounding of the heart. This disease process comes on suddenly (or appears to) but usually starts slowly with mild symptoms such as the inability to relax, irritability, an intolerance to heat, difficulty sleeping, a fast pulse. These warning signs can expand to include an even faster resting pulse (mine was 100), severe weight loss, increased perspiration and bowel movements, hand tremors, low libido, dry and brittle hair, changes in menstrual flow, tinnitus, a goiter, and eventually brittle bones. Graves' dermopathy results in thick, orange-peel-like skin on the shins, top of feet, or elsewhere. In 30% of people, Graves' ophthalmopathy/orbitopathy will occur, caused by carbohydrate metabolism dysfunction; antibodies attack and inflame the soft tissue behind the eyeball, pushing it forward. If the disease is left untreated, complications can consist of heart rhythm disorders, changes in structure and function of the heart muscles and coronary heart failure, and blindness. In pregnancy there is the threat of miscarriage, preeclampsia, fetal thyroid dysfunction, and poor fetal growth.

Although rare, the most serious complication is thyroid storm. Life-threatening, this event requires immediate emergency care. Symptoms of fever, profuse sweating, vomiting, diarrhea, severe weakness, seizures, a markedly irregular heartbeat, yellow skin and eyes, and severe low blood pressure that can lead to coma make this event out of range of naturopathic care.

Are you too nervous to read on, cringing to think that naturopathic medicine should even be considered to treat this serious disease? Let me explain further.

In my first bout of Graves' disease, I trembled not just from the "hyperness" of a fast pulse but from the fear of how I could save my thyroid while avoiding the allopathic standard of radioactive iodine therapy or thyroidectomy, especially after calling the medical director at my alma mater and learning that naturopathic medicine continued to avoid treating hyperthyroidism.

I was undeterred; I had to get to the bottom of this disease in order to heal myself. How did I rein in the attacking antibodies forcing my thyroid cells to overproduce? They couldn't be magically acting on their own, I thought. The thyroid, like any other organ, does not work alone. To compartmentalize it, to isolate it, seemed absurd. The phrase "it takes a village" came to mind.

I was grateful to NATO scholar Ryan Drum, PhD (who used to take my patients on herb walks): "Please stop blaming the thyroid gland for thyroid dysfunction. ...Rather a person's behavior contributes significantly. ... Please engage the thyroid gland as an obligate ally rather than a mass of misbehaving errant tissue, which must be disciplined with medications, radiation ablation or surgical removal. The thyroid gland is probably usually doing its best to respond to events and demands."

Ah, events and demands.

Before delving into that hornet's nest, I reviewed the feedback loop from the hypothalamus (TRH; thyroid releasing hormone), to the pituitary gland (TSH; thyroid stimulating hormone) and finally, the thyroid (T3, T4). I remembered that the hypothalamus responds to stress, strong emotion. Ditto the pituitary.

After 25 years of not needing to, I reread the risk factors. I was female but no longer under 40, not pregnant, had no family history, didn't have another autoimmune disease, didn't smoke (something that also increases the risk of Graves' ophthalmopathy), and had no physical stress. I had emotional stress from grief but I was handling that. Wasn't I?

While I calmed myself in a variety of ways – meditation, slow walks, homeopathy, Chinese herbs, acupuncture, massage, along with Tapazole (the trade name for methimazole) – I looked deeper into my situation. I was determined to put my finger on what I needed to understand to heal a disease that I was taught not to treat.

Thankfully, history reframed my predicament. Leaning into the past, I learned that the constellation of symptoms which would become known as Graves' disease was first described in 1786 by Dr. Caleb Parry in England, 25 years earlier before Dr. Robert Graves did in Ireland. It was as if these medical men were standing in my home, offering their insights on the core expression of what they had observed, clapping that someone was paying attention.

Graves, published in the *London Medical Journal* in 1853, noted the cause "...a bereavement following the death of a loved one, a marital breakup, major financial concerns... an overwhelming grief, an upset." He spoke of a sense of doom, something that I more and related to over time as denial of my emotional state waned.

Although I am not keen on diseases' being named after men, I feel deeply indebted to these doctors for their observations, a discussion that never entered the room with any of my medical doctors. If these 19th-century men hadn't written down their conclusions 200 years earlier, my thyroid, like thousands of others, would have gone the way of the knife, or been shrunk in size through radiation, leaving me, in either case, if nothing else, dependent on thyroid medication the rest of my life. And yet nothing for my aching heart.

Although I don't want to make any assumptions (and am begging for a researcher to step forward), each person whom I have come across diagnosed with Graves' disease confirmed the historical literature of a sudden grief: a child or sibling murdered, a mother dying, financial woes ... or shock from a fall, an accident, something physical.

Our practices are filled with people with unresolved psychological trauma, whether we delve in and treat at that level or not. This is the crux of the body-mind connection or psychoneuroimmunology – physical symptoms that stem from emotion. This was the concept that, along with my love of plants, had pole-vaulted me toward naturopathic medical school almost three decades earlier.

The more I knew about Graves' disease, the more shocked I felt that not one medical doctor mentioned stress to me. No one even suggested that I see someone for anxiety. Just part of the symptom package that would be healed through one caustic method or another.

This malady of omission is, of course, rampant, even though medical professionals have stepped forward in the last century to voice the role of emotions and stress in causing ill health. It's only lately that I learned that Hans Selye, in my hometown of Montreal in the 1950s, concluded that seven distinct conditions, including Graves' disease, had stress as an underlying cause. So why does it continue to be ignored?

I was in the first class at Bastyr that offered counseling. I gobbled it up, but it was the Vancouver Diocese that really concentrated my awareness in the mental/emotional root of physical symptoms. As I began treating survivors of sexual abuse

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Lab

(Serum) **TSH**: thyroid-stimulating hormone or thyrotropin. In hyperthyroidism the TSH is low – in my case less than .004, barely detectable – telling the thyroid to slow down, it has too much T4 and T3. The conventional range is .5 to 5.5 mcg/dL but many endocrinologists now recommend .3 to 3.0. Mary Shomon, a consumer thyroid advocate, believes that optimal values should be close to 2.0.

(Saliva or urine) **Free T3** (triiodothyronine) and **Free T4** (thyroxine): the metabolically active thyroid hormones. (Total T3 and T4 can be omitted.)

(Serum) **TPO**: thyroid peroxidase antibodies test. This is the most sensitive test for determining autoimmune thyroid disease, whether Graves' or Hashimoto's. It measures an enzyme that catalyzes the oxidation of iodide on tyrosine residues in thyroglobulin for the synthesis of T3 and T4. Only 60% to 80% of patients will have them, although some authors say up to 95%. 5% to 10% of healthy people test positive for TPO, so it is not a definitive test.

(Serum) **TSI**: Thyroid-stimulating immunoglobulin binds to tissues in the eyeballs and beneath the skin, contributing to exophthalmos (protruding eyes) and pretibial myxedema (skin thickening on legs). This confirms Graves' disease and indicates to 30% diagnosed that they will likely develop Graves' ophthalmopathy/orbitopathy. Imaging tests, CT scan, and/or MRI are needed, so this is for information only.

Additional Tests

(Salivary) **Adrenal function test**. Four measurements of **cortisol** essential.

(Salivary or urine) E1, E2, E3, and progesterone.

Any others indicated to affirm that "it takes a village."

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with PTSD (post-traumatic stress disorder), it was relatively easy to link physical complaints such as migraine, digestive disorders, dysmenorrhea, painful intercourse, endometriosis, fibromyalgia, and more to a story of abuse. Once this connection was made and patients could track the cause through active listening, visualization, simple witnessing, and/or creative expression, symptoms would disappear. It didn't matter what the presentation, something would change dramatically. This is true holism ... to explore the whole picture, the whole person.

The trauma in Graves' may be more sudden, more apparent, as the body goes into overdrive to deal with the shock of a profound upset, but I believe that our knowledge of, and our commitment to, *tolle causam* and *vix medicatrix naturae* is exactly what people suffering autoimmune hyperthyroidism need. This is not to say that pharmaceuticals aren't necessary, especially at the beginning. It depends on the severity of the disease. And it doesn't mean you have to be directly involved in emotional therapy. Just be aware of this possible central core and refer out if need be.

What I want you to understand about the emotional root is that it is fundamental to the disease and therefore its healing. Graves and Perry, excellent observers, knew of what they spoke/wrote. And I know that this gave me the incentive to probe my own grief, allowed me to recognize the work that I needed to do to heal my autoimmune hyperthyroidism. I had to grasp this rather amorphous entity, dig myself out of its entrails of emotion, releasing feelings in order to move forward to a happy ending. I accepted that my personal narrative had been the origin, or at least played a large role in my illness.

That said, the opposite is also true, as we know: the physical affects the psychological. Graves' disease has been described historically as " ... a heightened sensitivity of receptors to sympathetic nervous system activity possibly mediated by increased alpha-adrenergic receptors in some tissues." This acknowledges the adrenal glands, the body's bell ringers that call together the "village" of the thyroid, including the pancreas, liver, and kidneys, for a concerted response to a shock or grief. Undoubtedly, there is much that our medicine – scientific knowledge coupled with natural modalities – can do, without nailing a psychological event.

For instance, how much do endocrine disrupters affect the thyroid? What is the outcome when essential minerals are displaced in our metabolic processes? How do allergies, environmental and food, or vitamins D and B12 and other micronutrients play a role in hyperthyroidism? What about viruses or bacteria? One theory has *Yersinia*, the cause of bubonic plague, as a possibility.

We know that the liver converts 60% of thyroid hormone, making transport proteins such as thyroid binding globulin that carry T4 and T3 to tissues, and is a factor in estrogen dominance, a condition that can increase free T4. The need for a healthy liver is obvious. Ditto all the other organs. Including carbohydrate metabolism. I have often

Highlights of a Treatment Plan

Use your own autoimmune, anti-inflammatory protocols and consider adding a few ideas here that pertain to Graves' disease (many of which I hope will become variables in research. Right now it's hit and miss.)

Food

Millet. Studies reveal that millet, rich in C-glycosylflavones, produces goitrogenic and antithyroid effects similar to those of antithyroid medications.

The **goitrogenic cruciferous family**, preferably raw: kale, cauliflower, broccoli, brussels sprouts. Soy and peanuts are suggested as well, but they have mild activity and there are other reasons not to recommend them.

Minerals

Iodine: Essential to thyroid hormone. T3 has three iodines and T4 four. In the old days, high iodine was given, as it can have the opposite effect of reducing thyroid hormone production.

It's unclear whether iodine starvation is a good idea, especially with radiation leaking over from Japan. Otherwise no seaweeds, seafood, or iodized salt. Google a list of foods that contain iodine.

Selenium, zinc, and the other minerals as you would in hypothyroidism.

Botanicals

Motherwort (*Leonuris*) and **bugleweed** (*Lycopus*) are two plant antithyroid drugs. Less powerful than synthetic drugs but can be adequate in less severe cases. Not noticeable for 1 to 2 weeks and can take 3 to 4 to really feel a difference. (*Leonuris* also relieves palpitations and tachycardia.)

Lemon balm (*Melissa officinalis*) Sedative. (Also antiviral, which might help in Graves'.)

Others include **valerian**, increases GABA; rose: calming.

Hydrotherapy

Cold immersion only.

Classical and acute.

Homeopathy

For nonhomeopaths: Start with Iodum 30 C once or twice a day until a constitutional case can be taken.

Mind-Body (remember, engage the parasympathetic!) Meditation, breath work (4 inhales to 8 exhales).

Visualization, hypnosis, tracking, or other psychoneuroimmunology techniques to ferret out an unconscious cause of the disease

Restorative yoga (no inversions; too stimulating). Gentle exercise: swimming, walking.

Chinese medicine/herbs.

I don't practice acupuncture or prescribe Chinese herbs, but their ability to balance meridians and evoke calm is evident in certain hyperthyroid formulas that are rooted in thousands of years of experience, even if the doctors didn't call it hyperthyroidism.

wondered at my "luck" at escaping protruding eyes. Is it that I have eaten an anti-inflammatory diet since my teen years? We won't know until we do the research!

There is no question that, as the pioneers of integrated medicine, we are good – no, excellent – at optimizing metabolic pathways to effect optimal health. Without restoring gut function, detoxifying the liver, managing cortisol levels, and regulating blood sugar, there can be no regular pulse, no optimal lab values for the thyroid. Not to mention a bright and relaxed facial expression.

So where does this leaves us? Can we partner with endocrinologists and refer when necessary in severe cases but take on more moderate presentations?

Botanicals *Lycopus* (bugleweed) and *Leonuris* (motherwort) work like prescription antithyroid medication. They disable thyroid hormone production by inhibiting iodine binding to tyrosine. The grain millet does this too. Synthetic drugs include either propylthiouracil (PPO) or methimazole. Methimazole is not to be taken by pregnant women in their first trimester because of the risk of birth defects; both can generate a skin rash and joint pain as well as liver failure and a decrease in white blood cells.

A little scary, these antithyroid medications are usually necessary at the acute stage, prescription tablets that can be slowly tapered down to nothing as the anxiety and heart racing is calmed. Have it prescribed through a medical doctor with the notion that is for the short term. (Note: Neither the botanicals or the prescription drugs are immediate in action; they don't act on already stored thyroid hormone and will take 3 to 6 weeks to work.)

The other prescription drugs at the onset of treatment are beta blockers, whether propranolol (Inderal), atenolol (Tenormin), nadolol (Corgard), or metoprolol (Lopressor, Toprol XL). They do not inhibit thyroid hormone but rather block pathways affected, giving fairly rapid relief of fast and irregular heartbeat, tremors, anxiety, irritability, heat intolerance, and sweating. Unfortunately these may trigger an asthma attack in people susceptible and may also cause complications in diabetes. I appreciated these as I worked to increase my parasympathetic nerves with my longtime favorite, meditation.

On the other hand, I am vehemently opposed to the other two standards. Surgery means either a complete thyroidectomy or subtotal thyroidectomy; either procedure risks damaging vocal cords and parathyroid glands. Radioactive iodine therapy, measuring the uptake of radioactive iodine, will determine the rate the gland is taking up iodine. Destroying thyroid cells over time, the gland shrinks and hyperthyroid symptoms gradually decrease to the point of lifelong mandatory hormone replacement.

I believe that allopathic medicine's refusal to question underlying proclivities warrants naturopathic physicians' and educators' taking a much larger role in this at times life-threatening disease. We can do much to alleviate suffering from what is considered an incurable disease, and save people from the standard treatments that seem barbaric and out of touch.

For no matter what our specialty (ies), we each have a lot to offer to sufferers of Graves' disease, a disorder that lends itself to a holistic approach. It underscores both the mind-body connection and the need for more research to understand the possible causes, including grief and environmental toxicity. It also delineates the need to augment our education regarding tools to uncover an emotional root.

I believe that once the underlying forces are evident, psychologically and physically, Graves' disease is no longer scary. A holistic treatment plan can utilize the full spectrum of the modality arc, from meditation to antithyroid medication, making this "incurable" disease on its way to being understood and healed.

Are we up for the challenge?

To Learn More

To explore more about autoimmune hyperthyroidism, please check out my radio play, *Dr Graves, We Healed Your Disease*, on YouTube or my website, www.drheatherherington.com.

I would be happy to lecture on various ways to track the psychological, straightforward techniques to help bring to light the emotional core of Graves' disease.

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As a 1987 Bastyr graduate, board certified in classical homeopathy, Heather specializes in PTSD and autoimmune disease. You can access her radio plays, *Dr Graves, We Healed Your Disease* and *A Conversation with an Ovary or Two* (about PCOS), at www.drheatherherington.com. An excerpt of her latest novel – highlighting yellow fever in New Orleans in the 1800s – will appear in the March issue of Hpathy.com. She is currently writing a booklet, *Preparing for Influenza, the Coming Supervirus*. For speaking engagements, please call Mary at 818-646-3403.

Solar Cycles and Moon Medicine

by Laura Repola, ND

Nature is set to a metronome created by planetary movement. Rhythms and cycles of human physiology are created by forces from the universe, specifically from the interaction of the earth, sun, and moon.

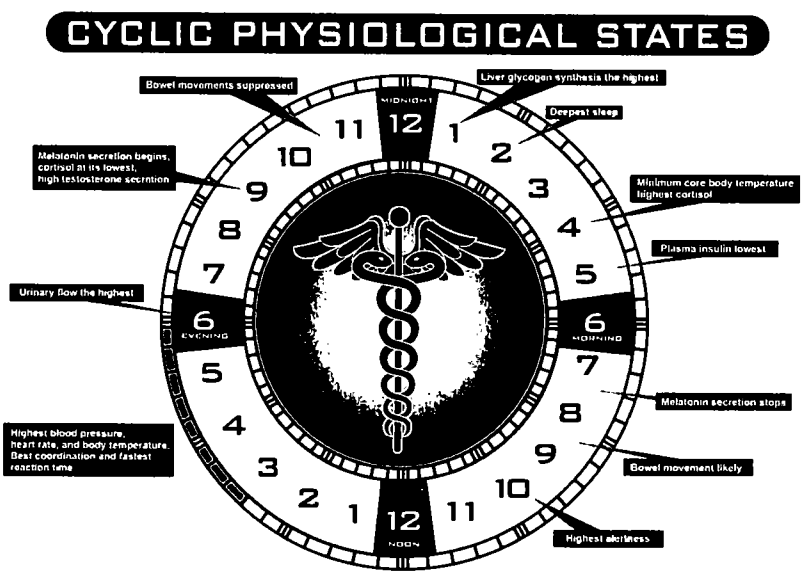
The sun and the moon have always dominated human culture through the creation of the sleep/wake cycle, the tides, the seasons, and moon phases. These forces set off immeasurable chain reactions that influence the migration of animals, the harvest of food, societal rituals, reproductive cycles, and the construction of the calendar. The solar system creates the biorhythm of the earth.

Human understanding of the solar system began with great reverence. The sun and the moon were worshipped in most primitive societies. Myths from the great Mayans and ancient Egyptians are built around the gods of the moon and sun. The celestial bodies have long been honored for the power of giving life and providing wisdom.

The age of modern science, technology, and the advancement of astronomy have contributed a large amount of data to support these primitive perspectives. The use of isolation facilities to investigate circadian clocks, the study of biological entrainment, and a multitude of scientific discoveries in the fields of chronobiology and genetics have increased the understanding of these influences. Even though society is removed from the raw influences of the sun and moon, the importance of their impact on human culture and human physiology has not lessened.

Cycles in Nature: The Solar Day, the Lunar Cycle, and the Tidal Force

The movement of the solar system generates cycles. These cycles include but are not limited to the solar day, the lunar cycle, and the tidal cycle. The solar day is the light and the dark cycle of the sun setting and rising. It is approximately 24 hours plus or minus 30 seconds. The lunar cycle is based on the length of time that it takes the moon to orbit the earth, 29.53 days. The reflection of the sun on the surface of the moon at different angles creates the moon phases. Another outcome of planetary movement is the tidal cycle. The tidal cycle is a result of gravitational force, not light exposure. It lasts 12.8 hours. The impact of these cycles on humans is incompletely understood, though newer research continues to substantiate ancient beliefs that celestial bodies hold power.



Circadian Rhythm and the Solar Day

Circadian rhythm. *Circadian rhythm* refers to the intrinsic molecular clock that maintains homeostasis between organisms and the environment. It is synchronized with the solar day through a process called entrainment. The circadian rhythm influences many biological processes and has been observed in plants, animals, fungi, and even prokaryotic cyanobacteria. To be considered circadian, a biological process must have an endogenous free running period of approximately 24 hours. This means the process has to persist in constant conditions, such as constant darkness.

The rhythm is entrained by external cues known as *zeitgebers*. *Zeitgeber* is German for "time giver," and examples include light, temperature, noise, exercise, and feeding regimens.

These environmental cues help regulate the circadian rhythm and translate to numerous physiological changes within a 24-hour period. Humans can be entrained to a 23.5-hour cycle up to a 24.65-hour cycle.[1] Zeitgebers enhance the regularity of the endogenously created circadian rhythm. Many organ systems are synchronized to the circadian clock, and perhaps every system in the body is attuned to it in some way.

The mammalian circadian clock. The circadian rhythm is generated in the suprachiasmatic nuclei (SCN) located in the hypothalamus in mammals. Each neuron of the SCN contains the molecular components to generate rhythmicity in the absence of external cues. These include the clock (Circadian Locomotor Output Cycles Kaput) genes that affect both the persistence and period of circadian rhythms. The core clock genes are CLOCK and BMAL1.[2]

The SCN, known as the master biological clock, also receives light/dark signals from photosensitive ganglion cells of the retina. These cells are different than rods and cones.[3] The SCN translates the retinal signal and passes it on to the pineal gland. The pineal gland secretes or suppresses the release of melatonin accordingly. Melatonin is the major communicating hormone of the circadian rhythm. Melatonin receptors are present all over the body. This is how the dark/light cycle and the lunar phases become signals that entrain the body's endogenous circadian rhythm.

Markers for measuring the timing of a mammal's rhythm are melatonin levels, body temperature, and cortisol. Different physiological states exist at different times of day.

Understanding Oscillators

The central oscillator is located in the suprachiasmatic nuclei (SCN), and peripheral oscillators exist in most if not every cell. Oscillators communicate to synchronize signals between the SCN and the periphery, which gives rhythm to biological functions.

The concept of oscillation is not commonly explored. In mathematics, oscillation is the quantification of the amount that a sequence or a function tends to move between extremes. More simply, oscillation is like a swinging pendulum. At the molecular level in humans, the term refers to a complex mechanism that drives the expression of clock genes and their proteins. Cyclic melatonin levels and other neural and humoral outputs from the SCN coordinate peripheral oscillator function to synchronize with the circadian rhythm.

Moon Phases and the Lunar Cycle

The lunar cycle is known by the brightness of light reflected from the moon's surface as it orbits the earth. This orbit takes 29.5 days in length. The exposure to cyclical changes in the amount of moon light affects hormone levels mostly due to pathways downstream from melatonin. The light of a full moon is 250 times greater than a new moon night.[5] Melatonin levels are lower within 4 days of the full moon compared with other lunar phases.[6] Perhaps with the expansion of this knowledge, a type of "moon medicine" will be more widely incorporated into clinical practice.

Gravitational Force and the Tidal Cycle

The alignment and distance between the earth, moon, and sun create a gravitational force and a centrifugal force. These forces generate the tides. A tidal cycle is 12.8 hours. The effect of this rhythmic change in the gravitational force does not produce measurable tides in smaller bodies of water, and therefore has previously been perceived as a weak force. It is undetermined to what extent the tidal cycle affects the human biorhythm and to what extent humans can alter the impact of the tidal cycle.

It is well evidenced that gravity can influence the direction of growth of plants, fungi, and animals, a feature known as gravitropism. Crustaceans exhibit endogenous circatidal and circadian rhythmicity.[7] New studies are investigating the impact of the lunisolar tidal force upon living and growing systems.[8] Does the tidal force change the flow of the cerebrospinal fluid or change cellular shape in the same way it impacts other fluid and solid matter? Without further scientific advancements, the discussion of the tidal cycle and its clinical applications is limited. The tidal variations do generate food cycles for oceanic species and influence the life cycle and culture of animals and people inhabiting the coastal zones. This is another example of how a moon, a planet, and a giant star work together to give rhythm to life.

Physiological Outcomes of Planetary Influences

Steady circadian rhythm and circalunar periodicity are essential for optimal health. The following are only two examples of how human physiology is intricately linked to the steadfast solar system.

1. **Fertility and the moon.** The relationship between moon phases and menses reveals patterns. The menstrual cycles of the most fertile women last 29.5 days, which is exactly equal to the length of the lunar cycle. Researchers have learned that most women with regular 29.5-day cycles have a menses within 7.5 days of the full moon.[9] Melatonin also inhibits the release of luteinizing hormone, changes testosterone levels, and is elevated in PCOS.[10,11] The exposure to bright light decreases the concentration of melatonin in circulation, and this is hypothesized to be useful in infertility treatments. These findings are supportive of the rudimentary perspectives that the moon is associated with fertility. Yet, a recent study reported that there is no synchronicity between the lunar cycle and the menstrual cycle.[12]
2. **Immune system and melatonin.** Melatonin is well known as a key player in immunity due to its properties as a potent antioxidant that can penetrate mitochondria. The interruption of the dark period with light or pulses of light rapidly reduces the output of melatonin from the pineal gland. The International Agency for Research on Cancer has classified light as a carcinogen in humans.[13] This may be due to reduction of the total output of melatonin and/or other consequences of chronodisruption. In an experiment with laboratory mice, oral melatonin supplementation increased the life span from 755 days to 931 days for mice on identical regimens.[14]

   Malignant tumors can modify the 24-hour oscillations of the clock genes, as was documented in liver and kidney tissue.[15] This may contribute to fatigue and sleep disorders observed in cancer patients. High-dose melatonin is widely used in naturopathic oncology care for its oncostatic properties.[16] Melatonin is part of a healthy immune system.

Clinical Applications

Disruptions of the biorhythm lead to a multitude of negative health outcomes. In my opinion, the greater the deviation from the rhythm, the greater the negative consequences. Modern lifestyles and the 24/7 model do not align humans with natural influences. Light and pulses of light during darkness can send misinformation to the SCN, contributing to chronodisruption. As scientists are concluding that planetary movement has significant impacts on physiology and behavior, holistic clinicians should be more judicious in addressing a patient's health in this capacity. ➤

Moon Medicine

➤

1. **Facilitate entrainment.** Greater consideration should be taken when choosing the timing and type of artificial lighting. The exposure to artificial lighting early in the morning or late into the evening disturbs the regular alternating periods of light and dark. The outcome is a shorter duration of melatonin secretion and less melatonin secretion overall.

   Different wavelengths and color temperatures have different effects on melatonin. Sunlight, containing mostly visible light and almost all wavelengths of the electromagnetic spectrum, shuts down melatonin. Daytime exposure to sunlight in homes and workspaces is ideal. Blue light from LCD screens and energy efficient bulbs has a strong suppressive effect on melatonin. Incandescent bulbs produce blue light, but less than most fluorescent and energy-saver types. Campfire and candles consist of red, orange, and yellow wavelengths, which means that they inhibit melatonin less than other choices of artificial light. In addition to light, a physician should utilize as many other synchronizers (zeitgebers) as possible to support the circadian rhythm.

Color Wavelengths (nm)

Red	780–622
Orange	622–597
Yellow	597–577
Green	577–492
Blue	492–455
Violet	455–390

2. **Avoid disrupting the synchronization of nature's cycles.** Habitual sleep loss and light pollution will send misinformation to the SCN and change the output of melatonin. Shift work, chronic jet lag, and nighttime activities that introduce artificial light should be avoided. The use of optical filters as bulb coverings or in glasses can filter blue light.

   A multitude of drugs can change the circadian and circalunar rhythms through various mechanisms. The substances that change melatonin levels impact the suprachiasmatic nucleus, and ultimately deregulate peripheral oscillators as well.

Case 1

Anita is a 35-year-old female with fertility concerns.

S: Anita is concerned that she cannot get pregnant because she has a history of irregular menses and has taken various types of hormonal birth control for the last 10 years. She stopped taking OCPs 3 months ago, and she has had one light menses since then. She is actively trying to conceive. She describes herself as light sleeper, and she wakes feeling tired.

O: Salivary hormone panel with progesterone, testosterone, estrogens, DHEA, cortisol ×4, and melatonin ×4.

A: Irregular menses.

P: Recommended Anita obtain a moon phase calendar for the next 3 to 6 months, which will help her to chart the following instructions.

Week 1: For the 3 days before and 3 days after the new moon: sleep in complete darkness and take 5 mg of melatonin nightly.

Week 2: Take 1 mg of melatonin for the following week (the moon is in its waxing phase).

Week 3: For 3 days before and three days after the full moon: Sleep with a light on, like a hallway light with room door open. Do not take melatonin.

Week 4: Take 1 mg of melatonin for the following week (the moon is waning).

Repeat this cycle for 3–6 months.

In addition, every morning sit within 2 feet of a light box for a minimum of 30 minutes. This can be accomplished during daily morning activities. She was instructed to open the curtains and brighten the indoor environment with natural and artificial lights during the day. She will spend as many hours in direct sunlight as possible to inhibit daytime melatonin secretion.

Case 2

Jim is a 45-year-old male with the chief complaints of difficulty falling asleep and fatigue.

S: Jim reports that he cannot fall asleep until after 2 a.m. most nights of the week, which leaves him drowsy most days. He gets irritable in the afternoons and feels depressed lately, which he considers normal for him during the winter months. He has recently quit drinking alcohol after 5 years of regular intake of 6+ drinks per day. He goes to a recovery counselor and attends regular AA meetings. He is otherwise healthy.

O: No acute distress, alert and oriented to person, place, and time. Normal physical exam.

A: Sleep disturbance, fatigue.

P: Educated Jim on sleep hygiene. This includes establishing routine sleeping habits, using only dim incandescent bulbs or candlelight for evening lighting, and turning off LCD screens and fluorescent bulbs 1 hour before desired bedtime. Remove all light sources from the bedroom, including alarm clocks, cell phones, and street lights. Consider using a sleep mask.

Supplementation: Melatonin dosing: 1 mg 30 mins nightly before bedtime and another 3 mg dose at bedtime.

Follow-up: Consider light box therapy, hormone panel with cortisol and melatonin.

Decreases Melatonin	Increases Melatonin
Calcium channel blockers, beta blockers, adrenergics, NSAIDs, SSRIs, benzodiazepines, alcohol, tobacco, caffeine, and high doses of B12 (3 mg/day)[17]	Most MAO inhibitors, *Hypericum perforatum*, *Cannabis sativa*[18]

Substance abuse can lead to long-lasting disruption of the circadian rhythm.[19] Treatment plans for these patients should stabilize sleep and the circadian rhythm for potentially better outcomes in relapse rates.

Conclusion

Primitive humans experienced the solar day and slept under the phasic light of the moon. They lived by the guidance of celestial bodies, both physically and culturally. Though disruptions in these cycles are abundant, the human species adapts. In my opinion, it is the role of the physician to encourage patients to align themselves with the dominant forces of nature. Our ancestors naturally praised these forces, and scientific evidence continues to prove that harmonizing with the solar day and lunar cycle benefits human health.

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Evidence-Based Medicine

by Katie Carter, ND

Evidence-based medicine (EBM) is an evolving philosophy that focuses on the changing bank of knowledge on which ideal medical clinical practice is based. It is the integration of research evidence, clinical experience, and patient values. The concept that there is a gold standard of medicine remains constant, while the data and knowledge base continues to shift.

EBM has its philosophical origins from mid-19th century Paris and earlier. Ancient medicine consisted of written historical or anecdotal accounts. During the 17th century, personal journals were kept and textbooks began to be more prominent. In the 1900s, knowledge could be shared easily in textbooks, and peer-reviewed journals became the basis for clinical practice. The term "evidence-based medicine" was first used in the 1990s, when investigators from McMaster's University defined it as "a systematic approach to analyze published research as the basis of clinical decision making."[1] This definition was replaced in 1996 when Sackett stated, "Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients."[2] This shift reflects the importance of integrating individual clinical expertise with the best available external clinical evidence from systematic research. By contrast, Trisha Greenhalgh and Anna Donald define EBM to be "the use of mathematical estimates of the risk of benefit and harm, derived from high-quality research on population samples, to inform clinical decision-making in the diagnosis, investigation or management of individual patients."[3] Here EBM is reflected in a narrower scope. This is the scope that promulgates quantitative and qualitative research and epidemiology separate from clinical expertise. The concept of evidence-based medicine is widened in the *EBM Notebook* designed by the *British Medical Journal*.[5] The authors describe that the goal of EBM is clinical expertise, which encompasses three distinct factors:

1. Research evidence
2. A patient's individual clinical state and circumstance
3 A patient's preferences and actions

The overlay of each of these concepts is presented to display that optimal clinical expertise must encompass and balance each of these factors if a successful and satisfying result is to occur. "Personalizing the evidence to fit a specific patient's circumstances is a key area for development in evidence-based medicine."[5]

In this light, one can see that the emphasis of Greenhalgh and Donald and others who are experts at analyzing data and providing a system for objective literature review is on one-third of the skills that provide a physician with clinical expertise. Of course, this particular model of EBM from the *British Medical Journal* does not include other limitations to clinical expertise such as health-care organizations and limited resources.

Separate from these external limitations, this model is presented as current in the evolution of evidence-based care. In light of this information, it is prudent to discuss each factor individually.

Research Evidence

Research evidence has three individual components:

1. A systematic review of primary studies that use explicit and reproducible methods:

   Medline database, checking the Cochrane controlled clinical trials register, reviewing other medical databases, reviewing foreign-language literature, being familiar with "grey literature" (non-peer-reviewed journals, theses, internal reports and so on), checking the references in the primary sources, reading the unpublished sources of known experts in the field, and, finally, reviewing the raw data from published trials.

2. A meta-analysis of the results of two or more studies that address the same hypotheses in the same way:

   The practitioner tabulates the relevant information including criteria, sample size, baseline patient characteristics, withdrawal rate, and results of both the primary and secondary end points of the studies available. In modern times, software has been created for this purpose (MetaView). Meta-analysis will reveal if there is heterogeneity or homogeneity reflecting whether the results of each individual trial are mathematically compatible with the results of any of the others.

3. The use of valid and reliable methods: This involves a review of materials, methods, and the accuracy of reporting of the research results.

A Patient's Individual Clinical State and Circumstance

As stated above, clinical expertise encompasses three factors. A discussion of the second component of clinical expertise outline by the *BMJ* focuses on the individual clinical state and circumstance of a patient. As medicine evolves, our assessments will shift regarding "clinical state."

Due to new knowledge, physicians may change their perception of an individual's clinical state. For example, the newly discovered illness anti-NMDA receptor encephalitis indicates that some patients previously considered psychotic were simply suffering from an autoimmune illness. In the past, these patients would end up in a psych ward and perhaps medicated permanently, to the point of catatonia (the disease also produces these results). As physicians, our perception shifts as we ascertain the true etiology of an illness. Slowly,

we are discovering more specific and underlying causes for many sorts of illnesses, and as these discoveries are made, we will find them shifting our clinical decisions.

Technology has affected science and medicine, opening up new possibilities in both the treatment and prevention of human sickness. J. D. Rucker describes one of the seven most important recent discoveries that could revolutionize medicine: mapping the human genome.[7] The ability to understand our patients' illnesses is advancing. The harnessing of information technology has brought such a sheer wealth of data, allowing us to solve complex medical problems like never before.

A Patient's Preferences and Actions

This is weighed as an important component to the clinical expertise subset of optimal evidence-based medicine. "Patients may have either no views or unshakable views on their treatment options, depending on their condition, personal values and experiences, degree of aversion to risk, healthcare insurance and resources, family, willingness to take medicines ... and so on."[5] In my own clinical practice, after reviewing the anecdotal clinical success with fecal implants, 2 years ago, I offered this treatment to a 20-year-old man who had been suffering with ulcerative colitis for 8 years. He found the suggestion disgusting and refused more information. According to Haynes et al., "The nature and scope of clinical expertise must expand to balance and integrate these factors, dealing with not only the traditional focus of assessing the patient's state but also the pertinent research evidence and the patient's preferences and actions before recommending a course of action."[5]

After Defining EBM, It Is Important to Discuss What It Isn't

It is not the imprudent use of the term *evidence-based medicine* to promote financial gain or detract from a patient-centered practice. According to a qualitative study published in *Family Practice Journal*, it is "inappropriate for GPs to see drug company representatives, tend to end their medical consultations with prescriptions and 'try out' new drugs on an 'ad hoc basis' and use this as evidence of the drug's effects. This publication stresses a need for a clearer understanding of GPs' perception of clinical autonomy, and necessitates an educational intervention called 'reflective practice', the goal is "to integrate other interventions and to change professional behavior."[6]

EBM is not the use of data in replacement of the doctor–patient relationship. Mayer et al. discuss a focus group study of Australian GPs. They state that "the evidence-based approach was regarded as particularly useful when patients required validation of their management or had specific queries."[8] However, the GPs also expressed some concerns, such as possibility of error when applying evidence from clinical trial to individuals, and the appropriateness of using research evidence with certain patients. They also feared a move away from the "Art of Medicine."

According to Sackett et al., "Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannized by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current best evidence, practice risks becoming rapidly out of date, to the detriment of patients."[2]

Evidence-Based Medicine Contributes to the Evolution of Medicine

Creating new definitions, categorizing, and the new naming of illnesses result from our ability to solve complex medical problems. This constant growing of knowledge is part of the evolution of medicine. Like anti-NMDA receptor encephalitis, chronic inflammatory response syndrome (CIRS) is defined as a new chronic illness involving multiple body systems following inhalation exposure to the indoor environments of water-damaged buildings. The World Health Organization and the US Government Accountability Office both report that there are toxins and inflammagens in the indoor air of a water damaged building (WDB).[9,10] These compounds have been identified within the complex mixture found in the air and in the dust of the interior environments of WDB. According to the WHO report: "Dampness-associated asthma, allergic sensitization and associated respiratory symptoms may result from repeated activation of the immune defenses, exaggerated immune responses, prolonged production of inflammatory mediators and tissue damage, leading to chronic inflammation and inflammation-related diseases, such as asthma."[9] This report also stresses that "in vitro and in vivo studies have demonstrated diverse inflammatory, cytotoxic and immunosuppressive responses after exposure to the spores, metabolites and components of microbial species found in damp buildings." The *Research Committee Report on Diagnosis and Treatment of Chronic Inflammatory Response Syndrome (CIRS) Caused by Exposure to the Interior Environment of Water-Damaged Buildings* reveals that "taken as a whole, CIRS-WDB is a chronic inflammatory response syndrome, resulting from exposure to WDB and is readily identified by current methods of clinical diagnoses, with thorough differential diagnosis the key to linking the abnormal physiology seen to the cause of the illness."[11] Within the model outlined by *Evidence Based Medicine*, a physician must assess a patient's individual clinical state and circumstance, a patients' preferences and actions, and research evidence.[5] A systematic treatment protocol based on these tenets is available for the diagnosis and treatment of CIRS.

Anti-NMDA receptor encephalitis and CIRS are examples of our advancement in medicine to achieve a cure. In the past, for these illnesses, we only hoped to subdue a set of symptoms. Also, the evolution of medicine allows us to discover new treatments for already known diseases. For example, the new treatment of *C. difficile* using fecal implants is an example of an innovative treatment for common illnesses. Dr. Robert Orenstein from the Mayo clinic states that fecal implants in *C. difficile* cases have been well established, but admits "much of the rest is mainly anecdotal."[12] Even without large-scale rigorous investigations of fecal transplants, the medical community appears to be coming around to the practice. In 2010, in a *Journal of Clinical Gastroenterology* editorial, it was stated that "it is clear ➤

from all of these reports that fecal bacteriotherapy using donor stool has arrived as a successful therapy."[15] In the US, there is a research logjam. The FDA is recalcitrant to ruling on investigational applications due to extreme variability in sources of donors.[14] Perhaps in light of the importance of clinical outcome, physicians' best approach in making their decisions in treating *C. difficile* patients is with limited research evidence. At present, the 27 published cases are small case series or individual case reports. Orenstein can be quoted, "There is some baseline evidence that it might be effective for IBS, but that hasn't been looked at in a controlled manner."[12] L. J. Brandt, MD, in an article in the peer-reviewed journal *Gastroenterology and Hepatology*, wrote, "I know of case series, case reports, and several unreported cases in which fecal therapy has been used to treat nongastrointestinal diseases, including insulin resistance, metabolic syndrome, morbid obesity, Parkinson disease, amyotrophic lateral sclerosis, and autism."[16] Here we have an example wherein the clinical expertise has focused on the clinical state and circumstance. Because of superior treatment outcomes, these physicians are disregarding lack of controlled research trials, and plowing ahead, treating patients and planning for clinical research trials in the future.

Traditionally, clinicians have been credited with clinical acuity reflecting their skills in making a diagnosis and prescribing or administering a treatment. The arrival of major investments in biomedical research led to new testing and treatments. This era has spurred the development of critical appraisal of the medical literature and evidence-based medicine. The application of current best evidence from health-care research is now an expected adjunct to clinical acumen. Initially, EBM focused mainly on determining the best research evidence relevant to a clinical problem or decision and applying that evidence to resolve the issue. This early method moved away from traditional determinants of clinical decisions, minimizing physiological rationale and individual clinical experience. As EBM developed, the philosophy emphasized that research evidence alone is not an adequate guide to action. Clinicians must apply their expertise to assess the patient's problem and incorporate the research evidence, in addition to consideration of the patient's preferences and values, before making a management recommendation.

Sackett elucidates this point, "Sometimes the evidence we need will come from the basic sciences such as genetics or immunology. It is when asking questions about therapy that we should try to avoid the non-experimental approaches, since these routinely lead to false positive conclusions about efficacy. ... *However* [emphasis added], some questions about therapy do not require randomized trials or cannot wait for the trials to be conducted. And if no randomized trial has been carried out for our patient's predicament, we must follow the trail to the next best external evidence and work from there."[2]

The utilization of science and technology grants us the understanding of the roots of diseases so we can more effectively treat their etiology. Systematic research and the application of this new knowledge contribute to clinical expertise. The unified definition of clinical expertise reflects effective and efficient diagnosis, external clinical evidence and the application of new knowledge, and thoughtful identification and compassionate use of individual patients' predicaments, rights, and preferences. When practitioners follow these guidelines, they are successful in their endeavor in practicing the expanding definition of evidence-based medicine. With this current focus of EBM, we are witnessing the evolution of medicine take place.

Katie Carter, ND, a 1986 graduate of National College of Natural Medicine, has a successful naturopathic practice in rural Polson, Montana, with a satellite in Kalispell. A role model for NCNM and Bastyr preceptoring students, she enjoys sharing her knowledge on practice-building, homeopathy, herbal medicine, nature cure, strain/counterstrain, neurotherapy, prolotherapy, ozone therapies, and biotoxins. Throughout western Montana, she is known for her expertise in autoimmune and endocrine disorders. She enjoys positive, cooperative working relationships with local physicians, specialists, pharmacists, and dentists. Dr. Carter has lectured annually at the Women for Wellness Health Fair, Salish Kootenai College, where her lectures are always filled to capacity. She has lectured for the Lupus Foundation of America, annually at the "Celebrating Women" HCP production, and in St. Anthony, St. Cloud, and Minneapolis, as well as Antigo, Wisconsin, and Marquette, Michigan. In Polson, she served on the Healthy School Task Force and taught weekly nutrition classes. Her organic orchard, skiing, mountain biking, hiking, tennis, beautiful family, friends, and patients keep her contentedly busy.

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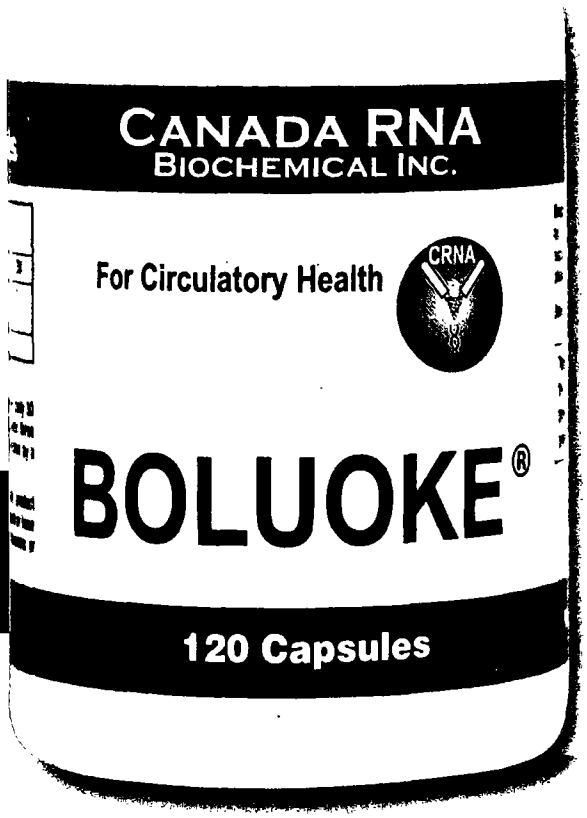

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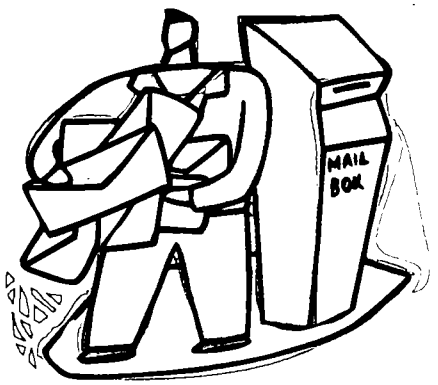

Letters to the Editor

All Hormone Testing Methodologies Have Strengths and Weaknesses

I read with interest Dr. David Zava's article titled "Steroid Hormone Testing in Different Body Fluids," in the January 2015 issue of this publication. I've admired Dr. Zava's work in the past, in particular "Assessment of Japanese Iodine Intake Based on Seaweed Consumption in Japan: a Literature-Based Analysis" (*Thyroid Research*. 2011;4:14), but in this recent *Townsend Letter* article there are some inaccuracies, obvious to any experienced practitioner using and monitoring bioidentical replacement hormone therapy (BHRT).

Dr. Zava correctly makes the point that all bodily fluids (including serum, saliva, urine, and dried blood spot) can be used to accurately measure endogenous steroid hormones. Dr. Zava also rightly describes the liquid and gas chromatography with tandem mass spectrometry (LC-MS/MS and GC-MS/MS) technologies as providing the most "accurate and precise assessment of the steroids present in the diagnostic medium." While it's true that the LC-MS/MS and GC- MS/MS methods require a commitment to advanced and complex infrastructure, it's plainly inaccurate to allege that these methods are cost prohibitive and outside the reach of clinicians and patients. Literally hundreds of physicians from Meridian Valley Laboratory use these tests every month, as do clients of Rhein and Genova Laboratories. Since the early 1980s, Meridian Valley Lab has invested in the LC-MS/MS and GC-MS/MS technology, retaining highly skilled technicians and refining procedures to make such testing practical and affordable.

Dr. Zava's statements about the measurement of topically administered steroids also require some fact-based refutation. The assertion that the urine cannot be used to detect any topically prescribed steroid hormone does a disservice to the clinical experience of the *Townsend Letter*'s readership. Clinical observation – my own and that of Meridian Valley Lab's clientele – has verified the utility of a 24-hour urine assay for monitoring topical testosterone, estradiol, estriol, and DHEA applications. 24-hour urine testing, when coupled with LC-MS/MS and GC-MS/MS methodologies, also affords the detection of many critical hormone metabolites not available in any other body fluid medium.

I doubt that a methodology as inaccurate and cost-prohibitive as Dr. Zava describes would last approximately three decades! Certainly there is competition among hormone testing laboratories, but that competition should be based on fact and not on unsupported allegation.

All testing methodologies – blood, saliva, and urine – have their strengths and weaknesses in measuring hormones. I agree with Dr. Zava that the appropriate selection of the best-suited method is an important aspect in monitoring a patient taking a steroid hormone prescription. However, it detrimental to patients to suggest that the 24-hr urine method should not be used to measure any topically administered hormones, as well as a disservice to patients and physicians new to BHRT to suggest that it is cost prohibitive.

Jonathan V. Wright, MD
Medical Director, Tahoma Clinic and
Meridian Valley Laboratory
Tukwila, Washington

Liposomal Vitamin C Worthy of Further Study

We at the Vitamin C Foundation would like to commend Steve Hickey, Hilary Roberts, and Damien Downing for their excellent article "Can Vitamin C Cure Ebola?" published in the November 2014 edition of the *Townsend Letter*. We did find ourselves questioning one apparent statement of fact in the section on liposomes: "Liposomal vitamin C is *not* more effective than IV for fighting acute infections. This suggestion is unscientific and unsupported by data."

We agree that there are no published clinical data. However, is not the scientific method to ignore anecdotes merely because they seemingly make no sense and we don't understand them.

Thomas Levy, MD, JD, and others have reported their clinical observation that true encapsulated liposomal vitamin C seems to have 10 times the clinical effectiveness of intravenous vitamin C (IV/C) directly into the vein in the treatment of acute viral infections.[1] Usually this is taken as 5 grams of liposomal vitamin C, which is clinically equivalent to a 50 gram intravenous infusion. As an experienced clinician, Levy was merely reporting an astonishing clinical observation that he literally did not believe at first because it was so counterintuitive.

The Vitamin C Foundation is receiving a stream of similar reports attesting to the astonishing effectiveness of liposomal vitamin C. A small amount of encapsulated vitamin C apparently can have a large impact on infection. We believe that the effect is profound and worthy of further study, not ridicule. Liposomes are known to be able to deliver their contents directly into the cytoplasm, and perhaps this is at least part of the reason for these anecdotal reports.[2]

Owen Fonorow
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Naperville, Illinois 60540
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Notes

1. Dr. Levy's statement regarding lypospheric vitamin C [online forum post]. dreddyclinic.com. http://dreddyclinic.com/forum/viewtopic.php?f=3&t=16203. May 16, 2009.
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Optimizing Metabolism

by Ingrid Kohlstadt MD, MPH
www.INGRIDients.com

Looking to Stay Healthy? 'Apply Here'

Introduction

As a medical doctor specializing in nutrition and optimizing metabolism, I was trained in using therapies that are ingested – medications and food. This training is given the name "internal medicine." Yet in my medical practice, consultations, and research, I dispense as many recommendations that could be called external medicine. Examples include *safe sun and sunlamp* exposure to promote vitamin D production, incorporating plant oils into skin care, and using air filters and propolis diffusers to reduce indoor allergens. In this *Townsend Letter* column, those looking to stay healthy may "apply here."

From Submarines to Kitchen Cabinets

How to clean the air handling system of a submarine – now there's a tough one. But it's the type of question that led parent company Indoor Air Professionals to innovate a tea tree oil spray and gel now sold to consumers under the brand Kanberra.

Tea tree oil has a distinctive aroma, so it is sometimes considered an air freshener to mask cooking odors, pet odors, cigarette smoke, and dankness. It's more. Along with neem, thyme, and rosemary oils, tea tree is organic pest control for plants. Tea tree oil applied to kitchen cabinets stops the growth of mildew.

Natural oils offer triple action – furniture oil, mold and mildew control, and organic pest control. Apply pine or juniper oils to unfinished wood cabinetry. For cedar closets, hand-rub the dried wood with cedar oil.

When to Bag It and When to Bag It, So to Speak

When it comes to bagging groceries, eco-friendly living and public health are sometimes at cross purposes. Medical personnel call grocery bags by the ominous-sounding name *fomite*. That's a surface that can spread germs from person to person or to someone's food. Enterovirus D68, norovirus, and drug-resistant salmonella are three among many good reasons to clean reusable grocery bags between uses ... but how?

Most grocery bags are not easy to wash. They hold water, interfering with the wash cycle. The handles get hung up in the washer apparatus or knot the dryer load like a cat with a ball of knitting yarn. Some bags disintegrate. At one time, I decided to use all-cotton bags with short handles so that I could wash them. However I overlooked the dark blue handles on an otherwise white linen bag, and my favorite white pillowcase emerged from the washer looking like the Greek flag.

My more recent system for public health plus environment is reusing bags with surfaces that can be wiped between uses. I field-tested many products: Some stain, some stink, some harm the environment, some are alcohol-based, and some don't do the job. Now I wipe the grocery bags and the children's reusable vinyl lunch boxes with an all-purpose spray made by Sun & Earth. There are several other eco-friendly brands.

For most kitchen cleaning tasks, you don't need a brand. For example, for cleaning most kitchen surfaces, simply use a 50:50 mixture of vinegar and filtered water with a few drops of liquid soap. For washing most fruits and vegetables, I add baking soda and lemon juice to the water.

Shawl I Tell You More?

For a long time, *Townsend Letter* contributors have cautioned about electromagnetic fields (EMFs) as a health disruptor. Population data are supporting a connection with thyroid dysfunction, relating the rise in EMF exposure to the rise in use of levothyroxine, one of the nation's 10 most prescribed medications. A Swedish study published in *Pathophysiology* October 2014 showed a dose relationship between mobile/cordless phone use and glioma. Medscape, a leading Web resource for health professionals, featured the article, suggesting that as the data grow, the concern and hopefully preventive actions as well will be mainstreamed.

For most of us, a little bit of prevention at a desk or work station can reduce EMF exposure. Some patients have EMF-related symptoms. Don't let them shrug off tingling fingers following keyboard use as muscle aches or mild carpal tunnel syndrome, before considering EMF exposure. Such symptoms add urgency to prevention:

- If you use a notebook computer with its built-in keyboard, your fingers are but a few inches from the antenna. Distance yourself by using a detachable keyboard.
- Consider wearing an EMF-blocking shawl or neck gaiter during computer work. The EMF protective materials can be purchased online, as can the fabric itself, which can then be cut to size. Consider draping the material over the multiplug surge protector often placed very close to the computer user's feet.
- When choosing office furniture, select wood instead of metal. Wooden chairs and desks don't conduct EMFs the way that metal does.
- Avoid using metal hairclips or jewelry, which can act as an antenna and possibly worsening the effects of the EMFs.

Rethinking the Salt Mines?

Few job assignments today are literally in the salt mines. But most of us would benefit from ending our day at the salt mines. If your workday ambushes you with electrosmog or leads to muscle strain, consider giving your body what it needs in return – minerals. Epsom salt baths have been promoted for a century for their ability to replete the body's magnesium and sulfur. Salts from famous spas around the world contain trace minerals that often confer the distinct colors for which the salts are known. Pink Himalayan salts have become popular. I interest children in my retelling of the story "Stone Soup," reminding them that there really is a rock which we eat – salt! Salts combined with plant oils reinforce the skin's protective barriers.

Combine external medicine with that delicious form of adrenal support – dark chocolate with sea salt. Adding sea salt makes dark chocolate more flavorful with less sugar. The sea salt adds to the energy boost by supporting weary adrenal glands' production of mineralocorticoids.

Conclusion

"Apply here" to boost your metabolism from the outside in.

- Apply tea tree oil spray to prevent mycotoxins, especially under the kitchen sink.
- Cut your risk of foodborne infection by spraying reusable grocery bags.
- Wear a fashionable scarf as an EMF shield during computer use and take other preventive actions to reduce workplace EMFs.
- End your day in the salt mines, otherwise known as mineral baths and salted chocolate.

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Editor, *Advancing Medicine with Food and Nutrients* (CRC Press; 2013)

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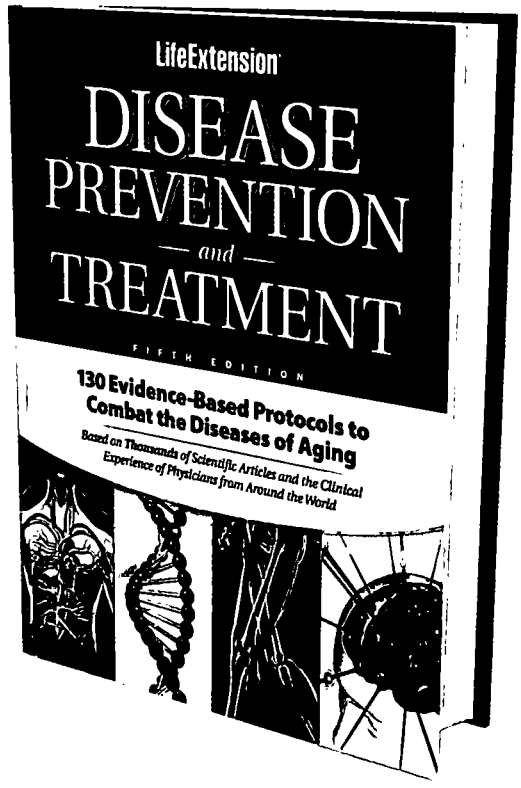

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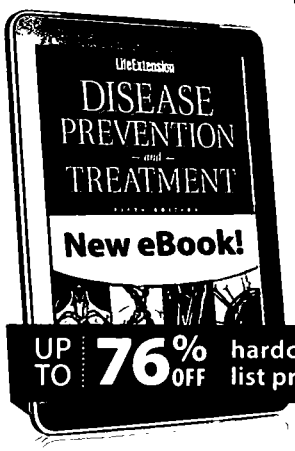

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Migraine Headache

The following article is an abridged version of the "Migraine Headache" chapter that appears in *Disease Prevention and Treatment*, 5th ed., an integrative-health textbook published by Life Extension.

Migraine headaches are recurrent, painful headaches often accompanied by nausea, light sensitivity, and/or sound sensitivity. A migraine is often one-sided and pulsating, and may occur with or without an aura (Cutrer 2012; Rakel 2011; Ferri 2012; NINDS 2012; Goldman 2011).

Avoidance of migraine triggers such as intense emotional stress, poor sleep habits, food allergies or intolerances, and unbalanced hormone levels may reduce the frequency and severity of attacks (Gaby 1998; Alpay 2010; Shugart 2012; Mayo Clinic 2011; Dzugan 2006). Several safe and effective natural treatment approaches are available to prevent migraines and reduce their frequency and intensity (Schiapparelli 2010).

What Is a Migraine Headache?

Migraine headache is often described as an intense throbbing or pounding head pain (Rizzoli 2012; NINDS 2012), is often made worse by physical activity (Walling 2012), and may interfere with a person's ability to function normally. Although migraine duration varies from patient to patient, a typical attack lasts for several hours but can last up to several days (Walling 2012).

Symptoms that precede a migraine headache by a few hours to a few days are called a *prodrome*. Prodrome can include appetite changes, loss of balance, mood changes, tiredness, neck stiffness, and changes in alertness (Rossi 2005).

Approximately 25% of migraine sufferers experience a premigraine phenomenon called *aura*, characterized by mostly visual, but also other sensory and/or movement symptoms (Cutrer 2012; Digre 2011c).

What Causes Migraine?

Migraine headaches are believed to result from complex dysfunction within the central nervous system (Charles 2009). Several factors may contribute:

Serotonin. The neurotransmitter serotonin is believed to play a role in migraine attacks, as migraine patients tend to have low levels of serotonin in their brains (Panconesi 2008). Also, tricyclic antidepressants, which increase serotonin signaling, reduce the frequency of migraine attacks (Cutrer 2012).

The role of hormones. Migraine disproportionately affects women – 70% of all migraine patients are female – suggesting a potential hormonal link (Dhillon 2011).

Although many hormonal events in a woman's life may influence the occurrence of migraine (Sacco 2012), menstruation appears to be the most important: 70% of female patients who experience migraine report some type of menstrual link (Calhoun 2012). A phenomenon called "estrogen withdrawal," which occurs in the late luteal phase of the menstrual cycle and is characterized by an abrupt decline in estrogen levels, is likely an important migraine trigger in some women (MacGregor 2009; Lay 2009).

Among women with menstrual-related migraines, hormone therapy that minimizes monthly declines in estrogen concentration may be effective in preventing migraine attacks (Calhoun 2009). Studies suggest that non-oral routes of estrogen therapy, such as in a cream applied to the skin, are more likely to improve migraine than oral estrogens (MacGregor 2009).

The Neurohormonal and Metabolic Dysbalance Hypothesis of Migraine

Some researchers suspect that an important cause of migraine is an imbalance between *estrogen* and *progesterone* levels, rather than simply the absolute amount of these hormones. Indeed, in preliminary reports, therapies aimed at improving the ratio of estrogens to progesterone have successfully relieved severe menstrual migraine (Holdaway 1991).

One link between hormonal imbalance and migraine may be the opposing roles of *estrogen* and *progesterone* within the brain. While estrogen stimulates neural excitability, progesterone exhibits inhibitory actions in central neurons (Finocchi 2011). Tailored *hormonal replacement therapy* (HRT) aimed at minimizing estrogen/progesterone imbalance and stabilizing estrogen levels may be effective for preventing migraines among pre- *and* postmenopausal women (Nappi 2009; Shuster 2011; Schurks 2010; Calhoun 2012).

Other sex hormones such as *testosterone*, *dehydroepiandrosterone* (DHEA), and *pregnenolone* may also play a role in migraines (Dzugan 2006).

Although well-controlled clinical trials designed to test this hypothesis have not yet been performed, several case reports have demonstrated positive outcomes using this novel approach (Dzugan 2006).

Women with migraines who have not received relief from other treatments may want to consider comprehensive hormone testing and restoration of hormonal balance using bioidentical hormone replacement therapy.

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Migraine Headache

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Diagnosis

History and physical examination are used to diagnose migraine headaches (Cutrer 2012; Katsarava 2012).

Some less common but potentially serious disorders can cause migrainelike symptoms, including subarachnoid hemorrhage, intracranial mass lesions, and cerebral vasculitis. Migraine headache is often misdiagnosed as sinus headache or tension-type headache (NHF 2012; Merck Manual 2012; Kwiatkowski 2009; Bope 2011; Ferri 2012).

Tests such as computerized tomography (CT), magnetic resonance imaging (MRI), and a spinal tap (lumbar puncture) to test cerebrospinal fluid may be used to help rule out other possible causes of headache (Mayo Clinic 2012; Kwiatkowski 2009).

Conventional Treatment

Most migraine treatment plans involve both *acute* and *preventive* strategies (Braun 2010).

Acute Treatment

The goal of acute treatment is to relieve the intensity and/or duration of an imminent or ongoing migraine (Hershey 2011). First-tier options for acute migraine management may include nonsteroidal anti-inflammatory drugs (NSAIDs) and/or mild analgesics (e.g., acetaminophen or aspirin) (Hershey 2011; Bajwa 2012). Caffeine, due to its vasoconstrictive properties, is sometimes combined with aspirin and/or acetaminophen as well (Aukerman 2002). The triptan drugs (e.g., sumatriptan, rizatriptan, eletriptan, and almotriptan), which are used for more severe migraines, promote vasoconstriction and block pain pathways by activating certain serotonin receptors in cranial blood vessels (Bajwa 2012).

Although the triptans are arguably the most effective treatment for acute relief of a migraine headache, they have a number of side effects (Cady 2011). For example, triptans should be avoided in patients who are at risk for cardiovascular events and stroke (i.e., patients with heart disease). Furthermore, triptans require careful monitoring because they are known to interact with a large number of other commonly used medications (Bajwa 2012).

Other drugs that may be used to treat migraine include ergot alkaloids, which cause blood vessel constriction, opioids, and, less commonly, corticosteroids.

Medicating as early as possible during a migraine attack increases the chances of successfully aborting an attack or reducing its intensity (Aukerman 2002).

Preventive Treatment

The main goals of preventive therapy are to reduce migraine frequency, severity, and duration, as well as to improve response to acute treatment(s). Preventive treatment options include headache trigger avoidance, daily medication, physical therapy, and/or behavioral therapy (Braun 2010).

Drugs used to prevent migraines include blood pressure medications (e.g., beta blockers, calcium channel blockers, ACE inhibitors, and angiotensin receptor blockers), tricyclic antidepressants (e.g., amitriptyline [Elavil]), and anticonvulsants (e.g., valproate [Depakote], gabapentin [Neurontin], and topiramate [Topamax]). These drugs should be started at low doses and given adequate time to reach peak effectiveness. Therefore, depending upon the chosen medication, a proper drug trial could take anywhere from 4 weeks to 3 months to produce the desired effect (Bajwa 2010).

Unfortunately, too much migraine prevention medication over too long a period can lead to "medication overuse headache," which can become a chronic, self-perpetuating condition called "chronic daily headache." This is characterized by daily headaches, and patients often inadvertently perpetuate it by continuing to medicate their headaches. To prevent medication overuse headache, migraine patients should (on average) limit use of NSAIDs to 15 or fewer days a month and limit triptan or over-the-counter combination analgesic use to 9 or fewer days a month (Garza 2012; Young 2001).

Lifestyle Considerations

Many migraine patients will not experience significant symptom relief from drug treatment alone, until healthful lifestyle modifications are made (Sun-Edelstein 2009a). The following lifestyle interventions may prevent migraines (Chaibi 2011b; Gallagher 2012; Linde 2009; Honaker 2008, Hauge 2011):

- avoidance of caffeine, nicotine, red wine, and other migraine triggers
- stress reduction
- improving sleep hygiene
- massage therapy
- chiropractic manipulation
- acupuncture
- sufficient exercise
- frequent stretching

Dietary Interventions

One out of every 4 migraine patients report that certain foods can trigger an attack (Mueller 2007). Furthermore, the avoidance of food allergies and/or sensitivities may reduce or eliminate migraine symptoms for some patients (Ross 2011; Gaby 1998).

Common migraine triggers in food include (Mueller 2007):

- *monosodium glutamate* (MSG), a commonly used flavor-enhancer found in some soups and Chinese food
- *nitrites,* preservatives found in processed meats such as hot dogs
- *tyramines,* natural compounds found in wines and aged foods (e.g., cheeses)
- *phenylethylamine,* a stimulant compound found in chocolate, garlic, nuts, raw onions, and seeds.

Other potential dietary triggers include cow's milk, wheat, eggs, alcohol, artificial sweeteners, citrus fruits, pickled products, and vinegar (Mueller 2007; Ross 2011).

Many experts recommend the use of simple and inexpensive food diaries to identify dietary migraine triggers (Sun-Edelstein 2009a). Trials have demonstrated that food allergy elimination based on testing for immunoglobulin G

(IgG) food antibodies successfully reduces migraine symptoms (Arroyave Hernandez 2007; Alpay 2010).

Additionally, not eating for over 4 hours has been linked to an increased risk of migraine attack (Gallagher 2012; Fukui 2008).

Integrative Interventions

Natural therapies (e.g., dietary supplements) are well tolerated, and many have been shown to reduce migraine symptoms (O'Brien 2010; Schiapparelli 2010).

Butterbur root: Butterbur (*Petasites hybridus*) extracts possess analgesic, anti-inflammatory, antispasmodic properties (Pothmann 2005; Oelkers-Ax 2008). Butterbur root extract (standardized to 15% petasins) has been shown to be both safe and effective for the prevention of migraines (Diener 2004; Lipton 2004; Pothmann 2005). In one study, researchers divided 245 patients into three groups that received 75 mg of butterbur extract twice a day, 50 mg of butterbur extract twice a day, or placebo. At the end of a 4-month treatment period, those taking the 75 mg dosage experienced a 48% reduction, on average, in the frequency of migraine attacks (Lipton 2004). The American Academy of Neurology (AAN) and the American Headache Society (AHS) have recommended butterbur extract as an effective treatment for migraine (Holland 2012).

Coenzyme Q10: Coenzyme Q10 (CoQ10) is a potent antioxidant (Ross 2007) and an important component of cellular energy production. Its anti-inflammatory effects and ability to improve mitochondrial function may account for its efficacy in prevention of migraines (Slater 2011). CoQ10 at a dose of 100 to 300 mg daily has been shown to prevent and reduce the frequency of migraine attacks among adults (Schiapparelli 2010; Slater 2011).

Riboflavin: Riboflavin (i.e., vitamin B2) contributes to cell growth, enzyme function, and energy production (AMR 2008). High-quality research indicates that riboflavin is effective for the prevention of migraine among both children and adults (Condo 2009; Boehnke 2004), and may decrease the need for conventional rescue medications (Boehnke 2004). It is believed that riboflavin's beneficial effects are due to its ability to enhance mitochondrial energy production (Brenner 2010). Riboflavin is especially effective among migraine patients with mitochondrial genetic abnormalities (DiLorenzo 2009).

One study involving 23 participants showed that supplementation with 400 mg riboflavin daily reduced headache frequency by an impressive 50% after 3 months, with that improvement persisting through 6 months (Boehnke 2004). Riboflavin is also cost effective and has minimal side effects (Condo 2009).

Feverfew: Feverfew (*Tanacetum parthenium)* is a small, daisylike flower (Goodyear-Smith 2010). Feverfew inhibits the production of several inflammatory mediators that may be involved in migraine, including arachidonic acid, cyclooxygenase-2, TNF-α, IL-1, and MCP-1. Though a promising natural treatment for migraines, trials of feverfew extract have had mixed results (Goodyear-Smith 2010; Saranitzky 2009; Chen 2007; Pittler 2004). A combination of ginger and feverfew, at a dosage of 100 to 300 mg up to 4 times per day, has been shown to be effective for migraine prevention with minimal side effects (Cady 2011; Ernst 2000; Pareek 2011).

Magnesium: Migraine patients commonly have low magnesium levels, especially during an attack (Qujeq 2012; Talebi 2011; Sun-Edelstein 2009b). A dosage of 600 mg of magnesium daily has been shown to be effective for the prevention of migraine attacks (Koseoglu 2008), and is inexpensive and well tolerated (Sun-Edelstein 2009b). In combination with CoQ10, vitamin B2, and ginkgo, magnesium has been shown to significantly decrease the number of migraine headaches (Esposito 2011). A form of magnesium called *magnesium-L-threonate* may be especially effective for migraine treatment, as experimental data indicate that it enters the central nervous system more efficiently than other forms of magnesium, though it has not yet been subjected to clinical trials (Slutsky 2010).

Melatonin: Melatonin, a natural compound produced by the pineal gland in the brain, helps regulate the sleep-wake cycle (Wilhelmsen 2011). Lower-than-normal levels of melatonin have been found in migraine patients (especially during an attack), which may play a role in migraine pathology (Masruha 2008; Masruha 2010).

Some migraine patients experience an improvement in symptoms with melatonin supplementation (Vogler 2006). In one clinical study, melatonin supplementation yielded a trend of two-thirds reduction in number of migraine attacks

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(Alstadhaug 2010). Melatonin has been found to be safe (Gagnier 2001).

S-adenosylmethionine (SAMe): SAMe is derived from the amino acid methionine and adenosine triphosphate, a nucleic acid (De Silva 2010). It is a naturally occurring substance that is important in the function of the central nervous system (Carpenter 2011). Some data suggest that long-term supplementation with SAMe may relieve pain among migraine sufferers, possibly due to its ability to increase serotonin (Gatto 1986; Fetrow 2001).

L-tryptophan: The amino acid L-tryptophan is a precursor to serotonin. An older clinical trial found that supplementation with 2 to 4 g of L-tryptophan daily was as effective at preventing migraine attacks as the ergot medication methysergide (Sicuteri 1973). A more recent trial found that dietary tryptophan depletion exacerbated migraine symptoms (Drummond 2006).

Additional Supplements: These natural substances may help manage migraine symptoms, though definitive clinical data are lacking:

- *Ginkgo biloba* (Schiapparelli 2010)
- alpha-lipoic acid (Sun-Edelstein 2009a)
- vitamin B6 (Ross 2011)
- ginger (Mustafa 1990)

Suggestions

- butterbur root, standardized extract: 150 mg daily
- riboflavin: 400 mg daily
- coenzyme Q10 (as ubiquinol): 100–300 mg daily
- feverfew (dried leaf): up to 1200 mg daily in divided doses
- ginger root, standardized extract: 250 mg daily
- magnesium: 140 mg daily as magnesium-L-threonate; 320 mg daily as magnesium citrate
- melatonin: 0.3–5 mg before bed (sometimes up to 10 mg)
- S-adenosylmethionine (SAMe): 200–1200 mg daily
- *Ginkgo biloba*, standardized extract: 120 mg daily
- R-lipoic acid: 300–600 mg daily
- vitamin B6 (as pyridoxal-5-phosphate): 100 mg daily
- L-tryptophan: 500–2000 mg daily

In addition, the following blood tests may provide helpful information:

- Food Safe Allergy Test
- Magnesium (RBC)
- Male Basic Hormone Panel
- Female Basic Hormone Panel
- Male Comprehensive Hormone Panel
- Female Comprehensive Hormone Panel

More information on the integrative interventions and lab tests mentioned in this article is available from Life Extension, an organization dedicated to scientific innovation. To receive a free copy of *Life Extension* magazine, visit www.lifeextension.com/Book6 or call (toll-free) 866-606-9803 and mention discount code DPT506A.

The unabridged version of this "Migraine Headache" article is available on our website www.townsendletter.com with the February/March 2015 digital articles.

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Migraine Headache

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Monthly Miracles

by Michael Gerber, MD, HMD
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Nevada Homeopathic and Integrative Medical Association Fall Conference 2014: Part 1

Roger Morrison, MD: Miasm

Dr. Roger Morrison hails from Wisconsin and graduated from the University of Tennessee School of Health Sciences Medical School. He spent two years studying at the Athenian School of Homeopathic Medicine in Greece under the tutelage of the famous homeopath George Vithoulkas. He has also studied in India with Rajan Sankaran. He is the cofounder of the Hahnemann College of Homeopathy in Richmond, California, and the author of numerous publications and books on homeopathy, including his desktop guide for homeopathic prescribing.

A cardinal principle of prescribing homeopathic remedies is to seek the simillimum, the remedy that mostly closely mirrors the patient's nature. Miasms, or inherited constitutional weaknesses, provide a means of grouping remedies to make prescribing more accurate and less time consuming. Morrison reviews the miasmatic groupings of several homeopaths, including Hahnemann, Boenninghausen, Kent, Knerr, Ortega, Vithoulkas, and Sankaran. There was almost no agreement as to which remedies apply to which miasm.

Vithoulkas defines miasms in three parts. Infectious – a miasm must be contagious. Heredity – a miasm or the susceptibility to a miasm must be transmissible from parent to child. Nosode – a nosode must be obtainable from the miasmatic disease.

Sankaran postulates that each remedy is assigned to a specific miasm and only one. Each miasm is given extremely clear and tight defining characteristics – both physical and mental – which are readily identifiable in the homeopathic interview. Each patient has only one miasm evident at any time.

Ortega gave the three miasms of Hahnemann specific characteristics. Psora: inhibition. Sycosis: excess. Syphilis: destruction. After studying with Sankaran, Morrison evolved the number of miasms to 10.

The New 10 Miasms

1. Acute (Hahnemann)
2. Typhoid (Sankaran)
3. Malarial (Sankaran)
4. Ringworm (Sankaran)
5. Psora (Hahnemann)
6. Sycotic (Hahnemann)
7. Cancer (Foubister)
8. Tubercular (Vithoulkas)
9. Leprosy (Vakil)
10. Syphilitic (Hahnemann)

Morrison offers brief descriptions of each:

Acute miasm manifests as life-and-death feelings, shock, terror, panic, and violence. Adrenaline, escape, and instinctive reactions. Changing and dependence, rapid heart rate, flushing. Childishness, magical thinking, and superstition.

Remedies: Aconite, Arnica, Belladonna, Cactina, Calendula, Camphora, Chocolate, Coffeinum, Croton Tiglium, Digitoxin, Elaterium, Ergotaminum, Hydrogen, Hypericum, Lithium, Melilotus, Morphinum, Oenanthus, Stramonium, Strychninum, Veratrum. Nosode is Lyssinum, Morbillinum, Diptherinum.

Typhoid miasm. Urgency and crisis, security and materialism, fear of poverty. Selfishness, hyperactivity, ruthlessness, ambition, aggression, contradiction, order and routine, do what it takes to get what you need, enough money makes you secure, they want to be at rest, go-go-go then collapse, intense febrile course, frustrated, excitatory, late-stage prostration, sepsis, diarrheal conditions, dentition, greedy appetite, craves beer and meat.

Remedies: Abelmoschus, Acetic Acid, Aethusa, Ailanthus, Anantherum, Argemon, Asclepias, Tuberosa, Baptisia, Benzoic Acid, Bryonia, Carbo Vegetabilis, Carnegia gigantean, Chamomilla, Doryphora, Euphrasia, Gallic Acid, Gambogia, Helleborus, Hyoscyamus, Ipecac, Lycopus, Mancinella, Nux Moschata, Nux Vomica, Paris, Petroleum, Polystyrene, Podophyllum, Pyrogenium, Rheum, Rhus Tox, Sacchrum Album, Sulphuricum Acidum, Thyroidinum, Veratrum Veride, Viscum.

Malarial miasm. Periodic attacks, IBS, stuck feeling/ frustration, never completely well. Migraines. Unfortunate,

miserable, abused, harassed, tormented, averse to touch, and are the biggest complainers. Whine, whine, whine. Periodic complaints: IBS. Painful complaints: gallbladder colic. Not life threatening, pinworms, neuralgia.

Remedies: Ammonium Muriaticum, Angustura, Antimonium Crudum, Aurum Muriaticum, Kalinatum, Berberis, Boletus, Cactus, Capsicum, Ceddron, Chelidonium China(and its salts), Cina, Clematis, Colchicum, Colocynthis, Eupatorium Perfoliaattum, Eupatorium Purpureum, Iris, Kalmia, Magnesia Muriatica, Menyanthes, Natrum Muriaticum, Peonia, Prunus, Ranunculus Bulbosus, Sarracenia, Spigelia, Sumbulus, Verbascum.

Ringworm miasm. Slowly progressive but not life threatening. Learn to live with it. Can't take it anymore, frustration, effort, and struggle. Oppression and weight gain. Acne, psoriasis, eczema, scleroderma, allergy, hay fever, sinusitis, prostate conditions, BPH, scalp and nail issues.

Remedies: Actea Spicata, Allium Sativa, Calcarea Fluorica, Calcarea Silicata, Calcarea Sulphurica, Dulcamara, Fagus, Gossypium, Magnesia Sulphuric Opunta vulgaris, Pseudotsuga, Rhus Venanata, Sarsaparilla, Taraxicum, Teucreum, Upas, Veronica officianalis, Viola Tricolorata. Nosode: Ringworm nosode.

Psora miasm. Confidence, effort required not without uncertainty. Success in the outer world, ego, ambition, dreams of failure, self-sufficiency, skin disorder, eruptions behind ears, ailments from suppressed eruptions, itching, redness, craves beer and eggs.

Sycotic miasm. Hidden and secretive, feels flawed and inadequate, shame and guilt, anticipation anxiety, avoidance, fixed, ridged, nothing can be done. Physically has pathological vegetations, warts, tumors, growths. Sinus conditions, green discharges, clearing the throat, allergies, asthma, food allergies, chronic structural pathologies such as osteoarthritis, bunions, etc. Craves oranges and ice, is better at sea.

Remedies: Argentum Metallicum, Borax, Bovista, Calcarea Bromata, Cannabis Indica, Caulophyllum, Crocus Sativa Digitalis, Gelsemium, Kali Bichromicum, Kali Bromatum, Kali Sulphuricum, Lac Caninum, Lac Delphinum, Natrum Sulphuricum, Palladium, Pulsatilla, Sabadilla, Sanguinaria, Silica , Thuja. Nosode: Medorrhinum.

Cancer miasm. Chaos and control, need to excel, desperation, overwhelmed, boundaries not good, sympathetic (Carcinosin is the most sympathetic remedy), very sensitive to injustice. They are prone to tumors, moles, malignancies, neurological disorders, diabetes, blue sclera, twitches, breast swelling and tenderness, and anorexia and crave hot spices, fruit, and fat.

Remedies: Agaricus, Anacardiium, Anhalonium, Argentum Nitricum, Arsenicum Album, Asarum, Baryta Arsenica, Bellis Perenis, Calcarea Arsenica, Calcarea Nitrica, Causticum, Conium, Ferrum Arsenicum, Ignatia, Kali Arsenicum, Kali Nitricum, Natrum Arsenicum, Nitricum Acidumk Opium, Physostigma, Ruta, Sabina, Staphysagria, Tabaacum Viola Odorata. Nosodes: Carcinocin, Scirrhinum. There are multiple carcinocins available depending on the organ of origin.

Tubercular miasm. "Wild man," rebellious, loves to try everything, knows better than his boss, behavioral issues, rebels without a cause. Frantic pace, romantic, independent, adventuresome, travel, freedom, fears suffocation, restless, destructive, addictive personality, rock climbing, gambling. Good for ADHD (also tarantula), lung disorders, emaciated, night sweats, wandering joint pain, worse in cold and damp, foggy weather, and pine forests.

Remedies: Abrotanum, Acalypha, Apis, Aranea, Arsenicum Iodatum, Atrax, Balsamum, Brucea, Bromium, Calcarea Iodata, Calcarea Phosphorica, Cereus Bonplandii, Cimicifuga, Cistus, Coccus Cacti, Coffea, Drosera, Elaterium Euonymus, Ferrum Iodatum, Ferrum Phosphoricum, Fluoric Acid, Ginseng, Iodum Kali Phosphoricum, Lactrodectus, Magnesia Phosphorica, Mygale, Myristica, Myrtus Communis, Natrum Phosphoricum, Oleander, Phelandrium, Phosphorus, Pix, Rumex, Salix Niger, Sambucus, Senega, Succinic Acid, Tarantula, Theridion, Ustilago, Verbascum, Vespa. Nosode: Bacillinum Tuberculinum, also TB avium and BCG.

Leprosy miasm. They have feelings of worthlessness, contaminated/dirty, disgusting, dreams of excrement, isolated, outcast, depression, self-mutilation, cursing, poverty, and childhood abuse. Physical signs of skin disorders, vitiligo, psoriasis, gangrene, melanoma, crusts all over body. Mentally abusive, morbid obesity, downturned mouth, cravings for bread and milk.

Remedies: Aloe, Ambra, Androctonus, Aristolochia, Aurum Sulphuricum, Azadirachta, Baryta Iodata, Baryta Sulphurica, Cereus Serpentinus, Cicuta, Coca, Coceinum, Comocladia, Curare, Cycloamen, Fumaria, Gratiola, Homarus, Hura, Hydrastus, Hydrocotyle, Indolum, Kola nut, Lac Defloratum, Laurocerasus, Ledum, Mandragora, Mephites, Ocimum sanctum, Rhus glabra, Secale, Sepia, Skatolum, Solanum Tuberosum Aegrotans, Spirea. Nosodes: Leprominium, Psorinum.

Syphlitic miasm. It is the most destructive of all the miasms. It gives emotional turmoil, train wreck, acute flares, extremes, rage, turning-point destructive, revenge, hopelessness, murder, suicide, all is black, terrorists, suicide vests, school shootings. They know that death is coming. State of acute crisis. Physically destructive, bone lesions and pain, vascular aneurysms, especially aorta, optic atrophy, progressive blindness, ALS night time aggravation, progressive degeneration (CNS, heart, bone), disorders of nasal septum, segmental complaints. Craves alcohol, sardines, and indigestible foods.

Remedies: Alumina, Anagallis, Aurum, Cenchris, Clematis, Crataegus, Echinacea, Elaps, Hepar Sulphur, Hydrocotyle, Lachesis, Lathyrus, Leptandra, Mercurius, Origanum, Osmium, Naja, Platinum, Plumbum, Plutonium, Psilocibe, Stillangea. Nosode: Syphilinum.

Miasms Are Deeper Remedies

Morrison reminds us that after an acute illness responds to homeopathy and then more chronic symptoms reappear, it is important to look for an underlying, miasmatic remedy. It seems as if he offers quite a few choices for the different miasms. I think it is most helpful to have a good homeopathic repertory to look at the various remedies and make the best selection for your patients. I also love my Biomeridian EAV computer to check on my homeopathic remedy selection accuracy and dosage.

◆

Rebalance Your Microbiome

review by Katherine Duff

The Microbiome Diet, by Raphael Kellman, MD
Da Capo Press; 44 Farnsworth Street, 3rd Floor, Boston, Massachusetts 02210
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The Microbiome Diet, by Raphael Kellman, MD, may be a new concept to some readers. *Microbiome* is a term used to define the pathogenic microorganisms that live in and on the human body, where they exist in symbiotic relationship with human cells. These pathogens, which are mostly bacteria, outnumber human cells by about 10 to 1. They are found in the mouth, vagina, skin, and, in the greatest amount, gastrointestinal tract. In an effort to better understand the role of these pathogens in human health, the National Institutes of Health launched a $150 million project called the Human Microbiome Project in 2007. Adhering to a policy of "rapid release," the research generated under the project is released quickly and prior to publication, resulting in a wealth of information about this emerging area of study. Kellman, who has long focused on the role of the gastrointestinal tract on health and weight management, has been able to avail himself of the most current research for this book.

The microbiome, comprising "good" and "bad" bacteria, is critical to our very survival. We learn that our genes were not encoded for every task that the gut must execute for us to survive. We depend on the microbiome to accomplish tasks such as regulating the immune system, extracting nutrients, producing certain nutrients, and influencing the production of neurotransmitters. It is when the microbiome is out of balance that these tasks are not accomplished well and health problems occur. The those problems include weight gain or inability to lose weight, mental health; digestive issues, metabolic disorders, endocrine problems, and autoimmune illnesses.

A microbiome out of balance means that the bad bacteria overwhelm the good, and there could be parasites and fungi present as well. This imbalance can come about as a result of diet, antibiotic use, and stress. To rebalance, the author offers his plan of the "Four Rs."

The first *R* is to Remove from the diet anything that interferes with intestinal health, such as foods that are highly reactive: dairy, soy, sugar, eggs, and gluten. Since leaky gut is a sign of a microbiome out of balance, these foods are to be avoided because they leak through the intestinal walls and create inflammation, which then leads to storing fat. Another example from the Remove list is to rid oneself of parasites. For this the author suggests using natural compounds such as berberine and wormwood.

The next *R* is Replace. Lack of hydrochloric acid in the stomach can result in incomplete digestion before food reaches the small intestine. This can lead to the possibility of food's crossing the intestinal wall, which can then trigger more inflammation. Also, when this happens, critical nutrients such as vitamin B6, calcium, and iron cannot be absorbed. Another problem arises due to the fact that the small intestine does not get the signal to produce needed digestive enzymes. Kellman prescribes supplemental hydrochloric acid and digestive enzymes.

"Our metabolism, weight, and overall health depend on the balance of microbial life within our gastrointestinal tract."

Food choices come into play in the third *R* – Reinoculate. Here we learn about the importance of diversity in the gut. Research has already shown that leaner, healthier people have greater diversity of species in their microbiomes. We achieve our diversity through a lifestyle of eating different foods and mixing in different environments. To boost our diversity, Kellman looks to probiotics and prebiotics. He offers advice on selecting a good probiotic supplement and lists the fermented foods that will introduce their own living bacterial cultures.

Another form of inoculation is to encourage the good bacteria in the microbiome. This can be done with the prebiotic foods that are high in plant fiber, such as asparagus, carrots, and jicama, to name a few.

The last *R* is to Repair the gut wall and intestinal lining. In a microbiome that is off balance, the microvilli and the tight junctions found in the small intestine are not functioning properly. The tight junctions become loosened and can allow passage of food through the intestinal wall. The microvilli become atrophied and lose their ability to gather nutrients to be absorbed. The remedies include minerals and herbs, healthful fats, glutamine, and butyric acid.

The author has applied the "Four Rs" to a three-phase regimen. The first phase includes meal plans for the first 21 days that will aid in healing the digestive tract. At its conclusion, the repair should be well under way. The microbiome is ever changing, and with a lifespan of 20 minutes for the microbes, even 24 hours can make a big difference.

The second phase of 4 weeks' duration will reduce the inflammation that is causing fat storage and boost the metabolism into fat burning. At this point Kellman expects 90% compliance with the diet. The last phase is the plan for staying healthy for life that assumes a 70% adherence to the diet.

While this is certainly a diet book for losing weight, it is also a good primer on gastrointestinal health. We learn the importance of maintaining a balanced microbiome because, as it turns out, those pathogens are our gastrointestinal system. And rather than being "a blind tube," as the author was taught in medical school, the gut is integral to the functioning of the brain and immune system. He states that 70% to 80% of the immune system is found in the gut and 95% of the body's serotonin is located there to assist in digestion.

The National Institutes of Health proposes that if the effects of a changing microbiome on health can be demonstrated, the result will transform medicine. This book is on the cutting edge of that transformation.

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FEBRUARY 19: THE NEUROENDOCRINE IMMUNOLOGY OF SMALL INTESTINAL BACTERIAL OVERGROWTH in Tampa, Florida. CONTACT: (800) 736-4381; info@apexseminars.com

FEBRUARY 19-21: AMERICAN ACADEMY OF OZONOTHERAPY ANNUAL MEETING & WORKSHOPS in Dallas, Texas. CONTACT: www.aaot.us/meetings-training/

FEBRUARY 19-21: INTEGRATIVE HEALTHCARE SYMPOSIUM in New York, New York. CEs for MDs, RNs, DCs, NDs, L.Ac. CONTACT: www.ihsymposium.com/annual-conference/

FEBRUARY 21: ORGANIC ACIDS TESTING: AN INVALUABLE TOOL FOR DISCOVERING THE UNDERLYING CAUSES OF CHRONIC ILLNESS WORKSHOP in San Diego, California. Presented by The Great Plains Laboratory, Inc. CONTACT: www.GPL4U.com/workshops

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FEBRUARY 21-22: NATIONAL COLLEGE OF NATURAL MEDICINE presents 3rd ANNUAL WOMEN'S HEALTH SYMPOSIUM in Portland, Oregon. CONTACT: womeninbalance.org/woocommerce/3rd-annual-womens-health-symposium/

FEBRUARY 25-28: PREVENTIVE MEDICINE 2015 – Annual Meeting of the American College of Preventive Medicine in Atlanta, Georgia. CONTACT: www.preventivemedicine2015.org/

FEBRUARY 25-28: A4M SPRING BHRT SYMPOSIUM in Los Angeles, California. CONTACT: www.a4m.com/anti-aging-conference-2015-02-la-bhrt.html

FEBRUARY 27-28: SOUTHEAST REGIONAL INTEGRATIVE MEDICAL CONFERENCE in High Point, North Carolina. Up to 9 CMEs. CONTACT: www.NCIMS.com

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MARCH 5-7: INTERNATIONAL ACADEMY OF ORAL MEDICINE & TOXICOLOGY (IAOMT) SPRING MEETING in Rio Grande, Puerto Rico. CONTACT: iaomt.org/conference/conference_agend/

MARCH 6-8: FUNCTIONAL MEDICINE ADVANCED PRACTICE MODULES – IMMUNE in Rancho Mirage, California. CONTACT: functionalmedicine.org/immune

MARCH 16-17: UTAH INTEGRATIVE HEALTH CONFERENCE: The Evidence, The Experience, The Application in Salt Lake City, Utah. CONTACT: www.health.utah.edu/health-promotion/integrative-health-conference.php

MARCH 20-22: EURO MEMBRANE MEDICINE CONFERENCE near Munich, Germany. Epigenetics, biohacking biofilm, stabilizing the brain and microbiome. Intensive Clinical PK Biomedical Course. CONTACT: NeuroLipid Research Foundation, 856-825-8338; fax 856-825-2143; www.neurolipid.org/our-focus/membrane-medicine-biomedical-conference-series/

MARCH 22: BASTYR UNIVERSITY presents ARE THE DRUGS MAKING YOUR PATIENTS SICK? A LOOK AT THE TRIAD OF HYPERTENSION, DYSLIPIDEMIA & TYPE II DIABETES in Kenmore, Washington (near Seattle). CONTACT: 425-602-3152; www.bastyr.edu/civicrm/event/info?id=1381&reset=1

MARCH 23-27: APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE in Tucson, Arizona. CONTACT: 800-228-0622; functionalmedicine.org/AFMCP

MARCH 26-29: PSYCHOTHERAPY NETWORKER SYMPOSIUM in Washington, D.C. CONTACT: www.psychotherapynetworker.org/symposium/2014/

MARCH 28-29: NATIONAL COLLEGE OF NATURAL MEDICINE presents FOOD AS MEDICINE SYMPOSIUM-NOURISHING PRESCRIPTIONS in Portland, Oregon. CONTACT: foodasmedicineinstitute.com/food-as-medicine-symposium-nourishing-prescriptions-2/

APRIL 9-12: NATIONAL AYURVEDIC MEDICAL ASSOCIATION 15th ANNUAL CONFERENCE in Newport Beach, California. CONTACT: www.ayurvedanama.org/page/NAMA15Anniversary/?

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APRIL 23-26: AMERICAN ACADEMY OF ENVIRONMENTAL MEDICINE INSTRUCTIONAL COURSES in Dallas, Texas. CMEs. CONTACT: www.aaemonline.org/courses.html

APRIL 23-26: AMERICAN ACADEMY OF MEDICAL ACUPUNCTURE 27TH ANNUAL SYMPOSIUM in St. Louis, Missouri. CMEs. CONTACT: www.medicalacupuncture.org/ForPhysicians/Symposium.aspx

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APRIL 26: ADVANCED APPLIED KINESIOLOGY-For Dysbiosis, Lyme, Foods, Metals in San Francisco, California. Treating the chronic patient. CONTACT: 970-201-1457; www.MichaelLebowitzDC.com/html/SF2015

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APRIL 30-MAY 3: NATIONAL ASSOCIATION FOR NUTRITION PROFESSIONALS 10TH ANNUAL CONFERENCE & EXPO in St. Paul, Minnesota. CEUs for NDs and nutritionists. CONTACT: www.nanp.org/conference/

MAY 1-3: 59TH ANNUAL NORTHWEST NATUROPATHIC PHYSICIANS CONVENTION – Wisdom of our Elders in SeaTac, Washington. CONTACT: www.nwnpc.com/

MAY 1-3: 14TH INTERNATIONAL CONFERENCE ON CONSCIOUSNESS IN AYURVEDA & YOGA in Edison, New Jersey. CONTACT: aapna.org/conferences/may-1-3-2015-edison-nj-usa

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MAY 8-10: ICMART XVII WORLD CONGRESS ON MEDICAL ACUPUNCTURE in Bali, Indonesia. CONTACT: icmart.org/events/upcoming-icmart-congress/upcoming-icmart-congress.html

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JUNE 12-14: 12TH INTERNATIONAL HERB SYMPOSIUM in Norton, Massachusetts. CONTACT: www.internationalherbsymposium.com/index.php?route=common/home

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JULY 17-19: 21ST ANNUAL INTERNATIONAL INTEGRATIVE MEDICINE CONFERENCE Melbourne, Australia. CONTACT: https://www.aima.net.au/21st-annual-*international-integrative-medicine-conference/*

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AUGUST 21-23: INTEGRATIVE ADDICTION 2015 in Myrtle Beach, South Carolina. CONTACT: 954-540-1896; Sharon@integrativeaddiction2015:com; integrativeaddiction2015.com

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OCTOBER 9-11: 17th INTERNATIONAL CONFERENCE ON AYURVEDA & *AUTOIMMUNE DISORDERS* in San Jose, California. CONTACT: **aapna.org/conferences/17th-conference-october-9-11-2015-san-jose-ca-usa/**

OCTOBER 24-29: 16TH ANNUAL SCIENCE AND CLINICAL APPLICATION OF INTEGRATIVE HOLISTIC MEDICINE in San Diego, California. CONTACT: www.scripps.org/for-health-care-professionals__continuing-medical-education-cme

NOVEMBER 11-14: 56TH AMERICAN COLLEGE OF NUTRITION ANNUAL CONFERENCE in Orlando, Florida. CONTACT: www.naturalhealthresearch.org/annual-conference/

NOVEMBER 12-14: SOCIETY FOR ACUPUNCTURE RESEARCH 2015 CONFERENCE in Boston, Massachusetts. CONTACT: www.acupunctureresearch.org/events

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NOVEMBER 14-16: 12TH INTERNATIONAL CONFERENCE OF THE SOCIETY FOR INTEGRATIVE ONCOLOGY in Boston, Massachusetts. CONTACT: www.integrativeonc.org/index.php/sio-international-conferences

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Women's Health Update

by Tori Hudson, ND
womanstime@aol.com

Old Problems with New Research and Clinical Favorites from the Recent Past

Green Tea Catechins for Xerostomia (Dry Mouth)

The perception of dry mouth (known as xerostomia) affects up to 40% of adults in the US and can have a significant effect on quality of life. Causes can include medications, diabetes, Sjögren's syndrome, and hormonal changes such as menopause. Previous animal and laboratory studies provided evidence that green tea polyphenols could be beneficial for xerostomia.

The current human study used a double-blind, placebo-controlled, randomized design comparing green tea to xylitol. The study involved 60 individuals (58 women and 2 men) with the complaint of dry mouth and who had Sjögren's syndrome meciated salivary gland hypofunction, with 30 taking the placebo and 30 the green tea medicine. The green tea proprietary formula contained green tea catechins and other ingredients (amounts not given, but Internet search reveals the following information: xylitol, sorbitol, natural flavors, green tea [leaf], acacia gum, jaborandi extract [leaf], magnesium stearate, silicon dioxide, sucralose). The placebo contained 500 mg xylitol and other nonplant ingredients. Participants took 1 lozenge every 4 hours for a maximum of 6 lozenges per day, over an 8-week period. Quality-of-life assessments and saliva collection with volume determined were used to evaluate response.

After 8 weeks of therapy, the xylitol-containing placebo failed to affect saliva output, while the green tea catechin-containing formulated resulted in a statistically significant increase in saliva output, with a 3.8-fold increase in unstimulated saliva output and 2.1-fold in stimulated saliva output, compared with baseline. This occurred within 1 week. Both groups experienced a quality-of-life score demonstrating significant improvement with no significant difference between groups.

Comment: Most commercial products for xerostomia contain xylitol, although it has not been known if xylitol does in fact play a role in saliva output. A xylitol chewing gum, a sorbitol-containing lozenge, and a xylitol-containing spray previously showed no efficacy in stimulating saliva in patients with xerostomia. A study using a maltose-containing lozenge found a potential benefit for xerostomia, and another with a 1% malic acid spray did show a modest increase in salivary flow rates. It is not clear why there is a discrepancy between salivary output increase in the treatment medication compared with placebo vs. the similar effects on subjective quality-of-life measures. A longer study with more participants would hope to clarify and produce greater results in the treatment group, not only in objective measures of salivary output but also in subjective quality-of-life values. Dry mouth is one of the stubborn complaints that I regularly hear reported in my clinical practice among menopausal women. I look forward to the use of this as another option to offer.

De Rossi S, Thoppay J, Dickinson D, et al. A phase II clinical trial of a natural formulation containing tea catechins for xerostomia. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2014;118:447–454.

D-Mannose and Chronic Recurring Urinary Tract Infections

This was a prospective, randomized controlled study comparing efficacy of daily D-mannose powder intake for preventing recurrent urinary tract infection. After initial antibiotic treatment of their acute cystitis, 308 women who met the criteria were randomly assigned to three groups. Group 1 received prophylaxis with 2 g daily of D-mannose powder in 200 ml of water for 6 months. Group 2 received 50 mg of nitrofurantoin daily for 6 months, and the third group did not receive either.

Criteria for study inclusion were >18 years old and a positive history of recurrent cystitis (at least two episodes of acute cystitis in the last 6 months and/or 3 episodes of acute cystitis in the last year). The study included a total of 308 women with acute cystitis and a positive history for recurrent cystitis as defined above. Overall, 146 patients were postmenopausal. The most commonly isolated bacterium during the acute cystitis was *Escherichia coli* in 236 patients (76.6%). Patients were excluded if they were pregnant, breast-feeding, or trying to conceive; had history of a current upper urinary tract infection and symptoms of systemic inflammatory response (fever over 38 °C, WBC >12,000), urinary tract anomalies, interstitial cystitis, diabetes, taking hormone therapy, or contraception; or had previously received prophylactic antibiotics.

The primary outcome was the number of UTIs following treatment with D-mannose or placebo. Overall, 31.8%, or 98 of patients had a recurrent UTI with an average time of 30

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days from starting their prophylaxis to the onset of symptoms. The onset of symptoms did not differ significantly between the prophylaxis therapy groups; that is, the D-mannose worked as well as the antibiotic. This included 15 (14.6%) in the D-mannose group, 21 (20.4%) in the nitrofurantoin group, and 62 (60.8%) in the no-prophylaxis group. Patients in the D-mannose group and the nitrofurantoin group had a significantly lower risk of recurrent UTI episodes during the prophylaxis treatment period compared with those with neither prophylaxis strategy. This is an absolute risk reduction of 45% compared with the control group. The difference between D-mannose and nitrofurantoin was not significant. Patients in the D-mannose group had significantly lower risk of side effects during prophylaxis as compared with the nitrofurantoin group.

Comment: The overall rate of UTI recurrence in prophylaxis groups (mannose or the antibiotic) was about 30% and about 60% in the no-prophylaxis group. Since about half of the patients in this study were postmenopausal, I can attest, through a robust amount of clinical experience in the area, that adding a vaginal estrogen regimen to the D-mannose (or the prophylaxis antibiotic) will greatly decrease the recurrence rate even more. One could point out that this study was not blinded or that researches did not calculate the total number of recurrences per patient.

D-mannose has been used by alternative-minded practitioners for some time, for this exact purpose. Until now, I believe that there have not been any clinical trials, and the only evidence for this has been the supposed mechanism of action in inhibiting bacterial adherence to uroepithelial cells, in vitro experiments showing that D-mannose binds to the pili of enteric bacteria, blocking their adhesion to uroepithelial cells, and reduction in bacteria in the urine in animal models. Nonetheless, it has become quite a staple in treating chronic recurrent cystitis at least in women and used as a prophylaxis regimen along with other therapies known to inhibit adherence to uroepithelium, such as certain species of *Lactobacillus*, and other therapies, including vaginal estrogen (especially in postmenopausal women with this condition), cranberry extracts, berberine-containing plants, and more. The results of the current study provide clear evidence that D-mannose can be an effective prophylactic agent in preventing recurrent UTIs in women.

Kranjeec B, Papes D, Altarac S. D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial. *World J Urol*. 2014;32:79–84.

Grape-Seed Extract Effect on Menopause Symptoms and More

The most common perimenopause and menopause symptoms are vasomotor symptoms, a.k.a. hot flashes and/or night sweats. In addition to having numerous perimenopause/menopause symptoms, postmenopausal women in particular are at increased risk for cardiovascular disease, dyslipidemia, hypertension, and type 2 diabetes. Plant compounds such as French maritime pine bark extract (Pycnogenol) that are rich in proanthocyanidins have been used in three studies to alleviate menopause symptoms such as vasomotor symptoms. Because of these studies and an analysis showing that grape seeds are even richer in proanthocyanidins, researchers have conducted and published a study examining the effects of grape-seed extract/proanthocyanidin on menopause symptoms, body composition, and cardiovascular markers.

A randomized, double-blind, placebo-controlled study was conducted in almost 100 premenopausal, perimenopausal, and menopausal women between 40 and 60 years old. The average age was 49 to 59 years, with 40% to 48% premenopausal women, 52% to 60% perimenopausal, postmenopausal, or surgically menopausal. Women were randomized to receive grape-seed extract tablets that contained either 100 or 200 mg/day of proanthocyanidins or placebo for a total of 8 weeks. Menopause symptoms were evaluated using the Menopausal Health-Related Quality of Life Questionnaire, the Hospital Anxiety and Depression Scale, and the Athens Insomnia Scale before the start of treatment as well as after 4 weeks and 8 weeks of treatment.

Significant changes were observed in hot flashes, anxiety, insomnia, increased muscle mass, and reduced blood pressure. The average physical symptom score for the nine items in the physical-health domain of the Menopause Health Related Questionnaire significantly improved in the high-dose grape-seed extract group after 8 weeks, as did the mean score for hot flashes. The mean depression score did not improve in any of the groups, but the anxiety subscale score improved in both the 100 mg and 200 mg groups and was significantly better in the higher-dose group than in the placebo. Mean body weight and fat mass did not change in any of the groups, but the mean lean mass and muscle mass increased significantly in both the 100 mg and 200 mg grape-seed extract groups. Lastly, the mean systolic and diastolic blood pressure was significantly reduced in both the 100 g and 200 mg groups and after as soon as 4 weeks. The mean systolic and diastolic blood pressure decreased by about 5 mm Hg with both doses after 8 weeks.

Comment: The menopause studies using pine bark demonstrated positive results in improving menopause symptoms at all three different doses tested in each of the studies, 60, 100, and 200 mg. Similarly, in the current study, the two doses of grape-seed extract (100 and 200 mg) both worked well for hot flashes, although the 200 mg dose was clearly better than the 100 mg dose in the anxiety subscale. This study appears to be the first report of proanthocyanidins' affecting body composition, increasing muscle mass with both doses. The positive effect on blood pressure using proanthocyanidins, including those in grape-seed extract, is not a new finding. I have been using pine bark extract for vasomotor symptoms in perimenopausal and menopausal women for the past several years, with mixed results. I am intrigued by the current study and look forward to using grape-seed extract in these two doses as another nonhormonal option, especially in women who not only need vasomotor symptom relief but are also struggling with overweight and prehypertension or stage I hypertension.

Terauchi M, Horiguchi N, Kajiyama A, et al. Effects of grape seed proanthocyanidin extract on menopausal symptoms, body composition, and cardiovascular parameters in middle-aged women: a randomized, double-blind, placebo-controlled pilot study. *Menopause*. 2014;21(9):990–996.

Clinical Favorites from the Recent Past

Several nutritional supplements and botanicals have made their way into a dominant place in my women's health practice in 2014. Whether studies were published in 2013 or 2014 or even earlier, these natural agents have come to play a reliable role in my women's health practice of the last 30 years and in some of the most challenging cases. I've written about many of these in past *Townsend Letter* columns, but the purpose here is to emphasize their role and to encourage others to incorporate them more widely in women's health.

Melatonin and Endometriosis

A randomized, double-blind, 2-group, parallel clinical trial conducted in Brazil compared the effects of melatonin with a placebo on endometriosis-associated pelvic pain, brain-derived neurotrophic factor (BDNF) level, and sleep quality. Participants were randomized into melatonin (10 mg/day; n = 20) or placebo (n = 20) groups for 8 weeks.

Forty women with chronic pelvic pain, who were between 18 and 45 years old, were recruited from gynecology outpatient clinics. Chronic pelvic pain was defined as a moderate to severe pain lasting for more than 6 months and eliciting pain scores of at least 4 or greater on a 10-point pain scale that required regular analgesic use. All participants had a diagnosis of endometriosis as confirmed on laparoscopy and included patients with any stage from 1 to 4. Three patients in the melatonin group and 1 in the placebo group withdrew due to treatment inefficacy.

The primary outcome of the trial was pain, as assessed by pain score diaries within the last 24 hours, painful menstrual periods, or dyspareunia, as well as the amount of analgesic used each week throughout the treatment period and the level of BDNF. Secondary outcomes were pain during urination or defecation and sleep quality.

Results: The melatonin group had significantly lower pain visual analogue scale (VAS) scores than the placebo-treated group, with a mean pain reduction of 39.3% in the melatonin group vs. the placebo group. The melatonin group also had significantly lower pain scored during menstruation, with mean reduction in analgesic use of 42.2% patients in the placebo group and 22.9% in the melatonin group. The placebo group was 80% more likely to require additional analgesics than the melatonin group. In the placebo group, acetaminophen was used by 66.7%, NSAIDs by 60%, and codeine or tramadol by 60%. In the melatonin group, 33.3% used acetaminophen, 40% used tramadol or codeine, and 35% used NSAIDs.

The adjusted mean BDNF level for the placebo group was 25.64 vs. 20.46 for the melatonin group with a mean difference of 5.94, which is significant; and the authors concluded that the effect of treatment on the BDNF level is not dependent on the pain level. This suggests that melatonin has a direct effect on pain pathways or on the levels of chemicals that are signals for pain. Patients in the melatonin group had better sleep quality than those in the placebo group, and melatonin produced a mean improvement of 42% in how patients felt upon waking in the morning.

Comment: This study demonstrated that melatonin at 10 mg/day reduces endometriosis-associated chronic pelvic pain, including a reduction in pelvic pain, dysmenorrhea, dyspareunia, dysuria, and dyschezia (pain during defecation) that is statistically and clinically significant. This reduction in pelvic pain due to melatonin was of a magnitude >35% overall, as well as an 80% reduction in analgesic use.

This study is consistent with evidence from animal studies in which melatonin caused regression and atrophy of endometriotic lesions. The current study also corroborates other randomized clinical trials on melatonin and pain in treating fibromyalgia and acute postoperative pain.

The mechanisms of action may include the antinociceptive effect of melatonin involving the activation of supraspinal sites and the inhibition of spinal windup. Other experimental evidence suggests that the analgesic effects of melatonin are mediated by opioids and GABA and anti-inflammatory effects by inhibiting the release of cytokines. The effect of melatonin on chronic endometriosis-associated pelvic pain may also be explained by its effect on diverse hormonal pathways.

Melatonin is well tolerated by most patients and appears to represent an effective option for pain symptoms related to endometriosis. A 2013 observational study on N-acetylcysteine also resulted in significant reduction of pain and size of ovarian cysts associated with endometriosis. I consider the two nutrients mainstays in our treatment strategies for endometriosis.

Schwertner A, Conceicao dos Santos C, Costa G, et al. Efficacy of melatonin in the treatment of placebo endometriosis: A phase II, randomized, double-blind, placebo controlled trial. *Pain.* 2013;154(6):874-881.

Valerian/Lemon Balm in Menopausal Sleep Problems

The purpose of this 2013 study was to determine whether a combination of valerian/lemon balm could improve sleep problems in menopausal women. A total of 100 postmenopausal women aged 50 to 60 years with sleep disorders were studied. Women were selected randomly after fulfilling the entrance criteria. The Pittsburgh Sleep Quality Index (PSQI) questionnaire was completed to assess the status of their sleep disorder in the month prior. The PSQI consists of various measurements, including general description of individual sleep quality and patterns, delay in the onset of sleep, sleep duration and pattern as well as waking in the night, use of tranquilizers, and daily performance problems due to lack of sleep. A score of 5 or greater constitutes a sleep disorder and the 100 women selected were those with such a scoring. Women were randomly divided into two groups, with 50 in the herbal treatment group, which received two capsules containing 160 mg of valerian and 80 mg of lemon balm, and 50 in the control group, which received capsules containing starch. Participants and investigators and the statistician were all blinded. The duration of the intervention was 1 month and then followed by another PSQI questionnaire.

One month following use of the valerian/lemon balm supplement, 36% of the treatment group and 8% of the

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placebo group showed an improvement in the quality of their sleep. Sleep disorder scores decreased by 5 points, which was statistically significant.

Comment: Perimenopausal and menopausal women are faced with hormonal changes that can result in not only nighttime hot flashes that can disrupt sleep, but lengthened time it takes to fall asleep, frequent awakenings, waking and poor return to sleep, early morning waking, and nonrestorative sleep. Botanical options that can improve any or all aspects of sleep disruption are an important part of a comprehensive approach to treating this. However, addressing sleep disorders in this population usually also involves strategies that target the fundamental issue, which is hormonal changes and the impact on neurotransmitters, cortisol, stress adaptation, and sleep cycle physiology.

In 2011, another study of valerian and insomnia was published. The participants were generally healthy women aged 50 to 60 years who were menopausal for at least 1 year, not using hormone therapy, and experiencing insomnia. One group was given capsules containing 530 mg of concentrated valerian extract twice per day and the other group placebo, twice per day, for 4 weeks. A statistically significant change was reported in the quality of the sleep in the valerian group when compared with the placebo group. The average score on the sleep scale before valerian was 9.8 and after valerian it was 6.02. The placebo group had an initial average sleep scale score of 11.1 and after placebo, 9.4. Overall, 30% of the women taking valerian and 4% taking placebo reported an improvement in their sleep quality.

Although not all research on valerian and insomnia has shown positive results, these two studies bring more focus to using valerian in menopausal women for sleep disorders.

Taavoni S, Ekbatani N, Kashaniyan M, Haghani H. Effect of valerian on sleep quality in postmenopausal women: a randomized placebo-controlled clinical trial. *Menopause*. 2011;18(9):951–955.

——. Valerian/lemon balm use for sleep disorders during menopause. *Complement Ther Clin Pract*. 2013;19:193–196.

Oral Lavender Essential Oil in Generalized Anxiety Disorder

This randomized, double-blind, placebo-controlled trial investigated two doses of oral lavender essential oil in comparison with a selective serotonin reuptake inhibitor, paroxetine, in patients who have been diagnosed with generalized anxiety disorder (GAD). The primary outcome of this study was the effect of lavender essential oil in comparison with placebo, on GAD, as measured by the Hamilton Anxiety Scale (HAMA) total score. This scale assesses 14 symptoms of anxiety through a scale ranging from 0 (absent) to 4 (severe). The secondary outcome was the effect of lavender essential oil compared with paroxetine on GAD.

A total of 616 patients were recruited and then 536 patients randomized to treatment. These were men and women, between ages 18 and 65 year old, from 57 general and psychiatric practices in Germany, who had a diagnosis of moderate to marked severity of GAD for an average of 2.5 years. Inclusion criteria were: with a HAMA score of ≥ 18, and scores for anxious mood and tension symptoms of 2 or greater, in addition to a score of 21 or less for psychic anxiety. An additional anxiety scale was used as well, the Cover Anxiety Scale (CAS), and the inclusion criterion was a score of 9 or greater. Individuals with any additional psychiatric illnesses were excluded. Psychiatric medications other than the paroxetine were not allowed during and for 30 days prior to entering the study. A total of 128 were in the 160 mg lavender group, 135 in the 80 mg/day group, 137 in the paroxetine group, and 136 in the placebo group.

Individuals were given a lavender essential oil made from the steam-distilled fresh flowering top of lavender that has then been standardized to contain approximately 70% of two constituents, linalool and linalyl acetate. The product was given as either a 80 or 160 mg dose and then 1 placebo or 2 placebo pills daily. The paroxetine was given in capsules of 20 mg. Treatment was given for 10 weeks, and measurements of safety and efficacy were done at 2, 4, 6, 8, and 10 weeks. During a week of "down-titration" following the study, patients on the paroxetine took the treatments every other day to account for any withdrawal problems caused by paroxetine. Patients in the lavender essential oil group took placebo.

After 4 weeks of the study and at other time points, the intake of 160 mg/day of lavender essential oil resulted in a significantly greater change in the HAMA score compared with placebo ($p < 0.01$). After 6 weeks and beyond, those taking the 80 mg/day of lavender essential oil had a significantly greater change in the HAMA scores compared with placebo ($p = 0.02$). At week 6, the HAMA score in those taking paroxetine approached significance ($p = 0.06$) but then were not significantly better than placebo after that point.

Significantly more patients in the 160 mg/d lavender group showed an improvement in the HAMA score of 50% or more compared with the placebo group (60.3% vs. 37.8%). This was also observed in the 80 mg/d group (51.9% vs. 37.8%). The HAMA score was <10 in significantly more of those patients taking the lavender product compared with the placebo (46.3% vs. 29.6%). According to the clinical global impression (CGI), all three treatment groups (the 80 mg/day, 160 mg/day, and paroxetine) contained a greater percentage of patients who were "much/very much improved" or had a "moderate/marked" therapeutic effect as compared with the placebo group. The adverse events reported were 25% of those in the 160 mg/day lavender group, (oddly higher) 34.8% in the 80 mg/day group, 40.9% in the paroxetine group, and 30.9% in the placebo group. These adverse events were reported as gastrointestinal disorders, infections, and nervous system problems.

Comment: Both doses of oral essential oil of lavender were effective in treating GAD and more effective than the conventional medicine, paroxetine. Adverse events in those taking lavender were similar in those taking placebo and lower than those taking paroxetine. This is another welcomed positive study in using an oral lavender essential oil standardized to linalool and linalyl acetate in

the treatment of GAD. Conventional medications, whether antidepressants, anxiolytics, or barbiturates, are fraught with side effects, which makes the lavender essential oil product that much more appealing.

Kasper S, Gastpar M, Müller WE, et al. Silexan is effective in generalized anxiety disorder – a randomized, double-blind comparison to placebo and paroxetine. *Int J Neuropsychopharmacol.* Epub January 23, 2014:1–11. doi:10.1017/S1461145714000017.

N-Acetylcysteine and Polycystic Ovarian Syndrome

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders in reproductive-aged women, with multiple manifestations and consequences. It affects approximately 6% to 10% of reproductive-aged women, and the metabolic disturbances associated with it have immediate and long-term potential outcomes, including infertility, hyperandrogenism, type 2 diabetes, cardiovascular disease, and even uterine cancer.

Insulin-sensitizing agents have emerged as an important strategy in addressing the fundamental underlying cause of PCOS, insulin resistance. In conventional medicine, the focus has been on metformin, an insulin-sensitizing agent which can decrease the levels of insulin, improve glucose tolerance, increase sex hormone binding globulin (SHBG), decrease circulating androgens, and increase ovulation rates in women with PCOS. N-acetylcysteine (NAC) is used by many alternative practitioners as a mucolytic medication and antioxidant effects. Lesser known is its role as an insulin regulatory agent. And previous studies have shown that it can improve circulating insulin levels and insulin sensitivity in hyperinsulinemic women with PCOS as well as being used successfully as an adjunct treatment with clomiphene citrate for ovulation in women with PCOS.

The purpose of the study reported on here was to evaluate the effects of metformin and NAC in patients with PCOS. This prospective trial randomly divided 100 women to receive either metformin 500 mg t.i.d. or NAC 600 mg t.i.d. for 24 weeks. Evaluations included hirsutism scoring, body mass index, serum samples for follicle-stimulating hormone (FSH), luteinizing hormone (LH), dehydroepiandrosterone-sulfate (DHEAS), 17 OH-progesterone, total testosterone, free testosterone, androstenedione, thyroid stimulating hormone (TSH), SHBG, prolactin, glucose tolerance tests (including glucose and insulin), tumor necrosis factor-alpha (TNF-alpha), and lipids.

Women were ages 17 to 38, and 75 of the 100 women with PCOS completed the study. All women in the NAC group completed the study and 5 of the 35 women in the metformin group did not complete the study. At baseline, there were no differences between the treatment groups. Following treatment, LH, total testosterone, and free testosterone decreased significantly and SHBG increased significantly in both groups. Hirsutism improved significantly in both groups, and the difference between the metformin group and NAC group was not significant. Menstrual regularity was restored in 9 patients in the metformin group and 11 patients in the NAC group (36% vs. 34 %), and both metformin and NAC women significantly improved menstrual irregularity. In the metformin group, total serum cholesterol levels were significantly lowered, but no significant changes were observed in LDL, triglycerides, and HDL. In the NAC group, total cholesterol and LDL decreased significantly, but no changes were observed in triglycerides and HDL. The changes in lipid profiles between the two groups were not significant.

Both metformin and NAC had positive effects on reducing fasting insulin levels, without change in fasting glucose, but this means that glucose-insulin rations were increased significantly following treatment with both medicines and, in addition, both led to a significant improvement in the HOMA (homeostatic model assessment) and were considered comparable. TNF-alpha levels were increased in both groups but not significant from baseline and similar in both groups.

Comment: Conventional medical treatments for PCOS have come to include a combination of hormonal contraceptives, progestins, statins, and insulin-sensitizing agents, especially metformin. This combination of treatments has not clearly led to adequate prevention of consequences of PCOS such as cardiovascular disease and type 2 diabetes and insufficient treatment of anovulatory infertility, hirsutism, and weight management in those PCOS women who are overweight/obese. In addition, these approaches are fraught with side effects, and for metformin this typically includes gastrointestinal symptoms that can lead to intolerance of the drug, as it did with the high dropout rate in the metformin group in the current study. However, metformin has been a very important addition to PCOS management, and two systemic reviews have shown that metformin reduces menstrual irregularity and improves ovulation rates, although it has poor impact on hirsutism.

A treatment such as NAC is a welcomed addition to improve insulin sensitivity in the management of PCOS. It turns out to be very well tolerated with no adverse effects. In the current study, both metformin and NAC reduced menstrual irregularity, resulted in regression of hirsutism, and reduced hyperinsulinemia in women with PCOS. In the current study, there were also significant reductions in free testosterone and total testosterone in both groups, likely due to decreasing insulin levels and increasing SHBG levels, and decreases in total cholesterol and insulin, which bodes well for long-term prevention issues as they relate to cardiovascular disease and type 2 diabetes.

Oner G, Muderris I. Clinical, endocrine and metabolic effects of metformin vs N-acteyl-cysteine in women with polycystic ovary syndrome. *Eur J Obstet Gynecol Reprod Biol.* 2011;159:127–131.

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The Illusion of the Asymptomatic Patient

In a recent study, researchers measured endomysial antibodies in the relatives of people who had celiac disease. A positive test is strongly suggestive of celiac disease, with a specificity of close to 100%. Forty individuals who tested positive for endomysial antibodies and were apparently asymptomatic were randomly assigned to consume a gluten-free diet or a gluten-containing control diet for 1 year. After 1 year on the diet, gastrointestinal symptoms improved to a significantly greater extent in the gluten-free diet group than in the control group. Compared with the control group, the gluten-free diet group also had significantly less indigestion, reflux, and anxiety.[1] Thus, a gluten-free diet was beneficial for apparently asymptomatic relatives of patients with celiac disease who were positive for endomysial antibodies.

While this study adds to our knowledge regarding gluten intolerance in the relatives of patients with celiac disease, that is not what led me to discuss it in an editorial. What caught my eye about the study is that it showed that "apparently asymptomatic" people are often not really asymptomatic, since some of the patients were experiencing symptoms such as indigestion, reflux, and anxiety. These symptoms may not have been severe enough to mention to a doctor, or they may have been dismissed as a normal part of living, but they were nevertheless symptoms. I have seen many patients over the years who answered "no" when asked if they suffered from symptoms such as fatigue, depression, or aches and pains. However, after embarking on a nutritional program and feeling so much better than before, they realized that these types of symptoms had been part of their daily lives for years.

For example, a woman in her late 30s who consulted me because of recurrent respiratory infections denied having a history of depression. She had clinical evidence of possible hypothyroidism, and was started on a low dose of thyroid hormone and a multivitamin. At her follow-up visit 6 weeks later, she stated that she felt better than she ever felt had. In retrospect, she had been depressed her entire life, but had just assumed that this was the way people were supposed to feel. Another woman in her mid-50s had unexplained osteoporosis. Although she denied having any gastrointestinal symptoms, she was tested for celiac disease (tissue transglutaminase and endomysial antibodies) and was found to be positive. After going on a gluten-free diet, not only did her bone mineral density improve, she also remarked that the "horrible" gastrointestinal bloating she had suffered from for most of her life had disappeared.

Why should we spend extra time on a medical history trying to identify symptoms that a patient may not consider important enough to mention or may not even be aware of? The reason is that the more you know about a patient's symptoms, the more likely you are to arrive at an accurate diagnosis and an effective treatment plan. A number of years ago, I was asked to demonstrate to a group of holistically oriented medical students how to take a medical history from a nutritional/metabolic/endocrine perspective. A 24-year-old female student volunteered to be the guinea pig. The interview went something like this:

Doctor: How would you rate your overall health?
Patient: Very good.
Doctor: Do you have any symptoms?
Patient: No.
Doctor: Do you suffer from fatigue?
Patient: No.
Doctor: How many hours do you sleep at night?
Patient: 10.
Doctor: How would you feel if you only got 8 hours?
Patient: Oh, I'd be exhausted!
Doctor: Do you have constipation?
Patient: No.
Doctor: Do you take a fiber supplement?
Patient: Yes.
Doctor: What would happen if you didn't take the fiber supplement?
Patient: I wouldn't be able to go to the bathroom.
Doctor: Do you have dry skin?
Patient: No.
Doctor: Do you put moisturizer cream on your legs?
Patient: Yes.
Doctor: Why do you do that?
Patient: Because my skin gets dry if I don't.
Doctor: Do you suffer from cold extremities?
Patient: No.
Doctor: Do you wear socks to bed?
Patient: Yes.
Doctor: Why?
Patient: Otherwise my feet get cold.

This "asymptomatic" young woman actually had at least 4 symptoms that are consistent with mild hypothyroidism. On physical examination, she had a delayed Achilles tendon reflex return, a finding strongly suggestive of hypothyroidism. Since this was just a demonstration, I did not do any further evaluation or recommend a treatment plan. However, the symptom pattern was similar to that of hundreds of patients I have seen who had "sublaboratory" hypothyroidism and who experienced an improvement in their health after taking low-dose thyroid hormone. Had I accepted a simple "no" for an answer and not followed up with additional questioning, I would have overlooked all 4 of these symptoms and would not have considered hypothyroidism as a diagnosis.

We all know the importance of going through the "review of systems" during a medical history, in order to identify symptoms and illnesses that patients may not have thought to mention. It is also important in certain cases to do some extra digging in order to find symptoms which patients are not even aware that they have.

Alan R. Gaby, MD

Notes

1. Kurppa K et al. Benefits of a gluten-free diet for asymptomatic patients with serologic markers of celiac disease. *Gastroenterology*. 2014;147:610-617.e1.

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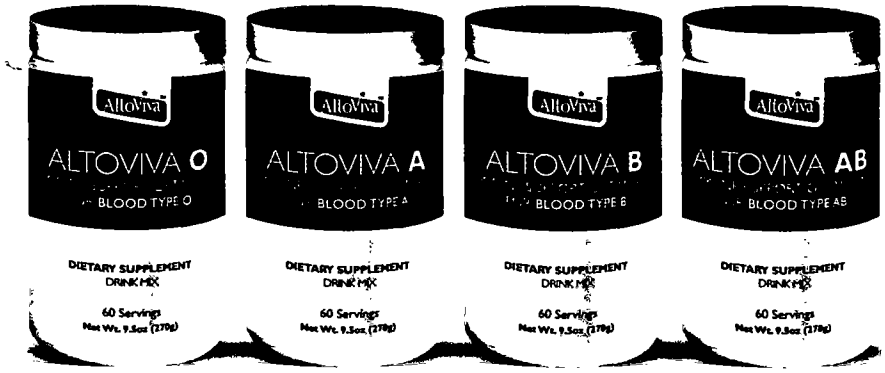

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