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Doug Lobay, ND
DEMENTIA, LOSS, AND LOVE

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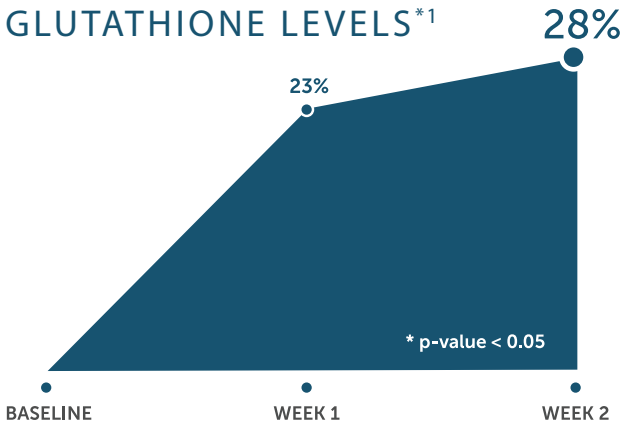

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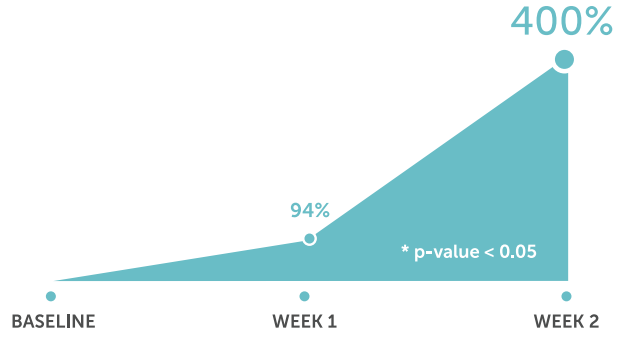

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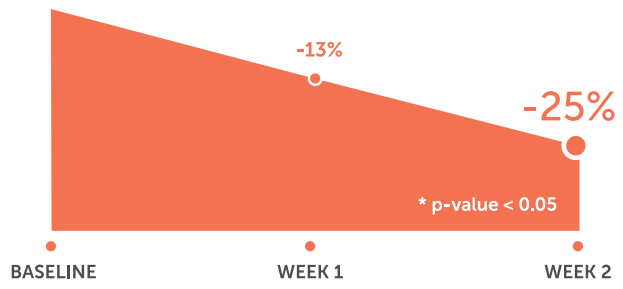

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[1]Sinha R, Sinha I, Calcagnotto A, et al. Oral supplementation with liposomal glutathione elevates body stores of glutathione and markers of immune function. Eur J Clin Nutr. 2018;72(1):105-111. doi:10.1038/ejcn.2017.132

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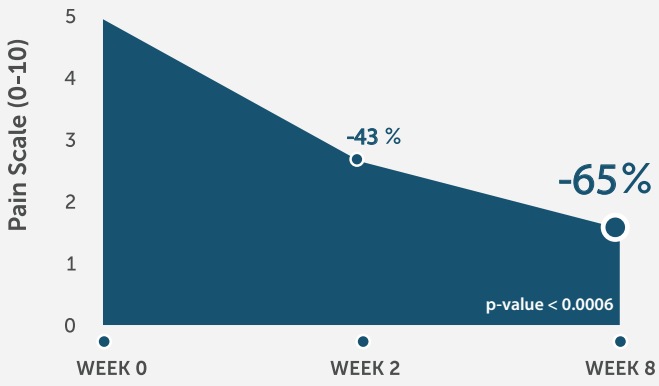

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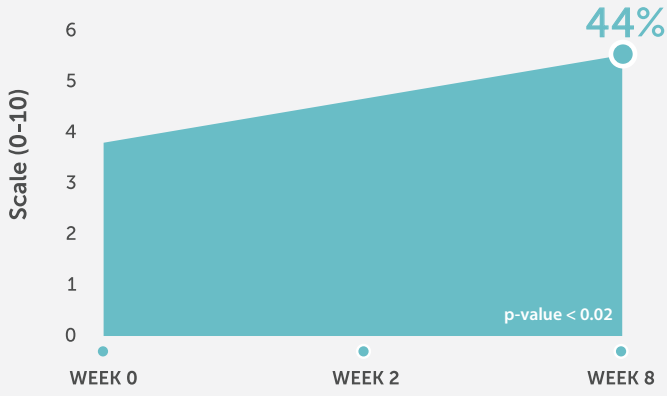

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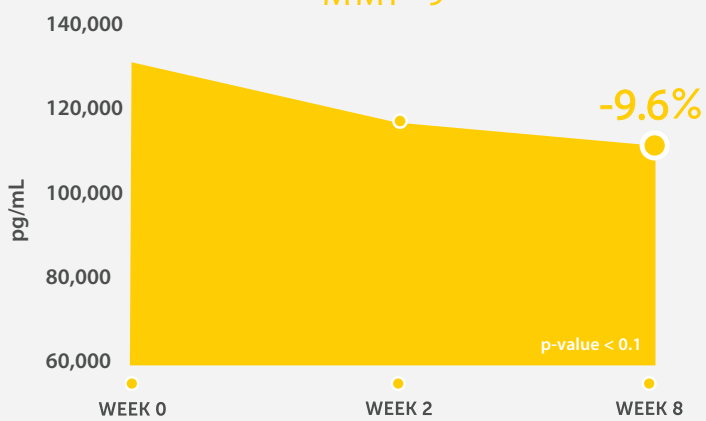

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Learn more: researchednutritionals.com/cytoquel

[1] Journal of Pain Research (D Hamilton, G Jensen). Pain reduction and improved vascular health associated with daily consumption of an anti-inflammatory dietary supplement blend. J Pain Res. 2019; 12: 1497–1508.

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From the Publisher

***The Virus and the Host* by Dr. Chris Chlebowski**

Like many practitioners and patients who have been unhappy with the public health response to the Covid-19 epidemic, Dr. Chlebowski not only thinks that things were not done right but also that practical and effective natural approaches were ignored. Of course, conventional medicine has never been on board with naturopathic medicine and chiropractic except grudgingly. Chlebowski who is both an ND and a DC as well as an herbalist and homeopath, practices in Ashland, Oregon, and has worked prodigiously over the past several years to help his patients prevent the coronavirus and treat the infection if they became infected. He states that not only have his patients not died but they have not required hospitalization. Of course, Chris employs a full armamentarium of medical therapy from herbs to homeopathics to ozone to chelation as well as other integrative therapies. He recognizes that patients develop infections much less frequently diagnosed, such as Lyme disease, Bartonella, Babesia, Entamoeba, and mold mycotoxin

illness. Chlebowski's chief concern is that most folks eat so poorly, remain sedentary, and are frankly over burdened with toxic metals and chemicals, that they are vulnerable to viral infections. He is not an advocate of the mRNA Covid-19 vaccines. Instead he advocates doing everything we are able to do to optimize our immune system and face the coronavirus and future viral outbreaks in robust health rather than depend on a vaccine.

As Dr. Chlebowski details in his new book, *The Virus and the Host*, published by Chelsea Green Publishing, cleaning up the diet is a major undertaking for most people. He likes his patients to follow his PLOW acronym: **P**lant-heavy meals, **L**ow to no sugar, **O**rganic and Clean, and **W**atch the carbohydrates. Chlebowski wants us to eat as organically as possible with locally grown food. His philosophy is that not only is an organic diet necessary to stop the intake of chemicals and other toxins, but consumption of locally grown organic foods is necessary to support farmers and revitalize the soils through organic farming. Healing the earth is as much a part of the program as everything else the patient is obligated to attend to in the medical protocol. There is no ground-breaking nutritional information here. However, he supports the logic that our nutrition is not just a matter of providing adequate protein and calories but is the foundation of cleaning up one's toxins. Dr. Chlebowski not only encourages exercise but recommends sufficient vigorous activity to cause sweating, a key to detoxification.

No matter how clean the diet, there is a need for supplemental nutraceuticals to bolster the immune system. Chlebowski not only offers nutraceutical dosing but food sources for those who prefer to obtain their nutrients directly through eating. The botanical chapter is a welcome introduction for patient and doc on using botanicals for immune support. Chlebowski would like us to grow the herbs so we can harvest our own medicine. What I enjoyed most was the chapter devoted to detoxification, all methods for one to easily do at home. Over the years I have appreciated the value of the "castor oil pack" and the "coffee enema." Chlebowski explains the how-to-do these detox methods that make sense for the patient.

Chlebowski is concerned about how we will face future viral pandemics. He thinks of an emerging virus as a signal. We have been educated to think of viruses as pathogens to humans or animals or plants; but viruses can infect without necessarily being pathogenic. As Chlebowski points out, about 8% of our genome is viral much of it representing prehistoric infections that were overcome or incorporated in the human genome. Viruses are opportunistic and serve to keep all organisms in check. There is no reason that an emerging virus can not be symbiotic with us; it does not need to act as a pathogen. The virus's pathology is based on our system becoming so imbalanced and devitalized that we are unable to survive the infection. For those who keep a clean, vital immune system, facing the future virus should not be a life or death experience or even a serious illness. However, one does need to detoxify now, not wait until the day we encounter a new virus.

From the Publisher

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Repurposing Ivermectin as a Coronavirus Treatment Takes Another Hit

Since the pandemic began (has it ended?), there have been efforts to repurpose drugs to treat the Covid-19 virus. In early 2020 the lupus drug, hydroxychloroquine, was thought to be an effective deterrent to severe disease. Not much later the FLCCC promulgated the use of ivermectin as an effective therapy, even a preventative. A number of early, small studies demonstrated positive outcomes using ivermectin. Then in 2021 a negative ivermectin study was besmirched by faulty data. Since then multiple interventional trials in the US reported in 2021-22 have continued to show ivermectin ineffectiveness.

A recent study reported in *JAMA* failed to show any benefit of ivermectin in reducing days to recovery, prevention of hospitalizations, and avoidance of serious adverse events[1]; 1591 individuals completed a study originally enrolling 3457 participants. Ivermectin was administered at a dose of 400 ug/kg to the study group of 817 for a period of 3 days. Time to recovery was 12 days for the ivermectin group and 13 days for the placebo group (not statistically significant). The ivermectin group had 10 individuals compared to 9 in the control group requiring hospitalization. The ivermectin group had 5 pneumonia cases compared to 7 in the placebo group, 1 thromboembolism event compared to 5 in the control group. Of note, the FLCCC protocol stipulates that treatment be administered for at least 5 days and continued until recovery. Since this trial's protocol only employed ivermectin for 3 days, it is reasonable that the insufficient treatment period caused the experiment to fail.

It is disturbing that the repurposing of ivermectin has become tainted by political advocacy/condemnation. Covid-19 prevention and treatment has divided into two polarized and vitriolic camps, those who subscribe to vaccination and pharmaceutical intervention and those who do not. Evidence based medicine gives ivermectin a low grade for Covid-19 treatment. Nevertheless, ivermectin is a relatively safe drug conveying minimal side effects. Its use during a viral infection deserves individual consideration.

Fat Is Fat, Right? Well, Not Exactly by Dr. Devaki Berkson

Dr. Devaki Lindsey Berkson is a recognized nutritional consultant who specializes in complex hormone and gastrointestinal case management. Dr. Berkson has served as a research fellow at the University of Texas at Austin as well as Distinguished Estrogen Scholar at the Center for Bioenvironmental Research. She serves in teaching CME for professionals at A4M and PCCA. Berkson has authored numerous books and presented at dozens of conferences here and abroad. Berkson authored a three-part article in the *Townsend Letter* beginning in August/September 2020 entitled "Estrogen Vindication," citing the evidence about estrogen's effectiveness and safety in bio-identical hormone treatment (see **www.townsendletter.com**). Dr. Berkson invites the readership to consult with her to help manage complex cases (**www.drlindseyberkson.com**).

We generally think of fat as the flab that surrounds our abdomen or balloons our thighs and upper arms. Indeed, white adipose tissue (WAT) is composed of fat cells that expand in size dramatically as we consume excess calories and glucose is converted into triglycerides. However, white fat is not static; it fluidly changes into brown adipose tissue (BAT) when our diet limit calories, we fast, and when our metabolism is altered with medication or nutraceuticals. Brown fat is responsible for keeping us warm and providing the body with energy while we don't eat. Curiously that white to brown adipose tissue conversion has an intermediary state, beige adipose tissue which confers properties of both white and brown fat to the adipose tissue. Berkson details the physiology of white, brown, beige fat as well as pink fat and bone fat. Those folks who are metabolically imbalanced fail to have good functioning bone fat, a risk factor for osteoporosis and bone degeneration. The complexity of fat metabolism and varying adipose cell types partially explains the difficulty we experience in losing weight.

Cover Article: The Last Ember by Douglas Lobay, ND

Townsend Letter readers are familiar with Dr. Douglas Lobay who writes frequently for the publication. Past articles include "The Canary in the Coal Mine or How to Improve Kidney Function" and "Practical Nutritional Supplement De-Prescribing," both available online. Lobay is the author of several books, including *Dr. Lobay's Natural Health and Healing* and *Dr. Lobay's Natural Medicine 101*. Dr. Lobay graduated from Bastyr College (now University) in 1991. Douglas practices naturopathic medicine in Kelowna, British Columbia. He is married to his wife, Natalie, and has two daughters, Rachel and Jessica. He states that "he enjoys hiking, hockey, skiing, tennis, travel, and playing the guitar."

When one has a Medicare wellness exam the primary physician reviews the patient's medical diagnoses and treatments, checks prescription medications and supplements, and does a physical exam. A short in-office test for dementia asks the patient to repeat a short list of objects 15 minutes after being asked to memorize the list. For those of us approaching our older years, remembering those five objects is a little challenge. For those with early dementia, it is a big challenge – impossible for anyone with advanced dementia. Diagnosing Alzheimer's is made with a scale just like a pain scale: 0 represents no signs of memory loss, 10 represents late-stage disease. Alzheimer specialists think we all fall somewhere on this scale from 0 to 10. We all see folks who probably fall between 2-3 particularly those above age 50. What do we do with someone having low grade memory loss? Those scoring above 3 are definitely in the early stage of Alzheimer's. What is the right course of action given the paucity of effective treatments?

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From the Publisher

➤ *continued from page 4*

Lobay reflects on how the disease affects the patient and the family from a personal perspective. His description of a warm fire in the wood stove dying out, the last ember, is a metaphor of what happens to the vital, strong individual who slowly deteriorates as the disease progresses. There are times when dementia may be a treatable condition that could be potentially reversed; too often, there is none. Then we can only offer emotional, spiritual, and psychological support.

Final Issue of the *Townsend Letter*

When I started a newsletter in 1983 in Port Townsend, Washington, I had high hopes that it would be a vehicle to serve the alternative medicine and naturopathic community. Frankly, I was surprised how it transformed into a little magazine one year later and then a larger magazine by 1986. Back then there was no internet and no other publications for MDs and NDs. Indeed, it also served as a medium for supplement companies, specialty labs, compounding pharmacies, and medical meeting organizers. Our hay day continued through the 1990s and early 2000s. Since that time period, numerous journals have appeared both in print and online, podcasts became available on YouTube, and advertisers chose to advertise only digitally, no longer in print. Over the course of the past five years, the paid readership of the *Townsend Letter* has dropped precipitously. Additionally, advertising revenues have plummeted. Ironically, the writing excelled, perhaps with some hubris on my part, at its best level ever.

With insufficient funding the *Townsend Letter* is no longer able to produce a magazine. We will only continue the website and the e-newsletter. Truthfully, we are very much "in the hole" and need your support. (For those of you willing to keep this publication going and are open to contributing to its financial solvency, we are very open to your donation, big or small.)

We invite supplement companies, specialty laboratories, compounding pharmacies, and meeting organizers to advertise online with us in 2023. As a digital newsletter, we will be able to offer extensive advertising opportunities beyond what was previously available in the print magazine. Please join us in 2023 – after all we are now offering digital advertising!

For those of you who have subscribed and advertised to the print magazine, thank you, thank you, thank you. It has been a great run just short of 40 years, not bad for a startup newsletter just trying to be a forum for docs.

Jonathan Collin, MD

Reference

1. Naggie S, Boulware DR, Lindsell CJ, et al. Effect of Ivermectin vs Placebo on Time to Sustained Recovery in Outpatients with Mild to Moderate COVID-19: A Randomized Clinical Trial. *JAMA.* 2022;328(16):1595–1603. doi:10.1001/jama.2022.18590

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

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

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Shorts

briefed by Jule Klotter
jule@townsendletter.com

Treating Transgender Youth

The American Psychiatric Association (APA), American Medical Association (AMA), and the American Academy of Pediatrics (AAP) all advocate "gender-affirming care" for the growing numbers of adolescents who experience distress – even depression and suicidal tendencies – because their biological sex does not match their gender identity. This care consists of gonadotropin releasing hormone agonists ("puberty blockers") to suppress puberty. The idea is to give youths time to become comfortable with their birth gender or to decide to take hormones (estrogen or testosterone) that help them acquire characteristics of their desired gender. "Gender-affirming surgeries may follow in later adolescence or young adulthood," according to APA's 2020 Position Statement on Treatment of Transgender (Trans) and Gender Diverse Youth. APA's statement says, "Trans-affirming treatment….is associated with the relief of emotional distress, and notable gains in psychosocial and emotional development, in trans and gender diverse youth." Maybe this is true for some; but others, like Chloe Cole who has testified before state legislators and medical boards, deeply regret the treatment they received as young teens.

Unlike the US medical groups, health authorities in other countries are more cautious about advocating this type of medicalized treatment in these young people. In 2022, five AAP members asked the AAP (which ignored the request) to review the evidence and update their 2018 policy statement. In their proposed Resolution 27, these pediatricians cited the Finnish Health Authority, the Royal Australian and New Zealand College of Psychiatrists, France's National Academy of Medicine, the Swedish National Board of Health and Welfare, and the UK's National Health System (NHS) – all of whom found low quality evidence to support the use of hormone treatments in children and youths. These groups also voiced concern about serious long-term effects from using puberty blockers and cross sex hormones. Carl Heneghan, professor of evidence-based medicine at University of Oxford (UK) and Editor in Chief *BMJ EBM,* and Tom Jefferson wrote in a 2019 BMJ blogpost:

> There are a large number of unanswered questions that include the age at start, reversibility; adverse events, long term effects on mental health, quality of life, bone mineral density, osteoporosis in later life and cognition. We wonder whether off label use is appropriate and justified for drugs such as spironolactone which can cause substantial harms and even death. We are also ignorant of the long-term safety profiles of the different [gender-affirming hormone] regimes.

In 2022, the NHS announced the Spring 2023 closure of the Tavistock Centre in London, which provided England's only gender identity development service. A review, led by past president of the Royal College of Paediatrics and Child Health, Dr. Hilary Cass, found safety issues related to the center's "'unquestioning affirmative approach.'" The NHS will, instead, set up regional centers that focus on child health and development as well as mental health services to help the rising numbers of children with gender dysphoria. "In 2021/22 there were over 5,000 referrals to [Tavistock Centre], which compares to just under 250 referrals in 2011/12," according to Owen Evans. An NHS statement reported a "'dramatic change in the case-mix of referrals from predominantly birth-registered males to predominantly birth-registered females presenting with gender incongruence in early teen years.'" Many of the children also exhibit neurodiversity, mental health issues, and risky behaviors that cannot be attributed solely to gender dysphoria.

Adolescence – even in the best of societies – is a time of identity exploration and intense emotion. I cannot imagine trying to navigate this challenging period with the added stresses of social media, online sexualized videos, and panic-promoting media.

AAP Resolution 27. In Support of a Rigorous Systematic review of Evidence and Policy Update for Management of Pediatric Gender Dysphoria. March 31. 2022. https://genspect.org/wp-content/uploads/AAP_Resolution_27_2022.pdf

Evans O. Tavistock Transgender Clinic for Children to Close. *The Epoch Times.* July 28, 2022.

Heneghan C, Jefferson T. Gender-affirming hormone in children and adolescents. February 25, 2019. https://blogs.bmj.com

Making Public Health Decisions

On October 7, 2022, Florida's State Surgeon General Joseph A. Ladapo, MD, PhD, recommended that males between the ages of 18-39 years not receive mRNA Covid-19 vaccines/boosters due to increased risk of cardiac-related death. "Those with preexisting cardiac conditions, such as myocarditis and pericarditis," according to a press release, "should take particular caution when making this decision." His recommendation was based on an analysis of data from Florida's reportable disease repository (Merlin), Florida State Health Online Tracking System (FLSHOT$), and death records data from vital statistics. The analysis used the self-controlled case series method, an epidemiological design in which individuals act as their own controls. A 2016 *BMJ* article explains that this method was developed to evaluate vaccine safety. Florida residents, age 18 years or older, who died within 25 weeks of vaccination since the start of the vaccine roll-out (December 15, 2020) were included. The residents were excluded if they had a documented covid infection or covid-related death, received a booster, or got their primary series after December 8, 2021.

The analysis found a statistically significant increase in cardiac-related deaths for the entire population (RI=1.07, 95% CI=1.03-1.12). Those aged 25-39 had the highest increase (RI=2.16, 95% CI=1.35-3.47). (Data was sparse for the 18-24 age group.) "Risk was significantly higher during the risk period for males (RI=1.09, 95% CI=1.03-1.15) but not for females (RI=1.05, 95% CI=0.98-1.11)." In comparison, the all-cause death showed no increase overall during the same period. Moreover, participants over age 60 had a statistically significant decrease in all-cause mortality in the 28 days after vaccination (RI=0.97, 95% CI=0.94-0.99). The increased risk was associated with mRNA vaccines (Pfizer-BioNTech and Moderna), not non-mRNA products.

The analysis has several limitations, including its use of surveillance data and the sample size. It also does not take into account the use of multiple boosters. The authors also say that the data is from the first months of the vaccines' availability, and the risk/benefit has likely changed since then: "In the fall of 2022, most people have either been vaccinated or have natural immunity to COVID-19. Many have had multiple vaccine doses, multiple infections, or both. Research to assess the current risks and benefits of the COVID-19 vaccine to help update vaccine recommendations should be studied in this context."

Dr. Ladapo has a medical degree from Harvard University as well as a PhD in Health Policy from Harvard's John F. Kennedy School of Government. As he explains in his book *Transcend Fear – A Blueprint for Mindful Leadership in Public Health* ((Skyhorse Publishing, 2022), his PhD studies focused on decision sciences, "a field that focused on optimizing decisions by characterizing the risks, benefits, and trade-offs associated with different choices." After his residency in internal medicine, he obtained a faculty position as a clinician researcher at New York University and later University of California-Los Angeles and received multiple grants from the National Institutes of Health to conduct clinical trials focusing on behavioral interventions that help prevent cardiovascular disease.

Although Ladapo was successful professionally, long-standing anxiety, rooted in childhood trauma, threatened his relationship with his wife and three young sons. In late 2019, he began working with Christopher Maher, an ex-Navy SEAL, who used a combination of techniques based in Chinese meridian theory to heal his own emotional, physical, and spiritual pain. Maher wrote *Free for Life*; his website is truebodyintelligence.com. Ladapo credits the work with Maher for saving his marriage but also for allowing him to remain clear-headed when the covid pandemic hit.

Instead of being swayed by media-fed panic, Ladapo's "internal housecleaning" and his background in decision sciences allowed him to use data in a consistent way – acknowledging what was unknown while making recommendations on what was reasonably sure. Throughout 2020, he wrote articles for *Wall Street Journal*, using his skills in decision making and research. "The messages in these articles would have been considered bread-and-butter public health in the past: education of children is important, avoid divisive policies with little or no proven benefit, avoid using fear as a communication strategy, and consider both benefits and cost associated with policies," he wrote in his book. And it was this transparency in his articles and the consistency in his messaging that drew the attention of the governor who asked him to become Florida's state surgeon general.

Florida Health. Guidance for mRNA COVID-19 Vaccines. October 7, 2022. Floridahealth.gov.
Florida Department of Health. Exploring the relationship between all-cause and cardiac-related mortality following COVID-19 vaccination or infection in Florida residents: a self-controlled case series study. https://floridahealthcovid19.gov/wp-content/uploads/2022/10/20221007-guidance-mrna-covid19-vaccines-analysis.pdf
Petersen I, Douglas I, Whitaker H. Self controlled case series methods: an alternative to standard epidemiological study designs. *BMJ.* 2016;354:i4515.

Casualties of Unpopular Science

The November 2022 "Shorts" column included a piece about the review article by Seneff S, et al: "Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs," published in Elsevier's *Food and Chemical Toxicology* (*FCT)* in April 2022. The article's authors included MIT research scientist Stephanie Seneff, PhD; Greg Nigh, ND, LAc; microbiologist Anthony Kyriakopoulos, PhD; and Peter McCullough, MD, an internationally known cardiologist. The article presents evidence that the synthetic vaccine mRNA may interfere with the body's immune response against infections and cancers. The paper was submitted in response to a request by *FCT*'s editor-in-chief, Dr. José Luis Domingo, who sought papers on vaccine safety: "'…the goal in calling for research on potential toxicological effects of the vaccines, was to reduce skepticism to vaccination,'" according to *The Epoch Times.* Dr. Domingo is a respected toxicologist who has served on the editorial boards of over 11 scientific journals and became *FCT*'s Editor-in-Chief in 2015.

Recognizing that the paper was controversial and involved a "'very sensitive social and scientific topic,'" Dr. Domingo asked five outside scientists – instead of the usual two or three

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Shorts

➤ ***continued from page 9***

– to "scrutinize" the article: "They provided detailed written feedback and required the authors to do three rounds of revisions. After the third iteration, all five were unanimous in recommending the paper be accepted."

About a month after publication, Domingo began receiving "angry emails and messages. These included insults, calls to resign, demands to retract the paper, and even threats." Domingo received only one scientific response to the review article. He agreed to publish it as a Letter-to-Editor if it passed peer review, but three of four reviewers deemed it "'scientifically poor'" even after it was revised and re-submitted following a first peer review. Despite the pressure, Dr. Domingo refused to retract the Seneff et al paper.

On October 28, Dr. Domingo sent out an email to colleagues with the subject heading: "My resignation as Editor-in-Chief of FCT induced by the PUBLISHER…." Although his contract actually ends on December 31, 2023, Dr. Domingo explained that he sent publisher Jagna Mirska a letter of resignation on October 16, 2022. In this email, Dr. Domingo states that Bryan Delaney, PhD, was appointed the new Editor-in-Chief even before his resignation had been accepted. According to *The Epoch Times,* Delaney, a toxicologist, works for Haleon, GlaxoSmithKlein's consumer health unit. Dr. Domingo stated in his email that his public request for studies looking at "potential toxicological effects of the vaccines for the COVID-19" and his refusal to retract the Seneff paper "was the final nail in my coffin."

Also in October, coincidently (or not?), Peter McCullough, co-author of the *FCT* paper, was "terminated as the Editor-in-Chief of *Cardiorenal Medicine* and *Reviews in Cardiovascular Medicine* after years of service and rising impact factors." "There was no phone call, no board meeting, no due process. Just e-mails or certified letters," he wrote in an email to Steve Kirsch. Dr. McCullough is one of many doctors who advocated early covid treatment (see "Shorts" July 2021) and co-authored the book *The Courage to Face COVID-19: Preventing Hospitalization and Death While Battling the Biopharmaceutical Complex* with John Leake. As a cardiologist with over 500 peer-reviewed articles to his name, McCullough has been outspoken about the adverse cardiovascular effects of mRNA vaccines, particularly in young people. In addition to this termination, McCullough was stripped of his board certifications in internal medicine and cardiology "after decades of perfect clinical performance, board scores, and hundreds of peer-reviewed publications" on October 28, 2022.

Kirsch S. Dr. Peter McCullough is being progressively stripped of his medical credentials. October 29, 2022. https://stevekirsch.substack.com/
Margulis J, Wang J. Editor-in-Chief of Renowned Science Journal Ousted for Publishing Science Questioning COVID-19 Vaccine Safety. *The Epoch Times.* October 30, 2022.

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Dried Blood Spots (DBS) as an Alternative to Venipuncture Serum for Testing Hormones

by David T. Zava, PhD

Serum vs DBS – A Brief History

Serum/plasma derived by conventional venipuncture blood draw has been the mainstay for testing steroid, thyroid, and peptide hormones, blood lipids, and myriad other analytes associated with the endocrine system. However, finger-prick blood drops collected and dried on filter paper (Dried Blood Spot, DBS) and used for testing endocrine biomarkers is proving to be a convenient alternative to serum/plasma testing.

Dried blood spot testing has advantages over conventional venipuncture – especially when monitoring topical hormone treatment.

Nearly 60 years ago Guthrie and Susi[1] first reported on the use of heal-stick neonatal blood drops dried on filter paper for measuring phenylalanine to detect phenylketonuria, a genetic metabolic disorder. Today finger-prick DBS is proving to be an excellent alternative to conventional venipuncture blood serum/plasma collections for therapeutic monitoring of the clinical markers associated with the endocrine system.[2-10]

Advantages of DBS for Testing Endocrine Biomarkers

DBS collection has advantages over conventional venipuncture, the most significant being that the former can be done at home by the patient and shipped directly to the testing laboratory by regular mail without coolants (cold chain), which is required with liquid blood serum/plasma. Home collection of DBS and the ability to ship the DBS directly to the testing laboratory circumvents the need to drive to a blood collection center or doctor's office for venipuncture blood collection. DBS collection at home also allows for collection to occur at the most appropriate time of day and month, which is important when monitoring sex-hormone levels at specific stages of the menstrual cycle, or in individuals monitoring pre- and post-hormone therapies where timing of collection from last use of a hormone to time of collection is important.

DBS collection has also opened doors allowing anthropologists and endocrine researchers opportunities to study populations in remote areas where access to phlebotomists and equipment needed to process (centrifuge), preserve, and ship (coolants for shipment/refrigeration) liquid blood samples are not available. DBS collections also offer advantages for blood collections in the elderly and children where venipuncture is difficult (poor or small veins) or not possible (remote setting).

Numerous reviews have been published, mostly over the past 20-30 years, on the pros and cons of finger-prick DBS vs venipuncture liquid serum/plasma for testing a broad spectrum of analytes. The following review references are a handful of those available. Here I have focused mostly on the references where DBS has been used for testing endocrine biomarkers relative to serum/plasma.[3,8-15]

Since Guthrie first recognized the advantages of stabilizing amino acids like phenylalanine in blood by simply allowing the blood to dry on filter paper, myriad other blood markers have been shown to be stabilized in DBS for prolonged periods of time when processed, shipped, and stored at ambient temperature.[8,11] Drying of the blood on filter paper to create the DBS simply removes the water, which inhibits oxidation of biomarkers and effectively inhibits enzymes that otherwise degrade these biomarkers in liquid blood serum/plasma if kept at ambient temperature during shipment. Liquid blood/serum requires cooling or freezing to prevent analyte degradation.[8,11]

The consensus of many researchers who have reviewed scientific literature published on DBS technology is that most biomarkers that are measured in serum/plasma can effectively be measured in DBS with quantitatively equivalent results once the difference in DBS and liquid blood serum derived from whole blood are taken into consideration,[2,3,8-19]

In our experience of developing DBS tests over the past 25 years for steroid and peptide endocrine biomarkers,[4,5-7,20] essential elements and heavy metals,[22] and Covid antibodies,[21] we have found that steroid, thyroid, and other peptide hormone endocrine biomarkers quantified in finger-prick capillary DBS are quantitatively equivalent to serum/plasma levels, when validation methods take into consideration the expected average serum/plasma content of whole blood. However, there are several exceptions where DBS cannot be used to quantify serum biomarkers, or where the

levels of hormones in DBS vs serum are very different.

Perhaps the most significant drawback to testing endocrine biomarkers in DBS is that the amount of serum in the typical 3 mm or 6 mm disks punched from the original DBS is lower than needed for conventional testing by immunoassays. Testing the very low concentrations of estradiol in men, postmenopausal women, and children, and testosterone in women and children, is more of a challenge than with serum/plasma testing which uses higher volumes to compensate for lower concentrations of estrogens and androgens in these individuals. For example, one 6 mm disk punched from a DBS contains about 12 microliters (µL) of whole blood, about half of which is blood cells and half liquid blood serum/plasma, assuming a hematocrit of about 40-50%. In processing about 6 µL of blood serum from the 6 mm disk, it is necessary to dilute the blood extracted from the DBS disc about 10-fold to enable extraction from the disk and provide ample volume of sample necessary for analyte testing.

For some steroids such as DHEAS and cortisol, and testosterone in men, levels of these steroids are in the ng/ml range and are high enough to accurately measure them by immunoassays using 96 well plates or automated bead assay formats.[8] In contrast, measurement of estradiol and testosterone can be a challenge in some individuals with very low levels of these hormones. Lower analytical sensitivity of tests for some markers can be a limitation to DBS; however, we and others have found that the limitations of analytical sensitivity with steroid immunoassays can be overcome with more advanced and sensitive methods of steroid testing using LC-MS/MS.[3,9,11,19] In our laboratory (ZRT) steroids present in DBS are now only measured by fully validated LC-MS/MS methods as we originally reported.[20]

Many studies have demonstrated that drying blood on filter paper stabilizes most analytes (steroids) and most other small nonpolar molecules rendering them stable for at least a month at ambient temperature. This is ideal for research participants or for individuals who prefer to collect blood at home, avoiding clinical environments that may increase risk for exposure to pathogens.[3,11,21]

As mentioned above and available in references herein, many clinical research studies have shown that levels of analytes in liquid (serum/plasma) and dried blood (DBS) are quantitatively equivalent when corrected for serum/plasma blood volume. With DBS testing, the assumption is made that the punched disk(s) from the DBS that are used for analysis of biomarkers contain the same volume of liquid blood serum or plasma, which must be corrected as a constant with validation studies to derive a serum/plasma equivalent. Slight differences are seen when the blood hematocrit falls outside the normal range of about 35-55% or when disks prepared from blood drops are smaller (<20 ul of blood applied to the filter paper) than the recommended full hanging blood drop of 30-50 ul that optimally should be applied

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to filter paper.[9,17,21] Less accurate results are also seen when the blood drop applied to the filter paper is allowed to bleed through the paper to the backside nonabsorbent protective sleeve.[9] This is more problematic with 5-spot collection cards where the back protective cover is more difficult to separate from the filter card during blood spot collection, allowing some blood to flow through the filter card onto the backside cover. DBS collection instructions must be very clear to prevent bleeding of finger-prick blood drops through the filter card onto the back protective sleeve.

DBS and Serum Show Excellent Quantitative Concordance When Testing Endogenous Hormones

In our experience, testing many of the analytes associated with the endocrine system (steroids, thyroid, peptides, blood lipids) as well as essential and toxic elements[22] and viral antibodies,[21] we have found excellent quantitative concordance of finger-prick DBS with venipuncture serum/plasma results.[5-7,20,23-25] While most steroid hormone therapies and different delivery systems for them (oral, troche, topical, transdermal patch, vaginal, subcutaneous/intramuscular injections, pellets, etc.) give more equivalent results when tested by serum/plasma or DBS,[4,5] there is one very notable exception – therapy with topical steroid hormones.

Topically Delivered Steroids Don't Obey the Rules

For reasons that are not fully understood, but well documented throughout the literature, topically delivered steroid therapy results in dose-associated increases in the levels of the supplemented steroid in DBS and saliva with very little to no increase in venous blood levels of the steroid derived by venipuncture[6,7] until the dosing rises above physiological levels. Of interest, and relevant to the efficacy of topical steroid hormone delivery, physiological topical dosing results in physiological levels of hormones in finger-prick capillary DBS, but not venipuncture serum, plasma, or whole blood[6,26] derived from venipuncture. Levels of urine steroid metabolites also do not increase significantly and follow the pattern of serum in that levels of the supplemented steroids don't begin to rise above their baseline levels until the dosing is within high-physiological to pharmacological range.

What we find to be universally true for all topically delivered steroids (estrogens, progestogens, androgens, glucocorticoids) in postmenopausal women and older hypogonadal men is that a physiological dose of the topically applied steroid results in an increase from baseline to physiological levels seen in healthy younger individuals at about 12-24 hr post therapy. In sharp contrast, the same physiological topical dosing has little impact on venipuncture serum and urine levels of steroids, leaving the impression that the steroid is poorly absorbed.

Topical Progesterone at Physiological Dosing in Postmenopausal Women Increases Capillary Blood (DBS) to Peak Physiological Levels Seen at Mid-Luteal Phase

Some of the best examples demonstrating that topical delivery of physiological amounts of steroids results in physiological levels in DBS are research studies exploring the use of topical progesterone. What we and others find is that a topical progesterone dose of about 20-30 mg, the amount produced by the ovaries during peak of the luteal phase, results in a DBS level of about 10-40 ng/ml at 12-24 hr post-therapy. This dose of progesterone currently is available in many compounded progesterone formulations, as well as OTC products. With this same topical progesterone dose, no or very little change in serum/plasma or urine progesterone is seen.

In a clinical study[6] investigating progesterone levels in saliva, finger-prick capillary blood (DBS), venipuncture serum, and whole venipuncture blood following topical progesterone use, striking differences in body fluid distribution were seen. In this carefully controlled study women applied a high physiological dose (80 mg) of topical progesterone with gloved hands to the inner thighs for 14 days; and on the last day of application, saliva, DBS, venipuncture serum, and venipuncture whole blood were collected. Blood samples were numerically coded and sent to our laboratory for testing. Testing was performed and the coded results were sent back to the clinical coordinating center for data analysis and correlation with levels in different body fluids. What our research group showed is that progesterone rose dramatically above baseline several hours later in saliva and DBS, but did not increase at all in venipuncture serum or venipuncture whole blood. That progesterone was not present in venipuncture whole blood, despite having used this dose for 2 weeks prior to testing multiple times over a 24 hr period with the same dose, dispelled the notion that the progesterone was being carried on the red blood cells and from there delivered to tissues. In fact, in this study we found that venipuncture whole blood had half the value of progesterone because nearly all the progesterone released into the blood-vascular system is carried in the serum/plasma, and not the red blood cells.

I and others had originally proposed as an explanation for the wide discrepancy in saliva, and DBS vs serum progesterone levels, that the reason progesterone was not detected in serum was due to it being held by the cellular compartment (red blood cells) of blood and removed from serum by centrifugation of blood. This does not appear to be the case since we showed that whole venipuncture blood was lower (about half) than blood serum levels, demonstrating that the much higher progesterone levels detected in finger-prick capillary blood could not be accounted for by binding of progesterone to red blood cells that are removed with clotting and preparation of serum.

Topical Testosterone Therapy in Men and Women Follows the Same Pattern as Topical Progesterone

It is important to recognize that what we see with body fluid distribution of progesterone following topical progesterone therapy is also true for other steroid hormones delivered topically. For example, topical testosterone

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Relax Sauna - Heavy Metal Report

Karen Russell, a Los Angeles health consultant, who accumulated high levels of heavy metals, mercury and lead. Tried DMSA treatment, supplements and foot detoxify treatments in the past 3 years but still had trouble detoxifying heavy metals. Dr. Doris J Rapp, MD recommended a Relax Far Infrared Sauna.

Karen used her sauna everyday and successfully got the mercury level back to normal.

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Laboratory Report:

Karen's case was shared with a local MD, an authority on heavy metal detoxification therapy. The medical doctor clearly points out. Heavy metals have two chemical bonds that stick to fat tissue.

It makes heavy metals almost impossible to remove from the human body. Some standard heavy metal detoxification treatments are Meso-DMSA, DMPS, D-Penicillamine, CaNa2EDTA, and BAL (Dimercaprol). Chelation therapy is done by inserting chelation drugs into the body through an IV. Pill form is also available.

Those treatments can be painful, expensive and can also cause serious side effects

Relax Sauna is a Detoxification Tool

An electrical engineer patient, who had not been diagnosed with heavy metal toxicity participated in the same experiments as Karen. His urine samples were collected before and after using the Relax Far Infrared Ray (FIR) Sauna. When they analyzed the urine samples, the were interesting, to say the least.

The laboratory data showed Triple amounts of Arsenic and Nickel had been removed from his body. The before and after results from his urine tests detected (Arsenic: Before- 89.2 ug/g-creatinine; after- 220 ug/g-creatinine).

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therapy also raises DBS and saliva levels of testosterone in a dose-dependent fashion but has little, or much less, impact on serum levels. WADA (World Anti-Doping Association) researchers investigating topical testosterone abuse in sports[27-29] recently published studies on male and female volunteers who used topical testosterone and measured levels in venipuncture serum and finger-prick DBS and saliva. What these investigators discovered is that topical testosterone users had a much higher (10-20x) level of testosterone in DBS and saliva than in serum. These results are more evidence that topically delivered steroids are transported slowly throughout the body without entering venipuncture blood, as we have reported for topical progesterone.[6,26]

Blood or Lymphatic Delivery of Topically Applied Small Non-Polar Molecules to Tissues?

The most logical explanation for topically delivered steroid hormones showing up in saliva, finger-stick capillary blood (DBS), and tissues[6,26,30] is that the hormones are being delivered systemically from the site of application to the tissues without moving through the blood vascular system. As I have discussed in previous publications,[6,7,26,31] it is likely that small nonpolar molecules such as steroids, enter the lymphatics present at the surface of the skin and are slowly transported through the lymphatic system to tissues rich in lymphatics such as the salivary glands, tips of the finger, reproductive tissues (uterus, breasts), and brain (glymphatics). In fact, this may explain why the level of salivary hormones increases more dramatically than the fingertip because the salivary glands have a greater abundance of lymphatics. It would also explain why the breast tissue, and likely other reproductive tissues rich in lymphatics, respond so well to the protective effects of topical progesterone[31] without affecting serum progesterone levels.

First-Pass or No-Pass Effect with Topical Steroid Therapy

That topically delivered steroids are not present in the saliva and fingertip DBS samples until about 2-6 hr after distant application is consistent with slow transport from site of application to lymphatic-rich systemic tissues. As we reported[6,26] in the study with women using topical progesterone daily for 2 weeks prior to measuring progesterone in different body fluids, there was essentially no progesterone in venipuncture serum or whole blood, meaning that there was no "first pass" effect with progesterone, but rather a "no pass" through the liver via the blood vascular system. This would explain why we see in our clinical testing for DBS and saliva that other hormones such as DHEA delivered topically, but not orally, rise in a dose-dependent fashion without a similar increase in DHEA sulfate or 7-keto DHEA, as measured by LC-MS/MS. Again, another example of a "no pass" effect with topical steroid delivery.

Potential for Overdosing When Measuring Serum or Urine with Topical Steroid Hormone Therapy

The novel concept of steroid hormones being delivered through the lymphatics when applied topically has certainly caused considerable confusion among health care professionals using topical hormones, as these results, based on conventional venipuncture serum testing, could be interpreted to mean that topical hormones are poorly absorbed and that higher, more pharmacological doses, are necessary to raise the serum, and presumably, the tissue levels of the supplemented topical hormone. An alternate explanation, and one that seems more logical based on serum, DBS, saliva, and urine test results and clinical efficacy of low dose topically delivered steroid hormones, is that topical steroid hormone therapy, which increases saliva and DBS levels in proportion to dosing, would seem to be more accurately portraying tissue levels of the hormone than is serum/plasma derived from venipuncture. It is important to keep in mind that levels of all the steroids and other analytes (thyroid and peptide hormones) we have tested and validated for commercial testing are quantitatively very similar in serum/plasma and in DBS when the hormones are produced endogenously or exogenous steroid hormones are delivered by other means such as intramuscular or subcutaneous injections, pellet, oral, troche/sublingual, or even transdermal patch therapies.

More Research Needed

Clearly more research is needed to elucidate the mechanism of transport of topically delivered steroids to systemic sites such as the fingertips, salivary glands, reproductive tissues (breasts and uterus), and the brain. Clinical studies with application of physiological amounts of topical estradiol and progesterone have shown that estrogenic and progestogenic effects can be seen in breast and uterine biopsies post therapy without significantly affecting serum levels.[26,31] If the mechanism of lymphatic transport of small non-polar molecules such as steroids from the skin to reproductive and other tissues is accurate,[26] then use of serum/plasma and urine testing may be giving the false impression that the patient using topical steroid hormone therapy is underdosed and may lead to unnecessary dose escalation. It also raises concern for how small non-polar toxins such as pesticides and herbicides, or other non-polar molecules applied to the skin, might enter the body through the skin and be transported through the lymphatics to tissues where they would concentrate and potentially increase risk for dysfunction and cancer of lymphatics and reproductive tissues.[32] ◆

Dr. Zava earned his PhD in biochemistry and has extensive experience researching hormones and breast cancer. He established ZRT Laboratory in 1998 to provide health care practitioners and patients with a deeper understanding of the role hormones play in wellness, and remains a strong advocate of wellness through preventative health. He is the co-author of *What Your Doctor May Not Tell You About Breast Cancer* and the author of many peer-reviewed articles.

References are available online at www.townsendletter.com.

Test and Address: The Clinical Importance of Direct Assessment of Gut Microbial Abundance and Diversity

by Julia Malkowski, ND, DC

Gone are the days of simply identifying a gut pathogen, prescribing an antibiotic and moving onto the next biological system. Although the identification and eradication of pathogens remains important, it is no longer sufficient. Recent advancements, most notably DNA technology and culturomics, allow us to identify the details of vast microbial communities held within our human biology. We have discovered that many seemingly disparate conditions ranging from anorexia nervosa, neurotransmitter imbalance, extroverted behavior, major depressive disorder, sleep physiology and aging have all been linked to the gut microbiome.[1-6] Abundance and diversity are the foundation of the gut microbiome and intricately connected to various health outcomes. Diversity of species is an important component of health for any ecosystem, and the gastrointestinal (GI) microbiome is no exception. Even colic in infancy is associated with decreased gut microbial diversity.[7] Chronic preventable lifestyle diseases, those categorized as potentially more difficult to treat, also have a link to microbiome abundance and diversity.[8] As the father of medicine Hippocrates predicted, "all disease begins in the gut."[1] The key to understanding this sage adage may lie in testing and addressing gut microbial abundance and diversity.

To fully understand the human GI microbiome, we may begin with our past. The Hadza tribe of Tanzania are the closest living approximation to our ancestry as they have remained largely unchanged for thousands of years. They do not store any food yet subsist by hunting with hand-made bows and arrows and foraging for edible plants, especially tubers, akin to our modern-day potato.[9] Today, proponents of paleo and carnivore diets would lead one to believe the hunter-gather diet consists primarily of meat. Contrary to pop culture belief, nearly all warm climate hunter-gather diets consist of a mixture of plants and meats, actually approximating 50/50.[10] The fact remains that hunting is an endeavor ending in failure more often than not, hence the gathering of carbohydrates account for a sizeable portion of pre-agrarian diets. The most frequently consumed food of the Hadza, is also their least favorite, tubers.[9] These tubers contribute to their notable daily fiber intake of approximately 100-150 g QD.[10] In contrast the standard American diet contains approximately 15 grams of fiber QD, while the current Dietary Guidelines recommend approximately 30 grams QD.[11] This is relevant as fiber, specifically soluble fiber, is linked to gut microbial abundance and diversity, which is in turn associated with a wide variety of health outcomes. Generally speaking for produce, one-third of the fiber will be soluble and two-thirds of the total is insoluble.

A rich diverse gut microbiome is the foundation for human health.

Regarding the microbiome, native tribes denote some distinct findings. A key difference to our modern guts is that native guts comprise many bacteria that aid specifically in the digestion of carbohydrates, such as *Prevotella* species.[12] While *Prevotella* is found in modern humans, in excess populations this may be associated with dysbiosis. This complex finding underscores the unique nuances associated with the gut microbiome and host physiology. Findings may not be extrapolated across certain populations, and bacteria may exert different influences depending not only on environment, but neighboring bacteria as well. Second, native people across the globe display a significantly marked increase in gut microbial diversity compared to modern populations.[9] This is germane, as not only is microbiome diversity associated with health outcomes, it has been progressively decreasing over time.

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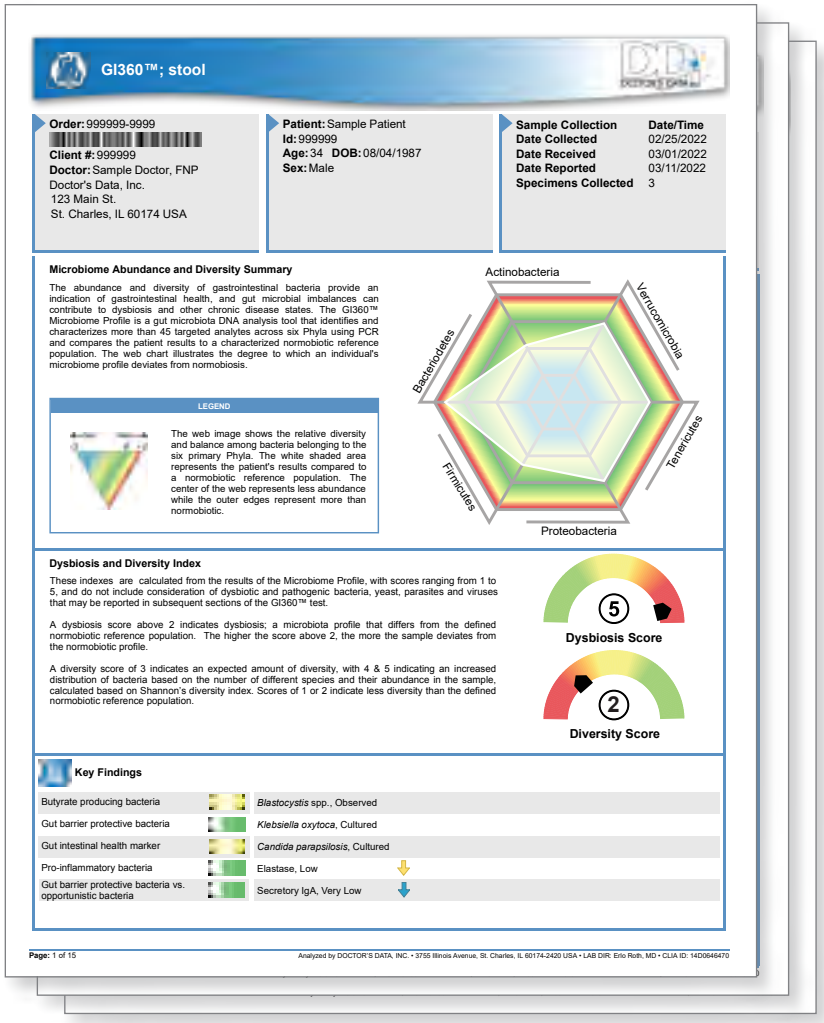

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Humanity began with rich diverse microbiomes, yet the advent of agriculture, industrialization, and urban living have all been accompanied by a decrease in gut microbial diversity.[12] This is pertinent as a rich diverse gut microbiome is the foundation for human health. Furthermore, immigration to a Westernized nation results in decreased gut microbial diversity and exacerbates with succession of each generation.[13] This phenomenon is in turn associated with the development of cancer, diabetes mellitus, obesity, asthma, allergies, neurodevelopmental disorders, autoimmunity and inflammatory bowel conditions.[13] Lifestyle, decreased gut microbial diversity, and the development of chronic disease seem to go hand in hand. To make matters worse, currently agreed upon healthy diets such as the Mediterranean diet do not foster gut microbiome diversity that equates to that of our ancestors.[12] Modern guts display decreased diversity in the long run, yet we may approximate a "new normal" healthy gut as a metric. Regardless of lifestyle, a rich diverse and abundant gut is best equipped to perform its functions.

The GI microbiome is a highly complex, intricate network of a multitude of bacteria (as well as yeast, viruses, archaea and their respective DNA) that operate synergistically. The microbiome largely develops as a result of geography, method of delivery, environmental exposure, and nutritional diet. Factors such as host interindividual differences and quorum sensing, the ability of bacteria to communicate, and even transfer genes play a role in the gut microbiome. Microbiome abundance and diversity consist of the numbers of bacterial species and their populations. While keystone bacteria, including but not limited to *Lactobacillus spp., Bifidobacterium spp., Akkermansia muciniphila* and *Faecalibacterium prausnitzii,* have proven valuable, they don't represent the entire GI bacterial community.

Once exclusively discussed by a subset of specialists, names like *Lactobacillus* have become a common household item. Generally recognized bacteria include *Bifidobacterium spp.,* especially in reference to the *Firmicutes/ Bacteroidetes* balance. Of note, research in this area denotes mixed results and this ratio may not be as conclusive as once thought[14] – again, highlighting the importance of abundance and diversity. *Faecalibacterium prausnitzii* and *Akkermansia muciniphila* have arisen as noteworthy bacterium in regards to human physiology. Although yet to join the common vernacular, *F. prausnitzii* is a keystone bacterium associated with butyrate production and its anti-inflammatory properties. Decreased levels of *F. prausnitzii* have been associated with GI inflammation, irritable bowel syndrome, inflammatory bowel disease, celiac disease, Parkinson's disease, bipolar disorder and major depressive disorder.[15] Low FODMAP diets have been shown to denote a deceased level of vital *F. prausnitzii* and subsequent fecal butyrate levels as well.[15] Consider appropriate stool testing for individuals participating in a Low FODMAP diet.

Akkermansia muciniphila is amongst the most en vogue bacteria of the moment as it emerges as a keystone bacterium. This bacterium is being touted as self-help for its anti-anxiolytic properties, and in commercial probiotics, and even online weight loss forums. *A. muciniphila* means mucus loving and the implication here is its influence over mucosal barrier integrity. Importantly, compromised intestinal mucosal barrier integrity is the precursor to intestinal permeability. Therefore, *Akkermansia* plays an important role in the pathogenesis of intestinal permeability, autoimmunity, and is implicated in inflammation, metabolism, and immune processes.[16] Recently the efficacy of cancer therapeutics has been shown to be influenced by GI microbial levels of *A. muciniphila.*[17]

In an effort to align host physiology and traditional monotherapy, the quest to identify a distinct bacterial species of greatest significance to human health has emerged. One serving of the typical probiotic on the market contains between 100 million and a few hundred billion bacteria of one or multiple strains.[1] In theory this may improve microbiome abundance and diversity, yet keep in mind factors regarding living bacteria such as manufacturing, stability, transportation, and the extremely acidic GI tract. Once that hurdle has been addressed probiotics may be appropriate at times, yet this is not root cause medicine. From a functional medicine perspective, probiotics do not address the root cause and may be utilized as an acute intervention. Clinical decision making based on probiotic theories is also complex. Keep in mind that rarely have more than two clinical trials with the same probiotic strain and same diagnosis been performed.[18] Diversity is paramount even when it comes to probiotic supplementation. More diverse guts have been shown to benefit from probiotic therapy via increased abundance and diversity, while less diverse guts have denoted a lack of significant changes to the microbiome.[12] Those very individuals in need of probiotic therapies may not even receive benefit if they have a less diverse microbiome to begin with. Lastly, the cost of probiotic therapies may not be financially feasible long-term. An approach to seed the colon with probiotics and feed these supplements with soluble fiber and polyphenols may prove efficacious.

In lieu of bacteria in a pill bottle, our ancestors likely inoculated their system by "washing" their hands in the entrails of hunted game as the Hadza do today.[9] In effect, essentially bathing the hands in microbes that are almost certain to travel to their mouths and eventually land in the colon. As this idea hasn't become a health craze yet, we may implore the next best logical solution; fermented foods, soluble fiber and polyphenols to support our gut microbiome. Fermented foods support a rich diverse and abundant gut microbial community. Fermented foods, such as

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yogurt, kimchi, kefir and kombucha, have proven to lead to increased gut microbial diversity.[12]

The next consideration is that these bacteria need proper energy sources to ensure optimal abundance. The preferred energy source of the bacterial residents of the GI microbiome is soluble fiber. Providing adequate dietary soluble fiber at 8-15 grams QD will typically support optimal populations. Polyphenols play a role as well. *Akkermansia* and *Lactobacillus spp.* consume polyphenols such as berries, green tea, chocolate, red wine, cranberries, pomegranate, curcumin, grapeseed, etc. An effective strategy to support proper gut microbial populations is to consume or supplement with polyphenols in addition to soluble fiber daily. Recall, bacteria are able to communicate and encourage growth of one another. Supporting keystone bacteria, may in turn support other species as well. To effectively address the GI bacterial ecosystem, one must consider the bacteria as the unique organisms they are supporting their abundance and diversity.

Supporting healthy gut bacterial communities is an aspect of human health and individualized medicine. As health care providers we may evolve beyond a simplistic "test and treat" approach regarding the gut microbiome, to a "test and address" lexicon integrating the significant roles our gut bacteria play pertaining to health. Predominant topics of health and medicine intersect at the microbiome where abundance and diversity are paramount. Addressing microbial gut diversity and abundance alongside existing therapies may improve health outcomes. We already see this approach in action regarding chemotherapy and cancer therapeutics with promising results.[17] Gut microbiome research is at the forefront of medicine and specific GI microbial applications may have a medicinal future, even as targeted cancer therapeutics.[17]

The best evidence supports a comprehensive evaluation of the gut microbiome as it relates to health outcomes. Current research suggests that optimal stool testing includes microbial abundance and diversity, as well as dysbiosis. GI360™ includes a summary for clinicians regarding abundance and diversity. Our research shows there is an inverse correlation between the Diversity Score and the Dysbiosis Index. The Diversity Score provides a wealth of information in a simple value. Research consistently demonstrates that microbiome abundance and diversity is of utmost consideration as it influences human health. GI360™ is unique in that it offers information regarding abundance and diversity, the Dysbiosis Index and Diversity Score, in addition to traditional stool marker. This is important as human physiology and countless health outcomes are rooted in the gut microbiome. We are at a time when chronic diseases are skyrocketing as gut microbiomes are dwindling. Recommending bacteria in a pill is not the best remedy. The evidence overwhelmingly points to a comprehensive "test and address" approach to the gut microbiome.

Dr. Julia Malkowski graduated with a doctorate in naturopathic medicine in 2017 (advanced standing) and a doctorate in chiropractic medicine from National University of Health Sciences in 2016. Dr. Malkowski's clinical rotation focused on drug-free and surgery-free approaches to improving health conditions. During this time, Dr. Malkowski completed the Biomedical Treatment for Autism Spectrum Disorders Seminar, Mastering Brain Chemistry and 100 hours in Functional Neurology applied to Childhood Neurobehavioral Disorders. Dr. Malkowski has spoken at International College of Integrative Medicine, Laboratory, Endocrine, & Neurotransmitter Symposium, National Nurse Practitioner Symposium, and Mid-Atlantic Conference.

References

1. Lyon L. 'All disease begins in the gut': was Hippocrates right?. *Brain*. 2018;141(3):e20. doi:10.1093/brain/awy017
2. Seitz J, Trinh S, Herpertz-Dahlmann B. The microbiome and eating disorders. *Psychiatr Clin North Am*. 2019;42(1):93-103.
3. Evans SJ, Bassis CM, Hein R, et al. The gut microbiome composition associates with bipolar disorder and illness severity. *J Psychiatr Res*. 2017;87:23-29.
4. Gacias M, Gaspari S, Santos PMG, et al. Microbiota-driven transcriptional changes in prefrontal cortex override genetic differences in social behavior. *Elife*. 2016;5.
5. Pedersen T. Gut Bacteria Impacts Toddlers' Behavior, Particularly Boys. Published online August 8 2018
6. Smith RP, Easson C, Lyle SM, et al. Gut microbiome diversity is associated with sleep physiology in humans. *PLoS One*. 2019;14(10):e0222394. Published 2019 Oct 7.
7. Sonnenburg J, Sonnenburg E. *The Good Gut: Taking Control of Your Weight, Your Mood, and Your Long Term Health*. Bantam Press; 2015
8. Hills RD Jr, Pontefract BA, Mishcon HR, Black CA, Sutton SC, Theberge CR. Gut Microbiome: Profound Implications for Diet and Disease. *Nutrients*. 2019;11(7):1613. Published 2019 Jul 16.
9. Schnorr SL, Candela M, Rampelli S, et al. Gut microbiome of the Hadza hunter-gatherers. *Nat Commun*. 2014;5:3654. Published 2014 Apr 15.
10. Pontzer H, Wood BM, Raichlen DA. Hunter-gatherers as models in public health. *Obes Rev*. 2018;19 Suppl 1:24-35.
11. Available at How much (dietary) fiber should I eat? (usda.gov). Accessed on October 12, 2022.
12. Sonnenburg JL, Sonnenburg ED. Vulnerability of the industrialized microbiota. *Science*. 2019;366(6464):eaaw9255.
13. Vangay P, Johnson AJ, Ward TL, et al. US immigration westernizes the human gut microbiome. *Cell*. 2018;175(4):962-972.e10.
14. Magne F, Gotteland M, Gauthier L, et al. The Firmicutes/Bacteroidetes Ratio: A Relevant Marker of Gut Dysbiosis in Obese Patients?. *Nutrients*. 2020;12(5):1474. Published 2020 May 19.
15. GI360 Resource Guide. Available at https://www.gi360.com/resource-guide. Accessed September 20, 2022.
16. Hasani A, Ebrahimzadeh S, Hemmati F, Khabbaz A, Hasani A, Gholizadeh P. The role of Akkermansia muciniphila in obesity, diabetes and atherosclerosis. *J Med Microbiol*. 2021;70(10).
17. Derosa L, Routy B, Thomas AM, et al. Intestinal Akkermansia muciniphila predicts clinical response to PD-1 blockade in patients with advanced non-small-cell lung cancer. *Nat Med*. 2022;28(2):315-324.
18. Brüssow H. Probiotics and prebiotics in clinical tests: an update. *F1000Res*. 2019;8:1157.

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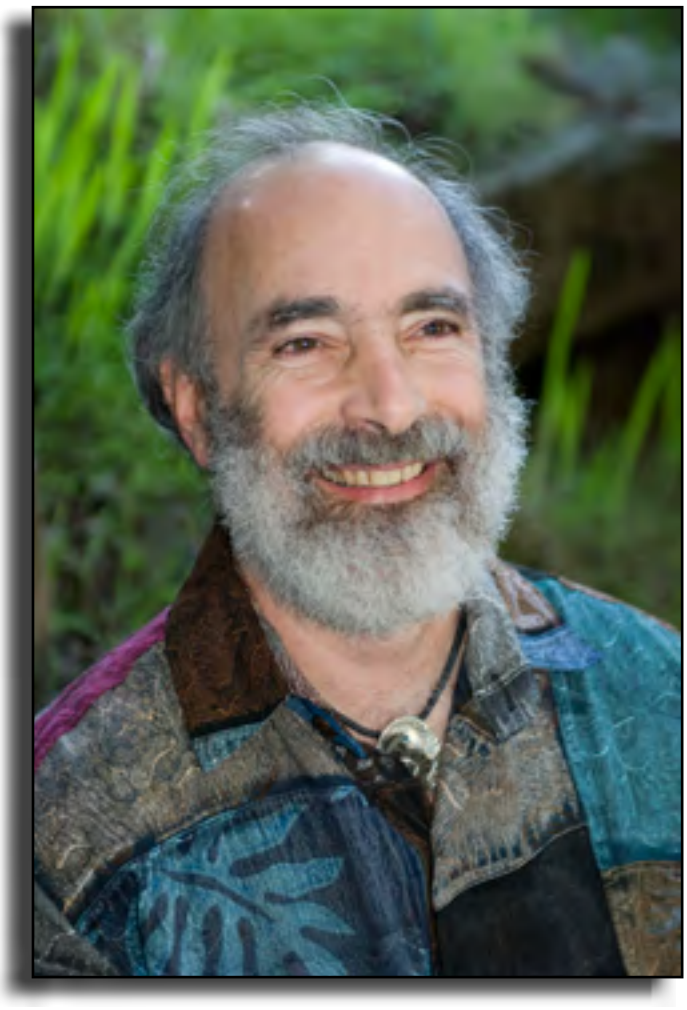

In Memoriam: David Getoff

Vice President, Price-Pottenger Nutrition Foundation

David Getoff left our world as we know it Sunday morning, October 30. David worked tirelessly to help others overcome modern diseases but lost his battle with acute myeloid leukemia in the second round, after seemingly fully recovering from its onslaught a year ago.

Our friend, David, has served more than just his patients, friends, and family. For more than 20 years, he has been a stalwart contributor to the Price-Pottenger Nutrition Foundation, most recently as the vice president of our board of directors.

If you're not one of the thousands who have met or heard from David during lectures at medical conferences or in seminars in the library at Price-Pottenger, he was a naturopath and board-certified clinical nutritionist. He had encyclopedic knowledge, quick wit, and a vast curiosity that propelled him to immerse himself to continually advance his learning and teaching.

David was committed to sharing the critical importance of diet and other ancestrally inspired metabolic-health practices to counter the plethora of damaging toxins present in every aspect of modern living. In "Detoxing for Health: An interview with David J. Getoff" in our winter 2017-2018 *Journal of Health and Healing*, David provides valuable information about healthful diet practices and methods to detox. This interview with our then-president of the board of directors, Mark Bielsky, provides only a small glimpse of David's expansive nutrition knowledge and expert guidance.

Most recently, David produced a five-part class entitled "Attaining Optimal Health: Essentials for Price-Pottenger." This 12-hour course is available at our website at a range of prices, depending upon ability to pay, including free. We encourage you to keep David and his teachings alive by watching this course and sharing the link with your friends.

While David was a huge proponent of natural and alternative healing practices, he never discounted the value of contemporary medicine, and, during his illness, received excellent acute care at Scripps Mercy Hospital, to which we are all grateful.

David is survived by his beloved wife, Linda, and his much-adored cat, Tomkha. More information is available at his website, naturopath4you.com.

In loving memory,
Steven J. Schindler
Executive Director
Price-Pottenger Nutrition Foundation

The Price-Pottenger Nutrition Foundation relies on your support. The work that we do is made possible because of donations from members and readers like you. If you value the information that we share, please take a moment and make a tax-deductible contribution. Any amount helps us to positively impact the health and wellness of communities worldwide.

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A Memorial to Coenzyme Q10 Scientist Bill Judy, PhD

by Ross Pelton,[1] RPh, PhD, CCN

William Judy, PhD, passed away on October 30, 2022. For decades, Dr. Judy was one of the world's leading coenzyme Q10 scientists.

Karl Folkers introduced Dr. Judy to coenzyme Q10 in 1968 and encouraged Dr. Judy to conduct CoQ10 clinical trials. Dr. Judy became so fascinated with coenzyme Q10 that it became his professional passion for the rest of his life.

Over a period of decades, Dr. Judy conducted numerous clinical trials on the safety and efficacy of CoQ10 supplementation for a wide range of diseases.[2] Later in his career, Dr. Judy published groundbreaking studies on the absorption and bioavailability of coenzyme Q10.

The Problem with CoQ10 Absorption and the Importance of Crystal-Free CoQ10

As a raw material, coenzyme Q!0 is a crystalline powder with a melting point of 118°F, which is 20 degrees above human body temperature. This creates absorption problems because at body temperature, CoQ10 crystallizes. In order to be absorbed, it must be dissociated into single molecules in solution. Dr. Judy's studies revealed that many commercial CoQ10 products have very low rates of absorption because the CoQ10 is crystallized.[3]

Dr. Judy emphasized that the ability to keep CoQ10 in solution depends on the mixture of oils and the heating and cooling process used in the manufacturing process rather than the form or CoQ10 in the supplement. A detailed explanation of these issues can be found at www.q10facts.com/absorption-and-bioavailability/.

The Ubiquinone vs Ubiquinol Controversy

Ubiquinol, which is the reduced form of coenzyme Q10, was launched as a new CoQ10 supplementation in 2007 with claims of superior bioavailability. This was great marketing, but these claims were not based on sound science. In a presentation at the 2015 International Coenzyme Q10 Association symposium in Bologna, Italy, Dr. Judy reported the results of his research which revealed ubiquinol is quickly and nearly completely converted to ubiquinone when it enters the stomach and duodenum. It is absorbed as ubiquinone and then converted back to ubiquinol in the lymph.[4] Ubiquinol is substantially more expensive than ubiquinone. Many consumers still purchase ubiquinol CoQ10 supplements but get no additional benefit for the extra expense.

Results from Dr. Judy's groundbreaking studies enabled him to make the following conclusions:

1. The oxidized form, ubiquinone, is the more stable and better documented form of coenzyme Q10. It is an electron acceptor that plays an essential role in the process of producing mitochondrial ATP, which is the primary source of energy used throughout the body.[5]
2. The reduced form, ubiquinol, is the antioxidant form. It is an electron donor. It neutralizes superoxides and other harmful free radicals. By its nature, it is less stable than the ubiquinone form.[6]
3. Regardless of whether the oral coenzyme Q10 supplement is ingested in the ubiquinone form or the ubiquinol form, the coenzyme Q10 will be absorbed in the ubiquinone form and will be rapidly converted to the ubiquinol form in the lymph. It will enter the blood circulation predominantly in the ubiquinol form.[7]

Dr. Judy also wrote a book titled *The Substance That Powers Life: Coenzyme Q10, An Insider's Guide,* which is available from Amazon.com.

I enjoyed a decades-long friendship with Dr. Judy, His keen mind and jovial spirit will be missed by his family, friends, and coenzyme Q10 scientists around the world.

References

1. Ross Pelton is The Natural Pharmacist. His website, bio and blog are at www.naturalpharmacist.net. His latest book, which is titled *Rapamycin, mTOR, Autophagy and Treating mTOR Syndrome* is available on www.Amazon.com
2. A complete list of Dr. Judy's coenzyme Q10 publications can be found at www.q10facts.com
3. Judy WV. The Single-dose Absorption and Steady-state Bioavailability of Different Coenzyme Q10 Formulations. *Integrative Medicine.* Feb. 2022;21(1):28-34.
4. Judy, WV. Presentation at the International Coenzyme Q10 Association symposium in Bologna, Italy, October 2015.
5. Mantle D, Dybring A. Bioavailability of Coenzyme Q10: An Overview of the Absorption Process and Subsequent Metabolism. *Antioxidants.* May 5, 2020;9(5):386.
6. Littarru GP, Tiano L. Bioenergetic and antioxidant properties of Coenzyme Q10: recent developments". *Mol Biotechnol.* 2007;**37**(1):31–37.
7. Judy WV. 2018. *Coenzyme Q10: An Insider's Guide.* ISBN: 978-87-7776-186-7. Available from amazon.com.

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Literature Review & Commentary

by Alan R. Gaby, MD
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Can Eating Avocados Prevent Heart Disease?

The association between avocado consumption and risk of developing cardiovascular disease (CVD) was examined in a prospective cohort study of 68,786 women from the Nurses' Health Study and 41,701 men from the Health Professionals Follow-up Study who were free of cancer, coronary heart disease, and stroke at baseline. Diet was assessed with food frequency questionnaires at baseline and again every four years. During 30 years of follow-up, a total of 14,274 incident cases of CVD (9,185 coronary heart disease events and 5,290 strokes) were documented. After adjusting for lifestyle and other dietary factors, compared with non-consumers, those with higher avocado intake (2 servings or more per week) had a 16% lower risk of CVD (pooled hazard ratio = 0.84; 95% confidence interval [CI], 0.75-0.95) and a 21% lower risk of coronary heart disease (pooled hazard ratio = 0.79; 95% CI, 0.68-0.91). No significant associations were found for stroke. For each half-serving per day increase in avocado intake, the pooled hazard ratio for CVD was 0.80 (95% CI, 0.71-0.91). Replacing half a serving per day of margarine, butter, egg, yogurt, cheese, or processed meats with the equivalent amount of avocado was associated with a 16-22% lower risk of CVD.

Comment: Avocados are rich in fiber, potassium, magnesium, monounsaturated fatty acids, and polyunsaturated fatty acids, as well as phytonutrients and other bioactive compounds. In national population studies, after controlling for lifestyle and socioeconomic status, avocado consumers tended to have higher HDL-cholesterol levels; a lower risk of metabolic syndrome; and lower weight, body mass index, and waist circumference, compared with avocado non-consumers. The present observational study supports the possibility that eating avocados can help prevent heart disease.

Pacheco LS, et al. Avocado consumption and risk of cardiovascular disease in US adults. *J Am Heart Assoc*. 2022;11:e024014.

Epigallocatechin Gallate for Uterine Fibroids

Sixteen premenopausal Italian women over age 40 years (mean, 47 years) with intramural or subserosal uterine fibroids at least 3 cm in diameter or multiple smaller fibroids with a total diameter of 3-10 cm received two tablets per day of a product providing daily 200 mg of epigallocatechin gallate (EGCG), 10 mg of vitamin B6, and 2,000 IU of vitamin D (Delphy; Farmares, Rome, Italy) for three months. The median uterine fibroid size decreased significantly by 17.8% or by 37.3%, depending on the method of assessment. The improvement was greater in women with predominantly intramural fibroids than in those with predominantly subserosal fibroids. The mean duration of menstrual flow decreased from 5.5 days to 4.6 days (p =0.04). There was no significant change in menstrual flow intensity or in the severity of menstrual pain. The satisfaction with treatment was in general very high, with no adverse effects reported.

Comment: EGCG has been reported to inhibit the proliferation of, and to induce apoptosis in, human leiomyoma (fibroid) cells in experimental animals and *in vitro*. This effect is thought to be due to the inhibitory effect of EGCG on catechol-O-methyltransferase, an enzyme that appears to play a role in the pathogenesis of uterine fibroids. In an earlier double-blind study from Egypt, administration of a green tea extract (green tea is a major source of EGCG) for four months decreased fibroid volume and improved symptoms in women with uterine fibroids.[1] However, in an uncontrolled trial conducted in Germany, treatment with a green tea extract (providing 390 mg per day of EGCG) for six months was associated with a nonsignificant 6.8% increase in mean fibroid volume.[2] Thus, it remains unclear whether green tea extracts are beneficial for women with uterine fibroids.

Grandi G, et al. Vitamin D and green tea extracts for the treatment of uterine fibroids in late reproductive life: a pilot, prospective, daily-diary based study. *Gynecol Endocrinol*. 2022;38:63-67.

Does Caffeine Consumption Increase the Risk of Developing Glaucoma?

Certain single-nucleotide polymorphisms (SNPs) are associated with increased coffee consumption. In the present study conducted in China, two SNPs that are associated with higher coffee consumption were also found to be associated with an increased risk of developing primary open-angle glaucoma. The presence of one of these SNPs was associated with a 24% increase in risk of primary open-angle glaucoma ($p < 0.02$) and the presence of the other SNP was associated with a 16% increase in risk ($p < 0.01$).

Comment: In a previous study, acute consumption of coffee resulted in a short-term increase in intraocular pressure (IOP). This effect appeared to be due primarily to the caffeine in coffee. In observational studies, however, higher caffeine consumption was not associated with higher IOP or with an overall increased risk of glaucoma. In contrast, among the subset of people who had a family history of glaucoma, higher caffeine intake was associated with an increased risk of developing glaucoma. Observational studies must be interpreted with caution because the results can be influenced by many different confounding factors. On the other hand, Mendelian randomization studies (such as the present study), despite being observational in nature, are less likely to be influenced by confounding factors. Therefore, the observed associations in the present study may be more likely to indicate causation. Glaucoma is a common condition and a major cause of visual loss. Further research is warranted to determine whether the risk of developing glaucoma could be decreased by limiting caffeine consumption.

Li X, et al. Habitual coffee consumption increases risk of primary open-angle glaucoma: a Mendelian randomization study. *Ophthalmology*. 2022;129:1014-1021.

Saw Palmetto Berries (*Serenoa repens*) for Chronic Prostatitis/ Chronic Pelvic Pain Syndrome

Two hundred twenty-one men (aged 18-50 years) presenting to one of 11 Chinese urological centers with a history of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) for at least three months were randomly assigned to receive, in double-blind fashion, in a 2:1 ratio, 120 mg of an extract of *Serenoa repens* (serenoa) twice a day or placebo for 12 weeks. At baseline, the mean score on the NIH Chronic Prostatitis Symptom Index (NIH-CPSI) was 26 on a scale of 0 to 43, with higher numbers indicating more severe symptoms. A response to treatment was defined as a decrease in the NIH-CPSI score by at least 6 points. The proportion of patients who had a response was higher in the serenoa group than in the placebo group (73% vs 33%; $p < 0.0001$). No serious side effects occurred. The mean reduction in the NIH-CPSI score was greater in the serenoa group than in the placebo group (9.39 vs. 5.21; $p < 0.0001$). The difference in the change between groups reached statistical significance by the end of the second week.

Comment: Serenoa is widely used as a treatment for benign prostatic hyperplasia (BPH). Many, though not all studies have found that treatment with serenoa improves symptoms, increases urinary flow rate, and decreases residual urine volume in men with BPH. In the present study, serenoa was also found to be an effective treatment for CP/CPPS. If the results of this study from China can be confirmed by additional research, it would represent a significant medical breakthrough because CP/CPPS is often a chronic and difficult-to-treat condition. However, a previous study conducted in the United States found that serenoa was not an effective treatment for CP/CPPS.[3]

Zhang K, et al. The efficacy and safety of Serenoa repens extract for the treatment of patients with chronic prostatitis/chronic pelvic pain syndrome: a multicenter, randomized, double-blind, placebo-controlled trial. *World J Urol*. 2021;39:3489-3495.

Eicosapentaenoic Acid for Pruritus in Dialysis Patients

Twenty-seven Taiwanese hemodialysis patients (mean age, 67.3 years) with severe pruritus received 1 g per day of a fish oil preparation (containing more than 90% eicosapentaenoic acid) for three months. Significant improvement was seen in pruritus at one, two, and three months compared with baseline. At three months, pruritus was severe in six patients, moderate in six, mild in eight, and absent in seven patients. Fish oil supplementation also improved dryness of the skin. None of the patients had a resolution of pruritus during the first two months.

Comment: Frequent and intense pruritus is a common problem among patients receiving hemodialysis for chronic kidney disease. Pruritus adversely affects quality of life and is independently associated with increased mortality. The results of this study suggest that eicosapentaenoic acid, which is a component of fish oil, is an effective treatment for pruritus in patients receiving hemodialysis for chronic renal failure.

Lin YL, et al. Omega-3 fatty acids improve chronic kidney disease-associated pruritus and inflammation. *Medicina*. 2022;58:796.

Gluten-Free Diet for Myofascial and Musculoskeletal Pain

Twenty-five women (aged 18-55 years) with a history for at least three months of moderate-to-severe myofascial pain in masticatory muscles due to temporomandibular joint syndrome were randomly assigned to consume a gluten-free diet for 4 weeks or to an untreated control group. Women on the gluten-free diet had a reduction in pain intensity ($p = 0.006$) and an increase in the pressure pain threshold of the masseter ($p < 0.02$) and anterior temporalis ($p = 0.03$) muscles. In contrast, the control group had no improvement.

Comment: In a previous study, consumption of a gluten-free diet relieved chronic low back pain in a large proportion of patients who had been diagnosed with fibromyalgia, spondyloarthritis, or both.[4] In a case report, a 46-year-old woman with a two-year history of severe heel pain diagnosed as plantar fasciitis had marked improvement within two weeks of commencing a gluten-free diet.[5] Symptoms recurred when she resumed eating gluten but again resolved with gluten avoidance. In the present study, a gluten-free diet improved myofascial pain in patients with temporomandibular joint syndrome. Taken together, these findings suggest that avoiding gluten can in some cases relieve various types of myofascial and musculoskeletal pain. Sensitivity to dairy products and other foods also appears to be involved in some cases of myofascial and musculoskeletal pain; but according to some investigators, gluten-containing foods are involved in the largest proportion of cases.

Araujo Oliveira Buosi J, et al. Gluten-free diet reduces pain in women with myofascial pain in masticatory muscles: a preliminary randomized controlled trial. *J Oral Facial Pain Headache*. 2021;35:199-207.

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Gaby's Literature Review

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Vitamin D Accelerates Recovery from Covid-19

Fifty patients admitted to a hospital in Belgium with Covid-19 between August 2020 and August 2021 were randomly assigned to receive, in double-blind fashion, vitamin D (25,000 IU per day for 4 days followed by 25,000 IU per week for up to 6 weeks) or placebo. Compared with placebo, vitamin D shortened the median length of hospital stay (4 days vs. 8 days; $p = 0.003$). At day 7, a lower percentage of patients were still hospitalized in the vitamin D group than in the placebo group (19% vs. 54%; $p < 0.02$). At 21 days, none of the patients in the vitamin D group and 14% of those in the placebo group were still hospitalized. Vitamin D reduced the median duration of supplemental oxygen use among the patients who needed oxygen (4 days vs. 7 days; $p = 0.01$).

Comment: It has been hypothesized that vitamin D could help prevent or decrease the severity of Covid-19 infection by regulating the renin-angiotensin system and by enhancing innate or adaptive immunity. Several previous studies found that supplementation with vitamin D or calcifediol (25-hydroxyvitamin D) improved outcomes in patients with Covid-19. The results of the present study support those findings.

A double-blind study conducted in Brazil and published in the *Journal of the American Medical Association* found that vitamin D supplementation did not decrease the mean length of hospital stay and had no significant effect on mortality, need for intensive care, or need for mechanical ventilation.[6] In that study, vitamin D was given as a single large dose of 200,000 IU. Administering vitamin D that way appears to be less effective than giving it in smaller, more frequent doses.

De Niet S, et al. Positive effects of vitamin D supplementation in patients hospitalized for COVID-19: a randomized, double-blind, placebo-controlled trial. *Nutrients*. 2022;14:3048.

Olive Oil Promotes Healing of Severe Burns: Revisiting an Old Iranian Paper

One hundred Iranian patients (mean age, 33 years) hospitalized with third degree and deep second degree burns on 10-20% of body surface area were given a very-low-fat diet and were randomly assigned to receive additional olive oil or sunflower oil (control group), to bring the total fat content to 20% of total energy. The mean time required for wound healing was 17% lower ($p = 0.04$) and the mean length of hospital stay was 17% lower (7.4 vs. 8.9 days; $p = 0.05$) in the olive oil group than in the control group. The authors concluded that ingestion of olive oil may accelerate wound healing and decrease the duration of hospitalization in burn patients.

Comment: In my writings during the past 10 to 15 years, I cited a number of research papers from Iran. Over the past several years I have developed concerns about the credibility of much of the nutrition research coming from that country. I have therefore begun taking another look at some of the research I cited in the past. The study described above, which was published in 2015, has a number of concerning issues.

Concerns about Najmi M, et al. Effect of oral olive oil on healing of 10-20% total body surface area burn wounds in hospitalized patients. *Burns*. 2015;41:493-496:

1. The paper stated, "Diet intervention was continued in all patients until they discharged from hospital with complete healing of burn wounds and donor sites." However, as noted in Table 3, the mean duration of hospitalization was 7.4 days in the olive oil group and 8.9 days in the control group. It seems implausible that major burns that require hospitalization would heal completely in 7 to 9 days.
2. The olive oil and sunflower oil that was added to salads provided 15% of total daily calories, and the total fat content of the diet was 20% of calories. That means that any meal that did not contain a salad had only 5% of calories as fat. It would be difficult to devise palatable meals that have such a low fat content and that burn patients would be willing to eat. In addition, many patients with major burns who are in pain and on morphine (as in this study) would not be willing to exert the chewing effort required to eat a salad. For patients who refused to eat salads, the extremely low fat content of the rest of the diet could put them at risk of developing essential fatty acid deficiency. Considering the importance of nutritional support in burn patients, it would seem that, if the ethics committee and the supervisor of the burn unit had some knowledge of nutrition, they would not have approved the study protocol.
3. It would be difficult to monitor how much of the oil each patient consumed because the amount of oil left at the bottom of the salad bowl would be highly variable, and the liquid at the bottom of the bowl would consist of unknown percentages of oil and water. Therefore, when studying the clinical effects of olive oil, it would not be logical to provide the oil in the way described in this study. Furthermore, in order to try to monitor the amount of oil consumed, the Master of Science student who conducted this study would have had to examine the food tray of every patient at every meal that contained a salad, over a period of 14 months. The logistics of accomplishing such a feat seems overwhelming.
4. The study was done as part of a Master of Science thesis. However, the paper also stated that the food was prepared in the hospital kitchen under the supervision of a student with a Master of Science degree in nutrition. It does not seem possible that the student could have already had a Master of Science degree, when the research was being done in order to obtain that degree. The possibility that two different students were involved also does not seem plausible, because it is not likely that a person would be willing to spend 14 months supervising food preparation in a hospital kitchen, just to help someone who is working toward a master's degree.

References

1. Roshdy E, et al. Treatment of symptomatic uterine fibroids with green tea extract: a pilot randomized controlled clinical study. *Int J Womens Health*. 2013;5:477-486.
2. Biro R, et al. Effects of epigallocatechin gallate-enriched green tea extract capsules in uterine myomas: results of an observational study. *Arch Gynecol Obstet*. 2021;303:1235-1243.
3. Kaplan SA, et al. A prospective, 1-year trial using saw palmetto versus finasteride in the treatment of category III prostatitis/chronic pelvic pain syndrome. *J Urol*. 2004;171:284-288.
4. Araujo Oliveira Buosi J, et al. Gluten-free diet reduces pain in women with myofascial pain in masticatory muscles: a preliminary randomized controlled trial. *J Oral Facial Pain Headache*. 2021;35:199-207.
5. Paoloni M, et al. Complete remission of plantar fasciitis with a gluten-free diet: Relationship or just coincidence? *Foot*. 2014;24:140-142.
6. Murai IH, et al. Effect of a single high dose of vitamin D3 on hospital length of stay in patients with moderate to severe COVID-19: a randomized clinical trial. *JAMA*. 2021;325:1053-1060.

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Quantum Functional Energy Medicine: Basic Concepts

by Michael J. Gonzalez,[1] DSc, NMD, PhD; Christine Shaffner,[2] ND; Jorge R Miranda-Massari,[3] PharmD; Jose Olalde,[4] MEENG

Introduction

Energy medicine entails several systems that work with energy fields of the body to help restore health. Most energy-related therapies challenge the current biomedical paradigm because they cannot be explained by conventional physical, chemical, biochemical, or physiological mechanisms. Quantum physics provides a more appropriate paradigm to explain these therapeutic approaches. Energy therapies involve low-level (subtle) energy field interactions, such as Healing Touch, homeopathy, acupuncture, magnet therapy, bioelectromagnetic therapy, electrodermal therapy, and phototherapy.

The term quantum functional energy medicine refers to the array of energetic possibilities that may influence the biofield. The biofield is the field of energy and information that surrounds and penetrates the human body. It is composed of electromagnetic energy and subtle energy (for example, Qi). One mechanism of action of the biofield phenomenon is that it acts directly on molecular structures, modifying the conformation of molecules in significant ways. Another potential mechanism of the biofield is that it may transfer bioinformation carried by energy signals interacting directly with different energy fields.[1] Living systems may be thought of as complex, nonlinear, dynamic, self-organizing energetic phenomena with negative entropy. At the highest level of organization, each life form may possess an innate biologic field, or biofield. This energy field maintains the integrity of the whole organism; regulates its physiologic and biochemical responses; and is integral to development, healing, and regeneration.[2-4]

The concept of life force is ancient and common to traditional healing systems such as Chinese and Ayurvedic medicine. These therapeutic modalities consider that a form of life energy flows throughout the body and that illness arises as a result of blockages, excesses, or irregularities in its flow. This energy has many names (for example, Prana, Qi, Ki, Mana, love, and spirit) and is similar to the present-day concept of the biofield, which is partly based on the electromagnetic field theory of modern physics. Additionally, many energy-guided healing systems, such as Reiki and Qigong, postulate that an individual's life force is connected with a universal life energy (aether). In the quantum physics realm, both a particle view and a wave view become necessary to fully describe the true nature of light and matter at the smallest level.

This dual model of the "complementarity principle" allows for explanation of a wide variety of energy effects.

"If you want to find the secrets of the Universe, think in terms of energy, frequency and vibration."

Nicola Tesla

Human Energy "Good" Vibrations

The dynamic human energy system is a complex network of different types of energies. Gerber[5] described this network as follows: (1) **biochemical energy** (e.g. glucose, adenosine triphosphate, fats, protein, carbohydrates); (2) **bioelectrical energy** (e.g. nerve signal transmission, cardiac electrical rhythms, neuro-electrical brain activity, piezo-electrical bone currents); (3) **biophotonic energy** (e.g. mitogenic radiation, ultraviolet biophotons emitted from DNA); (4) **bioelectronic energy** (e.g. inherent cellular/DNA activity; DNA vibrating at GHz frequencies); and (5) **biomagnetic energy** (e.g. perineural system, by-products of cardiac, nerve, and brain activity; by-products of cellular activity; and subtle energies [Qi, Prana, and etheric energy]). These energies are part of a bio-informational system that flows within living systems. This aspect of energy as information links to the concept of molecules as information and supports the orthomolecular understanding of health homeostasis.[6]

Energy supply is a necessary condition for the complexity of life (order, organization, compartmentalization), ➤

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and any disturbance in energy metabolism may increase the likelihood of pathological outcomes by disturbing the physiological balance that sustains the healthy state.[6]

Interestingly, cancer cells can obtain approximately the same amount of energy from fermentation as from respiration (Warburg effect[7]). By contrast, normal cells obtain greater levels of energy from oxidative phosphorylation than from fermentation.[8] Warburg showed that impairment of oxidative metabolism in cancer is due to mitochondrial dysfunction. Nevertheless, cancer research has focused on genetic mechanisms, erroneously considering that impaired oxidative metabolism is a side effect of malignant transformation rather than its central cause.[9,10] Continuous energy excites a state of coherent electrical polar vibrations that depend on water ordering in the cell (structured water).[11]

Energy transformation in mitochondria produces a special state of electrical vibrations. The inner membrane potential helps form layers of ordered water molecules around mitochondria, which provides vibrations that enable their high excitation. Disturbances in oxidative metabolism and coherence are a central issue in cancer development as well as most degenerative diseases.[12]

The mitochondrial dysfunction reported by Warburg is caused by inhibition of pyruvate transfer into the mitochondrial matrix. The number of protons transferred from the matrix is reduced, which in turn decreases membrane potential and changes the ordering of water molecules around the mitochondria. Decreased membrane potential leads to low vibrational energy, resulting in decreased energy production.

The Resonance Symphony Orchestra

The quantum principle of entrainment states that powerful rhythmic vibrations from one source will recruit less powerful vibrations from another source. This is known as resonance. Resonance is a phenomenon in which a vibrating system or external force drives another system to oscillate with greater amplitude at specific frequencies. Resonant systems can be used to generate vibrations of a specific frequency. This action may restore transmembrane potential and electron transport across cell and mitochondrial membranes, restoring cellular metabolism that correlates with health. This electromagnetic rejuvenation energy resonates at many different cellular frequencies and can tune each cell (by resonance) back to its original cellular frequency. Every organ and every cell in the body has its own resonant frequency. Together, they make up a composite frequency like the instruments of an orchestra. When one organ in the body is out of tune, it will affect the whole body. By restoring vibrational frequency, it may be possible to bring a diseased organ into harmony.

Life Energy: The Chi Mysticism

Everything in the universe is made up of energy vibrating at different frequencies. At the quantum level, the things that appear solid in our physical dimension as perceived by our senses are made up of vibrational energy fields. Every vibration produces a corresponding geometric form, and in this way crystals are built up. Crystals collectively form a body of an element according to its particular vibration. A unique vibration may produce a perfect state of resonance, its own pitch and tone.

A tone is a steady periodic sound characterized by duration, pitch, intensity (or loudness), and timbre (or quality). A simple tone has only one frequency, although its intensity may vary. A complex tone consists of two or more simple tones, called "overtones." Rhythm is a strong, regular, repeated pattern of movement or sound in time that can apply to a wide variety of cyclical natural phenomena. Beat is a pulse (regularly repeating event) in a basic unit of time. These relationships create what we call "harmony." Harmony is the simultaneous occurrence of frequencies, pitches, or chords that lead to balance, homeostasis, and therefore health.

All life exists within a sea of vibration (Energy, aether), and rhythm is fundamental to all of life. Therapeutic effects have been observed in several meditative and healing practices that use resonance and rhythm in the form of chanting and prayers to produce a trance state, a change in dimension (a change in frequency and vibration).

Frequencies, Dimensions, and Consciousness

In the human brain, alpha waves are in the frequency range of 7.5–12.5 Hz. Alpha waves are connected to deep relaxation, dreaming, and light meditation. The alpha waves are a gateway to deeper states of consciousness. They promote mental coordination, calmness, alertness, inner awareness, mind–body integration, and learning.

The Schumann resonances (SR) are a set of spectrum peaks in the extremely low frequency portion of the Earth's electromagnetic field. They are global electromagnetic resonances. The energy of the Earth vibrates at a 528-Hz frequency. This frequency is thought by some to be so powerful that it can help repair DNA damage and restore harmony and equilibrium. Alpha waves closely resemble the fundamental SR frequency at a smaller scale.

An individual's bio-frequency may directly correlate with health status. The higher the vibration, the healthier the human body. Consistent exposure to negative stressors can lower energetic frequency. Energetic clearing methods such as prayer, meditation, and other energy practices can be used to significantly increase baseline frequency (up to 15 MHz). In other words, energetic resonance can be elevated to restore harmony within the body. Electromagnetic imbalance can negatively affect the specific vibrational frequencies of molecules, cells, tissues,

and organs within the body. This energetic alteration often manifests as chemical imbalances that are associated with many diseases and illnesses.

The term consciousness is used in several ways. In general, "consciousness" refers to a state of total awareness or perception. Consciousness is one form of energy. We define consciousness as the highest level of energy (the Gamma state, Nirvana, Heaven, Moksha). Consciousness as a physical process is caused by the organization of energy in the brain. Consciousness increases the likelihood that an organism will direct its attention to whatever is most important for its survival. Consciousness is in an entangled state with the physical universe. In this quantum sense, information can exist outside the body.

Quantum Energy Therapies

There is an increasing appreciation of the electrical (energy) nature of biological functioning. One of the first scientists to explain this phenomenon was Georges Lakhovsky.[13] Lakhovsky proposed that exposure to a blend of higher frequencies stimulates the cell's life force (chi), restoring vigor and balance. Regeneration is the replacement of irreparably damaged or lost cells by new ones. It may happen in a natural way by inherent restoration of physio-metabolic resonance although it can also be achieved by lasers, hyperbaric oxygen, nutrients, stem cells, exosomes, and other regenerative biological-informational therapies. It is possible that cancer can be treated with high frequency therapies. Therapeutic strategies that restore mitochondrial function may trigger apoptosis in treated cells. In tumor tissues, reversing mitochondrial dysfunction with metabolism-modulating cofactors, oxygen, lasers, and information molecules may hold promise as an anticancer strategy.[12]

Biophoton Therapy: Let There Be Light!

Biophoton therapy is the application of light to particular areas for healing purposes.

The light (photons) is absorbed by the skin's photoreceptors and as wavelengths by internal photoreceptors. By stimulating certain areas of the body with specific quantities of light (wavelengths), biophoton therapy can help reduce pain as well as aid in various healing processes throughout the body. The theory behind biophoton therapy is based on the work of Morell,[14] and expanded by Popp and colleagues.[15] Morell and Popp theorized that light can affect electromagnetic oscillation, or waves of the body and regulate enzyme activity. The body's communication system might be a complex network of the interaction of resonance and frequencies. All photons that are emitted by the body communicate with each other in a highly structured light field that surrounds the body (biofield) and may also be the actual carrier of long-term biological memory. In addition, this light field regulates the activity of metabolic enzymes. The information transferred on biophotons is bidirectional. This means that as DNA sends information out, information about all the biophotons from the body is broadcast back to cells and, in particular, to tubulins, which are light-conductive system in the connective tissue. Illness may occur when biophoton emissions are out of sync. There is evidence that light emissions from patients with cancer is arrhythmic and scrambled, suggesting that cells are no longer communicating properly. Therapies are emerging that involve stimulating the body with specific quantities of light to reduce pain and promote healing processes.

Photobiomodulation: True Quantum Energy Medicine

"Photobiomodulation therapy" is the technical term for laser therapy. It is a light therapy using lasers or light-emitting diodes to improve tissue repair and reduce pain and inflammation.

It involves the delivery of light energy to modulate cellular mechanisms. Light is the most fundamental energy particle that is the source of life on Earth. Pigmented substances that accept photons in living tissue are called "chromophores." When a photon within a specific wavelength strikes a matching chromophore, the energy of the photon is transferred to the chromophore. This causes a biochemical change within the cell or tissue. If this change activates or improves cellular function, it is called "photobioactivation."

Mitochondrial Photobiomodulation: Mito Medicine

The mitochondria Is an important site of light action in cells and cytochrome c oxidase (the terminal enzyme of the mitochondrial respiratory chain) is the main responsible molecule for this activity. Mixed-valence copper components of cytochrome c oxidase are believed to be the photoacceptors. The excitation of the photo-acceptor molecule sets in motion cellular metabolism through a cascade of cellular signaling reactions or retrograde mitochondrial signaling. ATP is not only an energy currency inside cells but also a critical signaling molecule that allows cells and tissues throughout the body to communicate with one another.[16] ATP is believed to play a role as an important signaling molecule in many metabolic activities. Even small changes in ATP level can significantly alter cellular metabolism. Increasing the amount of ATP may improve cellular metabolism, especially in suppressed or malfunctioning cells. Degenerative conditions develop when the body's self-healing reserves lose their restorative power. It is thought that photons dissociate inhibitory nitric oxide from the enzyme cytochrome oxidase, leading to an increase in electron transport, mitochondrial membrane potential, and ATP production. Stem cells and progenitor cells appear to be particularly susceptible to photobiomodulation. A tumor-killing effect specific to ATP has been described.[17] ATP signaling acts, in part, to trigger apoptosis of tumor cells and/or to promote cell differentiation.

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At the cellular level, visible red and near-infrared light energy stimulates cells to generate more energy and undergo self-repair.

Quantum Functional Energy Medicine: The Physician-Healer

Ancient scholars came to understand that everything is composed of the same energetic substance that vibrates at different frequencies. Traditional Chinese medicine, for example, is based primarily on the understanding of the transformation of universal Qi throughout the human body. According to traditional theory, energy or Qi flows along energy channels or meridians that run throughout the body. When the flow of Qi is disrupted or blocked, it can be released by stimulating specific points along each channel.[18] Qi itself does not flow down the nerve but instead surrounds the electrical flow with an intangible field that can be manipulated to some degree. This is reminiscent of an electron flow in a magnetic field and also congruent with Ayurvedic medicine's concept of the chakras (Energy vortices) and nadis (similar to meridians). Correcting the flow of energy is considered necessary to ensure restoration or maintenance of health. Acupuncture deals with the body's own energy.

Conclusion

Today quantum physics proposes that all matter is composed of energy that is constantly vibrating at different frequencies. Underlying all of this motion is a ubiquitous force, an absolute energy medium, that has the ability to be everywhere at once. Quantum physics calls this force "vacuum energy" or "zero point energy." The wave-particle duality concept states that the movement of a particle through the absolute energy medium creates waves. A particle/photon in a quantum field, therefore, resembles a molecule in a chemical environment. The ability to electrostimulate living tissue at the subcellular level and thereby energize the life force has huge medical implications.

The right wavelength at the right time may have a specific therapeutic action. This is an orthomolecular principle with a quantum regenerative twist.

The human body is a magnificent quantum bio-physic phenomenon. It is an interplay of frequencies with molecules to provide the appropriate information to sustain the negative entropy state we call "homeostasis," or health.[19] Certain frequencies may repel disease, and there may be a link between frequency (vibration) and health. Quantum physics describes the universe as fluctuating fields of energy and matter. When an organ of the body becomes unable to reproduce the necessary equilibrium to sustain health, the resulting deficiency in electronic energy produces imbalance, often throughout the system, which may develop into injury or disease. Energy medicine, vibrational medicine, regenerative medicine, orthomolecular medicine, restorative medicine, and functional medicine are complementary informational systems. Together, they can create a holistic new treatment paradigm to achieve the state of health.

References

1. Rubik B, Pavek R. Manual healing methods. In: Alternative Medicine: Expanding Medical Horizons: A Report to the National Institutes of Health on Alternative Medical Systems and Practices in the United States. NIH Publication No. 94-066. Washington, DC: US Government Printing Office; 1994.
2. Rubik B. Can Western science provide a foundation for acupuncture? *Altern Ther Health Med.* 1995;1(4):41–7.
3. Rubik B. The unifying concept of information in acupuncture and other energy medicine modalities. *J Altern Complement Med*. 1997;3(suppl 1):S67.
4. Rubik B. Scientific analysis of the aura. In: Heinze RI, ed. Proceedings of the 19th International Conference on the Study of Shamanism and Alternative Modes of Healing. San Raphael, CA: Santa Sabina Center, Dominican University; September 1–3, 2002.
5. Gerber R. *Vibrational Medicine: New Choices for Healing Ourselves*. Sante Fe, NM: Bear & Co.; 1988.
6. Gonzalez MJ, Olalde J, Rodriguez JR, et al. Metabolic correction and physiologic modulation as the unifying theory of the healthy state: the orthomolecular, systemic and functional approach to physiologic optimization. *J Ortomol Med*. 2018;33(1):1–12.
7. Warburg O. On the origin of cancer cells. *Science*. 1956;123:309–14.
8. Mikirova NA, Casciari JJ, Gonzalez MJ, et al. Bioenergetics of human cancer cells and normal cells during proliferation and differentiation. *Cancer Ther Oncol Int J*. 2017;3:555623.
9. Seyfried TN, Shelton LM. Cancer as a metabolic disease. *Nutr Metab* (Lond). 2010;7:7.
10. Gonzalez MJ, Miranda Massari JR, Duconge J, et al. The bio-energetic theory of carcinogenesis. *Med Hypotheses*. 2012;79:433–9.
11. Pollack GH. *The Fourth Phase of Water: Beyond Solid, Liquid, and Vapor*. Seattle, WA: Ebner and Sons; 2013.
12. Lakhovsky G, Clement M. *The Secret of Life: Cosmic Rays and Radiations of Living Beings*. London: William Heinemann; 1939.
13. Gonzalez MJ, Seyfried TG, Nicolson GL, et al. Mitochondrial correction: a new therapeutic paradigm for cancer and degenerative diseases. *J Ortomol Med*. 2018;33(4).
14. Morell F, Scott AJ. *The MORA Concept: Patients' Own and Coloured Light Oscillations – Theory and Practice*. Stuttgart, Germany: Karl F Haug Verlag GmbH & Co.; 1990.
15. Popp FA, Li KH, Gu Q, eds. *Recent Advances in Biophoton Research and Its Applications*. River Edge,NJ: World Scientific Publishing; 1992.
16. Karu T. Mitochondrial mechanisms of photobiomodulation in context of new data about multiple roles of ATP. *Photomed Laser Surg*. 2010;28:159–60.
17. Mikhailov VA, Skobelkin OK, Denisov IN, et al. Investigations on the influence of low level diode laser irradiation of the growth of experimental tumors. *Laser Ther*. 1993;5:33–8.
18. Wang SM, Kain ZN, White PF. Acupuncture analgesia: II. Clinical considerations. *Anesth Analg*. 2008;106:611–21.
19. Gonzalez MJ, Sutherland E, Olalde J. *Quantum Functional Energy Medicine: The Next Frontier of Restorative Medicine*. J Restorative Med 2019; 8: 1-7.

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Fat Cells: Can't Live with Them or Without Them

by Devaki Lindsey Berkson, DC

Fat cells have a bad rap. Understandable, as too many of us battle excess adiposity. Thus, we often regard fat cells as ugly, dangerous nuisances, keeping us out of tight-fitting designer jeans – upping our risk of heart disease. fatty liver, type 2 diabetes, cancer, or promoting inflammatory "angry" and cognitively dull thinking.

But deep "scientific dives" into *fat physiology* reveal that we can't live without fat cells, as much as it seems frustrating to live with them. Fat cells, biology unveils, are a huge part of living healthfully, permitting humans to evolve and build cultures, as long as the fat cells themselves stay on a healthy "fat fate trajectory."

Fat cells, as it turns out, are quite the gooey, complex populace. Since fat is complex, the more accurate term for fat is *adipocyte tissue.* I refer to these cells as both "fat cells" and "adipocyte tissue."

A recent article published in the *New England Journal of Medicine*[1] plunged into the science of the "unappreciated adipose cell." It got me thinking.

I used to be a speaker for weight loss clinics in California. I spoke across that big state on the topic of "no-fair fat." The focus was partly on the explanation of the hidden mechanisms as to why certain persons struggle with excess fat cells more than others and how to minimize this fat handicap. I pointed accusing fingers at hidden food hypersensitivities as well as undiagnosed subclinical hypothyroidism and more.

Since that time, the galaxy of adiposity has enlarged. But even though science knows more and more, the planet is getting fatter and fatter. The rapidly growing global obesity epidemic,[2] its co-morbidity role in today's Covid pandemic,[3] its evolving role in promoting a growing epidemic of bone loss,[4] the role of too many unhealthy fat cells in driving major debilitating diseases from diabetes to heart disease in both young and old are all wakeup calls: it's time to understand fat physiology and translate this science into action so we can slow down this tsunami of adiposity, disease, and vulnerability.

Fat comes in varying colors secondary to their distinct physiologies and functions.

So far, not many efforts are really working. And our chaotic politically correct culture isn't allowing health experts to shout out the need to lose weight for fear of *fat-shaming*. Perhaps diving into fat physiology will hold some clinically effective answers to tame our fat cells to work "with" us rather than "against" us.

*First off, fat cells are dynamic***.** They can enlarge and shrink. No other cell can enlarge or shrink like *white adipose tissue* (WAT). White adipocytes can swell from a diameter of 30-40 µm to more than 100 µm, an increase in volume by a factor of more than ten. Thus, fat cells are capable of more than doubling in mass and can then return to their fat cell baseline. You might experience this by losing twenty pounds, only to gain that fat right back again, or even more.

Fat cells are "plastic." Over the last three decades, laboratories have collected a large body of evidence documenting and replicating that fully differentiated adipocytes have the physiological ability to "transdifferentiate." In other words, they can morph in and out of each other.[5,6] Mature adipocytes undergo genome reprogramming and can turn into different cell types, serving different physiological roles. White fat can morph into brown fat. Or beige fat. Or back again. This has huge implications for your overall health and even the health of your individual organs, such as the liver and brain. This is one reason that the environment, how we eat, how regularly we exercise and what type of exercise we do, the chemicals we are exposed to, and the nutraceuticals we swallow from pre-conception as well as from womb to tomb can all influence "stem" cells, which give "birth" to fat cells, nudging fat cell fate.

Fat stem cells. Stem cells are cells with the potential to develop into different types of cells in the body. There are two main types of stem cells: embryonic stem cells and adult stem cells. They serve as both "birthing" and "repair" systems for the body's cell populations. The "fat stem cell" microenvironment greatly contributes to terminal fat (or bone) cell fate. Fat and bone stem cells are in constant flux with each other, a fact that is also growing in appreciation, especially for its clinical implications. Unhealthy fat stem cells drive both the obesity and the growing osteoporosis epidemic.

Fat stem cells influence

- Whether white fat become brite or brown.[7]
- How fat cells behave.

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Fat Cells

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- How fat cells can be lysed (broken down or destroyed) for you to be able to lose weight… or not.
- How bone stem cells behave.
- Adipose-derived stem cells (ADSCs) repair and reboot tissues, via exosomes. used in regenerative medicine.[8]

Fat Cell Types

Fat cells aren't simple. There are many types. Fat is a "polychromatic" organ, meaning it comes in varying colors secondary to their distinct physiologies and functions.

White fat (*White Adipose Tissue, WAT*). This fat has a white, yellowish appearance. *WAT* protects organs. WAT stores energy as triglycerides, which are lipids. Stored energy allows us to interact with life without constantly needing to eat. When needed, free fatty acids are released during fasting periods. Stored calories allow humans to devote body, mind, and spirit toward building lives. If we eat too often, let alone too much, we store energy instead of using it, and those *excess* stored calories are a driving force of the obesity epidemic and why you are not fitting into those jeans.

Brown fat (*Brown Adipose Tissue, BAT*). Brown fat consumes energy and warms us by burning glucose and lipids to maintain thermal homeostasis. To do so, BAT is flush with mitochondria that are rich in iron-containing heme co-factors found in mitochondrial enzymes (cytochrome oxidases). Iron is brownish-red, giving brown fat its tone. WAT contains some mitochondria, but not enough to affect its color. These iron-rich brown mitochondrial enzymes enable BAT to convert chemical energy into heat, a process called *adaptive thermogenesis*. Brown fat requires "numerous" and "functional" mitochondria to perform adaptive thermogenesis.

When healthy, BAT[9] is supposed to keep us from getting obese. Healthy thermogenesis helps us stay thinner rather than fatter. Many pathological states are linked to dysfunctional mitochondria – such as chronic fatigue syndrome, fatty liver, type 2 diabetes, and even sleep apnea – which can make an ill patient more overweight and more fatigued. The potential list is long and ever growing.

Dysfunctional BAT[10] is a major contributor driving today's obesity epidemic. The formation of BAT is called brown *adipogenesis* (making more fat cells). If we can turn on more brown adipogenesis, we may help treat obesity and metabolic disorders. As WAT gets more respect for its complexity and it is seen that WAT can be induced or coaxed into becoming brown adipocytes, there has been a surge of research into adipocyte biology to try to turn the Titanic of humanity away from global morbid obesity.

Beige/brite fat is made in the muscles. WAT can be "browned"[11] into BAT or brite adipose tissue[12,13] when you exercise regularly; genetics, healthy biomes, and specific nutrients also play a role.

Pink fat is made in breast tissue from white fat mixed with glandular tissue, giving this fat its color. Pink fat helps produce milk for lactation. "Excessive pinking"[14] of breast fat may contribute to breast cancer.[15]

Bone marrow fat is inside bones. Bone marrow fat is an endocrine organ that secretes hormones. Its balance affects fat and bone stem cell function.

Dermis fat lies underneath the skin. Dermis fat (subcutaneous fat underneath the skin) contributes to bodily protection and shape.

White Fat Facts (WAT)

WAT exists as both visceral fat and subcutaneous fat. *Subcutaneous fat* is just under the skin and is normally harmless. It may even protect against some diseases. *Visceral fat* is fat that wraps around your abdominal organs deep inside your body. You can't always feel it or see it. In fact, you may have a flat tummy and still have visceral fat, called "thin fat."

Fat's number one job is the storage, use, and maintenance of energy. WAT stores energy as triglycerides, the main constituent of fat. When WAT enlarges with excess triglycerides, especially in dangerous locations like the torso, WAT becomes a nasty organ, capable of secreting pro-inflammatory molecules. We are learning that many diseases arise from excess inflammation (inflammation out of control).

Upper-body subcutaneous adipose tissue accounts for most of the systemic free fatty acids in the bloodstream. When fat cells break open or lyse (process of lipolysis) and release stored fatty acids, where the fat cells first came from (belly vs. thigh) affects where these fatty acids go into the rest of the body.

Belly vs Thigh Fat Dynamics

The first adipocytic environment that matters most is where fat cells are "birthed." In other words, the location of fat matters. Excess visceral[16] fat in the wrong locations (as they say in real-estate, "location, location, location") can contribute to disease by pumping out pro-inflammatory cytokines that can travel far and wide throughout the body. White fat on the thighs is different from white fat on the belly. Belly fat cells expand, and larger fat cells are harder to break open (lipolysis) to lose weight. Larger fat cells store more pollutants. Some pollutants make fat stem cells birth larger and nastier-acting fat cells.

Belly fat creates insulin resistance.[17] Accumulation of visceral belly fat over five years was found to be an independent predictor of the future development of type 2 diabetes,[18] independent of baseline adiposity levels. In comparison, fat cells on the thighs are smaller fat cells. They are better acting and easier to lose. They don't harbor pollutants or give off pro-inflammatory substances.

These fat cell differences are reflected in gaining extra weight.

- Weight gain in the upper body (abdomen/torso) comes mostly from expanded fat cells – large, potentially nastier-acting fat cells.
- Weight gain on the hips and thighs is in the form of new fat cells. Small. Less nasty acting.

Visceral fat lipolysis contributes a modest portion of free fatty acids in the bloodstream. Most visceral fat breakdown shunts much of these fatty acids to the liver. Excess belly fat is thus implicated as a major driving force in the sadly expanding fatty liver epidemic. Abdominal visceral fat drives insulin resistance, obesity, and other types of health issues far more than thigh fat.

An increase in visceral adiposity predicts diminished insulin sensitivity over ten years of follow-up,[19] independent of the size of this adipose depot at baseline. Also, belly visceral fat plays a huge role in releasing pro-inflammatory molecules

that can travel far and wide. They can cross the blood-brain barrier and inflame and shrink brain tissue. In essence, the bigger the belly visceral fat, the more shrinkage of precious brain tissue.[20]

This sad scenario hits lower body muscle mass, too. The larger the belly, the more thigh muscle is lost (thigh sarcopenia).[21] Thigh muscle helps prevent falls as we age. You don't want to allow your waistline to expand more and more. This shrinks your brain tissue, your thigh muscles, and makes your insulin receptors less sensitive to their major food, glucose.

Over the last two years, while much of the world has been isolating, I have been flying around the country lecturing. What I see is scary: too many Americans are letting their torso fat threaten their overall health. Especially their brain health![20] This is part of the consequence of letting body fat get the better of you. To protect the rest of you, getting rid of excess belly/torso fat should be a goal of your daily workout, along with your diet and nutraceutical strategies.

Brown Fat Facts (BAT)

Brown fat begins to form in the fetus during the late second trimester of pregnancy. BAT protects newborns from cold while they develop the ability to shiver (thermogenesis). Then BAT keeps us warm and thinner throughout life. The distribution of adult human BAT is found in specific anatomical areas: the neck, shoulders, posterior thorax, and abdomen. These BAT depots drain directly into the systemic circulation, leading to rapid distribution of "warmed blood" to the rest of the body. That's how BAT is supposed to keep us warm.

But I have patients that are on plenty of thyroid medication with normal thyroid labs, or endogenously healthy thyroid, but are still freezing. This can occur secondary to dysfunctional BAT. Since BAT is so flush with mitochondria, dysfunctional BAT can arise secondarily from mitochondrial dysfunction.[22]

BAT contributes to more than keeping us warm. Long-term activation of BAT contributes to a range of health benefits that positively influence multiple systems[10]: gastrointestinal, cardiovascular, and musculoskeletal systems.

Regular exercise "browns" white fat, called *adipocyte browning.*[23] As lifestyle choices become less healthy, and pollutants mess with fat stem cells, brown fat can shrink and/or become dysfunctional. Exercise, *regular exercise* and not just strolling along, helps make more brown fat out of white fat. Recruiting of muscles releases myokines (PGC1-α-dependent) that drive WAT browning into BAT.[24]

Humans have proportionally less BAT than smaller mammals, but contemporary humans may have even less BAT than is required to support their physiological and metabolic needs. Why? From too little exercise, too much eating unhealthy foods, and too much eating with too little time off for "fasting" and "food resting." Exercise, through a wide range of mechanisms, induces a phenotypic "switch" in adipose tissue from WAT to thermogenic beige/brite and brown adipocytes. This brown fat *activation* lowers the risk of heart disease. It can force-feed skeletal muscle cells to consume glucose and lipids, rather than have white fat store them. (Human muscle cells marbled with WAT become less healthy-functioning muscles).

BAT in adults appears to have a substantial clinical "weight homeostasis effect," as retrospective and prospective studies show an inverse association between BAT activity and BMI.

- The more BAT our bodies have, the less we have metabolic diseases.
- Brown fat releases substances (exosomal microRNAs) that can regulate gene expression. Not just in fat stem cells, but in other cells, such as some organ cells like the liver. BAT can release exosomes that are health promoting, such as reducing metabolic syndrome (shown in a rodent model[25]) and reducing inflammation.[26] Conversely, once cancer is present, WAT can morph into releasing tumor-promoting properties.[27] This may be one way that WAT contributes to worsening cancer dynamics. This may suggest that fat stem cell therapies may be contraindicated in some cases of cancer.

Stress, poor diet, mitochondrial unwellness, insufficient exercise, and even aging (less so if on HRT, in my opinion) promotes *BAT atrophy*. Too much white adipose tissue plus brown adipose atrophy and/or more "dysfunctional" BAT are driving the obesity crisis, along with endocrine-disrupting chemicals (EDCs) adversely affecting fat stem cells to birth nastier-acting fat cells (and potentially adversely affect bone stem cells).

Fat Cell Compartments

Fat cells are not an island unto themselves. Microscopic anatomical analysis has shown fat cells also contain "non-fat cells" that co-exist along with fat cells, but in different cellular compartments. These other cells have their own diverse functions. Many of these cells "cross-talk" with other tissues and organs, far-and-wide throughout the body.

What is stored in fat gets mixed and merged with our blood and, thus, the rest of our tissues. For example, a *stromal vascular fraction* of fat cells is made up of cells, such as fibroblasts, blood and blood vessels, macrophages, and other immune cells, and nerve tissue. Since fat cells are in constant communication with our blood, whatever endocrine-disrupting pollutants that fat cells may "horde," like lead for example, are in constant communication with the rest of the bloodstream. These pollutants can be carried far and wide to other tissues, like your brain. Yes, lead does cross the sacred-blood brain barrier. (The ability of lead to pass through the blood-brain barrier is due in large part to its ability to substitute for calcium ions.[28])

This also means that fat cells are in communication with our nervous and immune systems. For example, both WAT and BAT participate in immunomodulation, the suppression and activation of the immune system, and each fat tissue releases distinct mediators of the complement system.

WAT, and more recently BAT, have been identified as integral and regulatable components of lipoprotein and bile acid metabolism. This means that our fat stores affect digestion. White and brown fat get in on nutrient bioavailability. They both give off signals to liver and skeletal muscle that affect and help coordinate how these tissues use nutrients to fulfill their job descriptions. Digestion is not just about digestive enzymes or probiotics!

It's very clear that fat is not a lumpy island. *We are one of a thing.* Common sense says that all of our body

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communicates with all of our body. Inside our human body suit, we are made up of many things that all work communally together. At least we hope they are working together rather than the divide-and-conquer we are sadly seeing culturally today.

Brite Fat Facts

Beige/brite fats are results of white fat cell plasticity[29] and distinct thermogenic adipocytes that have features of both white and brown adipocytes. These "brown-in-white" (brite) or beige cells emerge in the white adipose depots in response to cold temperature,[30] a broad spectrum of pharmacological substances, and thank god, by exercise. Exercise promotes beige/brite fat as well as brown fat. Thus, brite fat is also known as "inducible brown adipocytes."

I have suspected for a long time that low-dose naltrexone[31] induces brown and brite fat in this manner, too, as so many patients lose those last several pounds on it. So much so that they have tried giving it for smoking cessation to avoid extra weight gain, but that has not shown great promise.

Activation/inducing of brite adipocytes (along with brown) promotes "fat burning" over "fat storing," making it less challenging to maintain a healthier weight. Brite fat cell induction (along with brown) also reduces diverse metabolic disease incidence.

Brite fat was first recognized in rodents. Lab animals were found to contain two populations of Ucp1-expressing adipocytes, with well-characterized thermogenic functions, or burning fat off as heat/calories. These were found in the classical interscapular brown adipocytes and in brite/beige adipocytes. Anatomical localization, gene expression profiling, and functional characterization of Ucp1-expressing fat cells indicate that brite and brown adipocytes also co-exist in human beings. Such adaptability of adipocytes is regulated by epigenetic mechanisms. This is why Dr. Bruce Blumberg found that exposure to certain endocrine-disrupting chemicals in the womb can affect epigenetics for the next several generations, making fat cells less able to have browning or beiging and keeping the animals fatter, even in fasting states. This is one way pollution exposure is partly driving today's obesity epidemic as much as or more than *what* we eat or *how much* we eat.

Some folks make brite fat much more easily than others and have an easier time staying slimmer. Some folks are exposed in the womb to chemicals that keep them fatter. DES – a synthetic estrogen, fifty times more powerful than our endogenous estrogen – is the model chemical for endocrine disruption. Exposure to this in the womb (from prenatal vitamins[32] containing it or from being prescribed it for a threatened miscarriage) alters the phenotype of the DES daughter,[33] making her epigenetically fatter.

Future generations get our genes. But these genes can be morphed especially while in the womb. Especially vulnerable are genes to fat and bone cells.

Methylation activates or represses gene expression depending on which residue is methylated. *Histone methylation* is an epigenetic marker for what nudges gene expression. mediates cellular memory to induce and maintain beige adipocyte characteristics. Enzymes that catalyze regulators of gene expression of brown adipocyte biogenesis can be tracked.[34] This tracking has demonstrated that *fat cells have cellular memory*, which can be nudged by environmental stimuli. The more you exercise, the more your fat cellular memory serves you well. But exposure to adverse stimuli, like environmental pollutants, can nudge fat cell memory in pro-fattening ways.

Exposure to endocrine disruptors that disrupt fat stem cells at the epigenetic level – which Dr. Bruce Blumberg calls *obesogens*[35] – can upset this histone cart. The functional response of the adipose organ to a range of metabolic and environmental challenges highlights its extraordinary plasticity[36] while also highlighting that today's dirty planet can morph our fat cells to act more nastily.

This illustrates that how we live affects how our fat cells live.

There is a "bi-directional"[37] ability of WAT to go to brite fat, but also, poor lifestyle choices and certain pollutants can reverse brite back to WAT. You are how you choose!

Pink Fat Facts

Emerging evidence suggests that pink fat is made from subcutaneous white fat, or WAT. In other words, pink fat comes from the trans-differentiation of subcutaneous white adipocytes. The "pink" component develops in subcutaneous depots during pregnancy. It is made from WAT and again demonstrates the plasticity of fat. Pink adipocytes are mammary gland alveolar epithelial cells whose role is to produce and secrete milk. Pink fat allows us to nurse the next generation. The pink adipocyte has recently been characterized in mouse subcutaneous fat depots during pregnancy and lactation.

Excessive "pinking" of breast fat may be a contributing factor to breast cancer. This remains to be explored but has been suggested by research from several labs.[38] The female breast is rich in adipose tissue. Adipose tissue has significant roles in the dynamics of breast changes throughout the life span of a female breast from puberty through pregnancy, lactation, and involution. There is a constant interaction between breast adipose tissue and surrounding cancer cells and vice-versa. Pollutants contained in breast fat can promote tumor microenvironment in favor of cancer.

Bone Marrow Adipoyctes (BMA)

Bone marrow fat is distinct from white, brown, and beige adipocytes, indicating that the bone marrow is its own "unique" adipose depot. Adipocyte tissue was first identified in human bone marrow more than a century ago, but we didn't understand much about it. Human arrogance thought it had little functional significance. When did Mother Nature ever invent anything without a purpose?

Bone marrow adipocytes[39] are the most abundant component of the bone marrow microenvironment. Recently, BMA was found to serve as an "endocrine organ" that secretes adipokines, cytokines, chemokines, and even growth factors.

Bone marrow fat cells, and even the total mass of bone marrow fat cells, have critical function and influence. Bone marrow fat *mass* needs to be in a state of Goldilocks "just right" balance – not too much and not too little – to keep physiology humming. When bone marrow fat increases in response to certain pathological signals coming from

a variety of sources, fat stems cells and even bone stem cells can take a serious hit.

Dr. Bruce Blumberg, whom I met at a Cooper conference and interviewed for my breakthrough book on endocrine disruption (*Hormone Deception,*[40] McGraw-Hill 2000) and on my podcast (Dr. Berkson's Best Health radio #133) has demonstrated that when bone marrow fat mass excessively increases, fat stem cells go rogue.

What can cause bone marrow fat to excessively increase? Endocrine-disrupting pollutants commonly found in food, air, water, and personal care products. Even exposure in the womb (in-utero) matters. When bone marrow fat mass increases beyond the balance point, this can upset the balance of bone stem cells.[41] Fat stem cells and bone stem cells are in a constant dance. When mass of bone marrow fat cells goes too high, nastier-acting fat cells are birthed that are much more resistant to weight loss measures, making it much harder to lose weight in 2022 than it was in 1952 (when we had much less endocrine disrupting chemicals inside our environment and bodies). Also, when the mass of bone marrow fat cells enlarges excessively, bone stem cells mass can pathologically lessen.

The Intimate Link Between Fat and Bone

Bone formation is complex and tightly regulated. We learn in school that we build bone with osteoblasts. and break down bone with osteoclasts. Throughout life, bone is in dynamic balance, constantly building up and breaking down. This harmony involves a complex coordination of multiple bone marrow cell types.

- *Osteoblasts* birth from a common archival cell, a cousin to adipocytes. Herein lies some of the intimacy. Osteoblasts come from marrow mesenchymal stem cells (MSCs).
- *Osteoclasts* come from hematopoietic stem cell precursors (HSCs) along the myeloid differentiation lineage.

Bone formation by osteoblasts and resorption by osteoclasts is responsible for continuous bone "remodeling." Imbalance between bone formation and bone resorption is a risk factor for a variety of health issues and pathologies, from bone issues such as osteopetrosis, osteopenia, and osteoporosis[42] to autoimmunity and even to cancer and obesity.

This balance between bone breakdown and buildup depends upon the tightly controlled commitment of MSCs[43] to ensure that bone will keep up with the body's demands, continually manufacturing when the body needs more bone. Thus, MSCs have a lot to do with bone homeostasis and indirectly with many downstream potential health issues.

Butyrate and resveratrol help 'brown' white fat and turn it into fat-burning brown adipose tissue.

Although a variety of cell types can be derived from MSCs, the "commitment" of MSCs to either adipocytes or osteoblasts has been specially implicated in certain diseases. If MSCs commit to making less new bone, then bone marrow fat content is increased, which increases the risk of osteoporosis. What tweaks MSCs to make less new bone? Aging, obesity, excessive inflammation, and certain blood cancers. With less bone stem cells and more bone marrow fat, the risk of metastatic cancer increases. Remember, bone marrow fat gives off growth factors. The more bone marrow fat, the more growth factors. These can encourage cancer cells to travel and kill. BMAs may function as a pivotal modulator of bone metastasis of breast cancer.[44]

It's All About Balance

There is a "yoga" to be maintained between bone stem cells and fat stem cells that affects bone health as well as fat cell health. If either goes rogue or behaves in an aberrant manner, they can adversely affect each other.

If fat stem cells nudge aberrant skeletal stem cells (SSCs), this reduces osteoblastic, or bone building, which in turn reduces bone mass while increasing marrow adipose tissue. Bones get thinner. You get fatter. Numerous in vitro investigations have demonstrated that fat-induction factors inhibit osteogenesis and, conversely, bone-induction factors hinder adipogenesis.

Disharmony between the delicate balance of adipo-osteogenic differentiation of MSCs creates excess fat at the expense of bone.

What's a growing trigger? Endocrine disruptors. Specifically, endocrine-disrupting compounds (EDCs) that specifically act on fat stem cells to make them commit to aberrant fates.

Dr. Bruce Blumberg and EDC Obesogens[45]

Dr. Bruce Blumberg has demonstrated that specific endocrine disruptors can hasten the morphing of increased fat stem cells at the expense of bone stem cells. He showed that tributyltin – the now banned chemical that was painted on the bottom of boats for many decades to prevent the buildup of barnacles, etc. – when given to pregnant rodents, epigenetically altered the fat stem cells of the next several generations, even without further exposure. They became fatter, and the fatness resisted weight loss measures. Even fasting didn't make the next generation of animals lose weight. And this was demonstrated by exposure to only ONE endocrine-disrupting chemical. We now live in a soup of many thousands of endocrine disrupting chemicals.

The peroxisome-proliferator-activated receptor γ coactivator 1-α (PGC-1α) is a critical "switch" of cell *fate* decisions whose expression decreases with aging and from exposure to endocrine disruptors. Loss of PGC-1α promoted nastier fat archetypal cells being made instead of skeletal ones – promoting obesity and at the same time, loss of bone density. Deletion of PGC-1α in SSCs impaired bone formation and indirectly promoted bone resorption while enhancing bone marrow fat accumulation.

Conversely, induction of PGC-1α blocked osteoporotic bone loss and MAT accumulation. How does PGC-1α do this? Mechanistically, PGC-1α maintains bone and fat balance by inducing TAZ,[46] a transcriptional co-regulator. TAZ[47] is a main regulator of bone organ growth and biology.

How we live effects TAZ. Excess sugar ingestion, excess processed foods, and/or excess stress hormones, as well as excessive production of the pro-inflammatory cAMP pathway (often

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inversely related to release of sufficient melatonin during a sufficiently "dark" night), increases loss of PGC-1α.

This may go to show that a worse diet, with more stress (anyone living outside this pandemic?) along with too much light at night (hey, that's the whole Western hemisphere), exposed to an endocrine-disrupting chemical soup, may be at risk of worse bones and worse fat cells, starting at the marrow level.

But there is hope. We are not born with all the fat cells we will ever have. We make new fats cells all throughout life.

If the "obesogen hypothesis" by Dr. Blumberg is accurate, then the more contemporary fat cells we are living with are more resistant to normal and proper behavior. However, the hope comes from the fact that normal fat cells have a "turnover" rate of eight percent a year. This means fat cells are recreated every fifteen years throughout our lives. This fat cell turnover is faster than many other cells, such as that of the heart cardiomyocytes, and similar to bone osteocytes. This means that there is hope about endocrine disruptors and fat cell fate. If we detox. Eat well. Eat less. Eat more plant foods. And exercise. That is one reason I recently formulated and designed two new products to help clear toxins and keep physiology humming (*Receptor Detox* and *Hormone Balance & Protect* available at https://drlindseyberkson.estorerx.com/).

This "renewal" of fat cells is done through "pre-adipocytes," which can be nastily tweaked by endocrine disruptors to act less normally and more frustratingly. But they can also be tweaked to act more normal and help you battle excess adiposity by detoxing, decreasing pollution exposure, and lifestyle choices in multiple life domains.

At the cell level, plasticity of the fat cell[48] is provided not only by stem cell proliferation and differentiation but also by direct trans-differentiation[49] of fully differentiated adipocytes via stimuli that induce genetic expression reprogramming – such as the chemicals you may be exposed to while eating fish flesh, or standing in an unfiltered shower, or through various exposures to diverse plastics.

Chronic exposure to some endocrine-disrupting pollutants – obesogens – can act on mature WAT and tweak them genetically to be more "problematic" fat!

If nothing else can encourage us to go more "green," perhaps the promise of less frustrating fat and the hope of thinner waistlines might. What a great motivation to go green.

When I was a distinguished scholar at the Center for Bioenvironmental Research at Tulane University, the last e.hormone conference we held was all about effective remediation. There are many scientific and lifestyle ways to turn the Titanic away from the global obesity and bone loss epidemics.

The Hormone Family and Fat

Hormones are a family of proteins that are the most powerful signaling molecules in the body. Like Rodney Dangerfield, they often "don't get no respect." But another underappreciated feature of hormones is that they *function and dysfunction together*. If one hormone, far off, is having issues, such as resistant leptin or too little testosterone, this can affect other hormones. Like thyroid. Or estrogen. Or adiponectin. If there is too much of one, it can diminish another. This is because they can often "sit" and "signal" on each other's receptors. Hormones are powerful. But potentially promiscuous. Fat cells, by producing hormones, get in on all these incestuous politics. Just saying….

Leptin keeps us in a normal-size body suit. It's a hormone made by adipose cells and enterocytes (gut wall cells) in the small intestine that regulate energy balance. Leptin keeps us from overeating by inhibiting hunger, which in turn diminishes fat storage in adipocytes. Some people suffering with obesity have "leptin resistance." Detoxing their receptors may be helpful in reversing this.

Adiponectin[50] – fat cells, muscles, and the brain make this hormone, which regulates glucose and fatty acid metabolism. But it's mainly made inside fat cells. It sensitizes insulin receptors. Of course, the brain mainly consumes oxygen and glucose most of the time. So does much of our body. So, adiponectin drives physiology on a huge scale. Adiponectin also helps the liver do many of its jobs more appropriately. The production of adiponectin increases following regular exercise! This is yet another way exercise improves energy and glucose metabolism. Low levels of adiponectin are associated with obesity, Type 2 diabetes, fatty liver, atherosclerosis and probably more.

Adipokines. Beyond these hormones, adipocytes and the other resident cell types produce dozens of other "adipokines" that affect local and distant physiology, good and bad. For example, adipokines can promote nasty pro-inflammatory molecules, such as proinflammatory tumor necrosis factor α (TNF-α) and monocyte chemotactic protein 1.

Estrogen. WAT produces the sex hormone estrogen in both genders. More WAT promotes more estrogen, but in the form of estrone, the more "pro-carcinogenic" form of estrogen. It signals "growth" via the first estrogen receptor (ER alpha) more than estradiol and estriol. Excess WAT makes lots more estrogen, which can lead to early puberty in young girls. In this way, fat cells can alter hard-wired biologic milestones of reproduction. Men who are overweight, sit too much, drink too much alcohol, and eat foods with high microplastic content can make excessive estrone that can lead to breast development in males, called gynecomastia, which is presently treated by surgery. This is on the rise. Lowering the WAT burden, cleaning up lifestyle factors, and sometimes replacing testosterone can get at cause rather than just the effect.

You can have too little WAT. Too little white fat stores occur in anorexia nervosa, some cases of amenorrhea, and lipodystrophies, all of which can interrupt menstruation. Too little WAT can halt menstruation as estrogen levels go way too low.

Fat Cells as Hoarders That Crosstalk

Fat cells are not totally separate from the rest of the body. About five percent of fat cells are in constant communication with our bloodstream 24/7. Whatever is stored inside fat cells slowly releases into the bloodstream from this five percent of the fat cell in communication with our blood. This has been known for a few decades (I wrote about this in *Hormone Deception* a number of years back). Thus, whatever is sequestered in fat cells over a lifetime merges with every cellular nook and cranny inside you. This

is a fundamental unappreciated action of adipose tissue.

This is partially what the concept of *detoxification* is about. Once we realized that fat (and other cells, like bone for example) can "sequester" pollutants, heavy metals, pesticides, etc. which, over a lifetime, slowly leak out and mingle and merge with all of our cellular real estate, that underscores the need for "cellular housecleaning" – detoxification. This also gives us some understanding as to why sudden and severe weight loss, over a relatively short period of time, can cause toxic exposure to the body (and brain). It sometimes results in such gallbladder pathology that the person – now happy to be suddenly thinner – unhappily learns they may need to have their gallbladder removed.

Fat cells chit-chat far and wide. Adipose tissue contains various cell subtypes that play critical roles in not only regulating adipogenesis and thermogenesis, but get this, "inter-organ communication!"

Adipose cells also contain proteoglycans inside an extracellular matrix. Proteoglycans[51] give fat physicochemical capabilities that allow fat to enlarge and shrink dynamically. Proteoglycans allow fat cells to withstand "pressure," and provide hydration and swelling pressure to the adipocytes, enabling them to withstand compressional forces. This allows fat to "protect" what it surrounds. Like organs. But proteoglycans can get glycosylated in "good" ways, as in enzymatic reactions, or in "bad" ways, because of dietary choices that drive unhealthy glycosylation.[52] The more processed foods, sugar, and high fructose corn syrup that you eat, the less compliant of a protective job your fat cells afford your organs. Diet affects everything!

Obesity

Obesity is a world-wide epidemic, but especially in the US. Obesity is the number one co-morbidity that drives severe Covid. One of my colleagues, an ICU doc in Idaho, confided that most of what she sees in the ICU are obese patients.

What drives obesity? Let me count the possible ways:

- Excessive triglyceride storage (which is why tracking triglyceride levels in patients is critical, and you don't want to go much higher than 150).
- Excess WAT
- Dysfunctional BAT
- Dysfunctional hypothalamus/body crosstalk (Animal studies suggest it may have something to do with the hypothalamus/hormone/body cross-talk going haywire, and we already know that obesity itself, besides extra WAT, also disrupts the ability of the hypothalamus to stimulate BAT energy expenditure in a normal way.)
- Dysfunctional hunger hormones

Fat Cells

- Dysfunctional sex steroid hormones
- Dysfunctional thyroid
- Gut illness/infections that contribute to BAT and hypothalamic/whole body cross talk miscommunication

Starting in early adulthood, lean Americans are mostly headed toward a chubbier future. Lean younger US adults tend to gain an average of 1.1 pounds ➤

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per year, which challenges the morphing quality of fat cells. They meet this challenge by enlarging.

- The larger the WAT cells, the more dysfunctional BAT and its mitochondria become.
- Increased pro-inflammatory signals are sent to organs far and wide.
- More health-damaging pollutants are stored and become in constant contact with our blood supply that reaches tissues and organs far and wide.

If children, teens, and young adults start out overweight or obese, their weight gain in mid-life can increase substantially. Covid and lockdown have not helped. When many patients come back into the office now, the first thing they say with a defeated smile is, "I gained that darn Covid 15."

By the fifth and sixth decades of life, a large increase in WAT stores more triglycerides and tamps down much of the protective effect of healthy fat cells. More WAT, less healthy functional BAT.

Ultimately, hypertrophic WAT keep growing and expanding. Getting more alien-like. Waxing WAT and waning BAT restrict the ability of oxygen to diffuse from the capillaries into the adipocytes. This *hypoxia* constitutes a biologic red alert for the cells, altering over 1,000 genes to express in unhealthy ways. More resistance to local insulin. More resistance to all adrenal hormones. More inflammation. More cellular damage.

When the WAT can no longer expand, then a flood of triglycerides rages throughout the body. Once the serum levels of triglycerides start to rise about 150, this is starting to occur.

Triglycerides accumulate in skeletal muscle. enter the liver, and worsen insulin resistance. Any attempt at losing WAT becomes near impossible with a fatty liver and the insulin resistance it imprints onto local tissues. Fatty liver is rising in epidemic fashion, even in children.

Obesity is a risk factor for fatty liver, but so is unhealthy *ergonomics*. Obesity works by putting pressure on musculature in the back of the throat from the extra weight. But so does unhealthy posture. Children who are raised on screens (phones and tablets) jut their chin forward and, in a manner, push their musculature similar to that of holding extra weight.

Fatty liver creates insulin resistance and makes it almost impossible to lose weight. If one has fatty liver, this must be identified and fixed in order to lose more weight, and to have the liver available to perform so many of its myriad other functions.

P.S. You might identify some cases of fatty liver by a below normal, high-density lipoprotein (HDL) blood level, as HDL is only manufactured in the liver. Ultrasounds of the liver can identify fatty liver, but the new liver elastography (FibroScan) is much more sensitive to fat deposits and to fibrosis and scarring.

Excess triglycerides hiding away in organs and creating havoc is called "lipid toxicity," which drives all metabolic diseases and the potentially worse outcomes of Covid. Why? Because lipid toxicity damages immune responses. That's why obesity is also associated with an increased risk of many types of cancer, including cancer of the breast, uterus, ovary, esophagus, stomach, colon, or rectum, liver, gallbladder, pancreas, kidney, thyroid, and meninges, as well as multiple myeloma.

Nutrients and Hormones That May Help Lessen the Obesity Epidemic

The main function of brown adipose tissue (BAT) is to burn off energy as heat. This is a process mediated by "uncoupling protein 1" (UCP1), which is located in the inner mitochondrial membrane. This protein releases ATP, which uncouples oxidative phosphorylation so energy can be turned into heat. White adipose tissue can be "nudged" into expressing UCP1 cells. This is the back-copy of what is happening with the "browning" of WAT to BAT. The browning of WAT into BAT helps keep us warmer, healthier, and not too overweight.

The UCP1-mediated browning of WAT can be enhanced by specific nutrients – butyrate,[53] a short-chain fatty acid, and resveratrol,[54] a plant compound found in some foods and skins of grapes and some nuts. And fermented foods.

Butyrate. Short-chain fatty acids (SCFAs) play an important role in the host system. Among SCFAs, butyrate has received particular attention for a robust effect on host immunity, particularly in supplying energy to enterocytes, the single layer of cells that make up the gut wall, as well as help producing local gut immune cells.[55]

Butyrate also is an inflammation controller to help control human host homeostasis. How can butyrate control inflammation? Let me count the ways.

Butyrate enters the cells through the Solute Carrier Family 5 Member 8 (SLC5A8) transporters, then works as a histone deacetylase inhibitor (HDAC) that inhibits the activation of nuclear factor-dB (*NF-κB*), which "down-regulates" the expression of *IL-1β*, *IL-6*, *TNF-α*. This means that butyrate tamps down inflammation. In this way, butyrate is famous in functional medicine circles as an anti-inflammatory and immune modulatory[55] tool for the gut wall.

Meanwhile, butyrate also acts as a ligand to activate G protein-coupled receptors *GPR41*, *GPR43*, and *GPR109*, promoting the expression of anti-inflammatory factors.

Further, it can also suppress the expression of pro-inflammatory chemokines to reduce inflammation. By the way, it also suppresses excessive appetite![56]

Butyrate is not only a gatekeeper of the gut wall and of taming excessive inflammation; it also helps us avoid getting obese. Let me count these ways, too. Butyrate has been shown to prevent diet-induced obesity, hyper-insulinemia,[57] hyper-triglyceridaemia and fatty liver (hepatic steatosis). Butyrate does this through several mechanisms.

Butyrate helps maintain healthy "gut-brain neural circuitry."[56] This has input into our energy intake, portion control, and enhances burning off fat by fat oxidation. Butyrate also improves insulin sensitivity and increases energy expenditure in mice and most likely does this in humans, too.

Where butyrate especially shines in helping with weight loss, as well as healthier levels of triglycerides and insulin, is by *boosting browning of WAT to BAT.*

How do we consume butyrate? Butyrate is found in resistant potato starch, raw green organic banana flour, lentils, white beans, and cooked and cooled potatoes and rice. Foods rich in butyrate are ghee, organic cow's milk, butter, goat's milk, breast milk, and parmesan cheese. When celiac disease was not well understood, one of the first

doctors to save failure-to-thrive infants, accomplished this by giving them raw green bananas. The resistant starch helped heal their gut and keep them alive. This was the first use of resistant food starch as medicine.

Resveratrol. Resveratrol[58] is a polyphenol, the micronutrients inside plants, and there are about 8,000 identified so far. Resveratrol also helps brown WAT into fat-burning BAT through quite a number of routes. Resveratrol and its derivative pterostilbene[59] activate BAT from white fat by promoting the browning action, by promoting the mitochondria that make brown fat brown, and by protecting activity against glycation, which protects the inner membranes of mitochondria, especially in brown fat.

Both resveratrol and pterostilbene induce thermogenic capacity in interscapular BAT by increasing mitochondriogenesis, as well as enhancing fatty acid oxidation and glucose disposal. This says that patients with mitochondrial dysfunction ought to make sure they eat and supplement robustly with resveratrol. It's a mitochondrial "Adam," birthing more mitochondria so your brown fat can serve you better.

Resveratrol promotes browning of BAT by another platform – by upregulating an insulin receptor, the peroxisome proliferator-activated receptor (PPAR). This underscores resveratrol as an "insulin sensitizer." Resveratrol also induces brown fat-like phenotype by activating peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α). It also reduces lipid accumulation inside fat cells (WAT), possibly by activation of mammalian target of rapamycin (mTOR). Resveratrol has yet another trick up its "browning" sleeve: it promotes biome diversity and healthy biome infrastructure, which also nudges WAT toward BAT. It is so influential in this that there is an axis named the *Gut Microbiota-Adipose Tissue Axis.*[60]

Resveratrol is found in grape skins, peanut skins, pistachio skins, microgreens, tomatoes, cocoa, and blueberries, bilberries, cranberries…and wine. The more resveratrol on hand, the healthier calorie-burning BAT. That is one reason to eat less "junk processed food" and consume more plant food.

Resveratrol is not easily absorbed. To get tissues rife with this protective flavonoid, plant foods and/or supplementation need to be taken regularly for months, if not years. Slowly, through healthy choices over time, our tissues accumulate healthy levels of resveratrol. If you do supplement, consider companies that have, in safe ways, "processed" their resveratrol to enhance its bioavailability. It is so poorly absorbed that it takes a lot of exposure, over lots of time, to make sure your piggy bank reserves are full enough. It is fat soluble, so it is better absorbed when consumed with a high fat meal.

Fermented foods for better fat metabolism. Foods that are fermented have been naturally processed to create healthy substances, such as lactic acids that boost weight loss and healthier biomes. An international team of scientists from Japan found that fermented soybeans improve fat metabolism and help block some effects of diet-induced obesity and possibly pollution. They showed that mice on a high fat diet, supplemented with fermented veggies, gained less body mass and had lower levels of fat and cholesterol after three weeks as compared to mice on the same diet but not fed any fermented food (they used fermented okra,[61] but also miso from soy in some other peer-reviewed studies). Mice fed fermented soy also had less visceral and subcutaneous fat than mice on a high-fat diet without any fermented food.

Why? Fermentation creates *Aspergillus oryzae* and *Aspergillus sojae,* which are typical aspergillus fungi used to produce soy sauce and miso, and okra. They do the magic. But you would have to consume the fermented food regularly – at least five days a week over a few months – to get the benefit.

There are many types of fermented foods: kimchi, yogurt, kefir, fermented pickles, fermented string beans, umeboshi plum paste (1/2 to 1 tsp/d makes it very easy to get this), and on and on. I love a cup of miso in the evening and add 1 tsp. of fermented gluten-free soy sauce and some granulated garlic to give it more nutritional and taste bang for my buck. Fermented soy has more protein and a higher total phenolic content – an indication of higher antioxidant properties – but due to the fermentation process, folks who are reactive or allergic to soy can often handle it better without adverse issues, than soy foods that are not fermented.

Nitric oxide. In a rodent model, sustained nitric oxide was given as well as a high-fat diet. This boosted the hormone lipase (which my new product Hormone Balance & Protect also does); and compared to control rats, there was loss of fat, increased browning of white fat, no loss of muscle, a reduction in the size of fat cells in epididymal white adipose tissue, improved glucose tolerance, and decreases in fasting serum insulin and leptin levels as well as protection against non-alcoholic fatty liver disease.[62]

Aging, Hormones, FSH. Most of us think as we age, we inevitably get fatter. And the battle gets harder. What drives this? Hormone loss. But it turns out it is not just hormone loss, as also an elevation of FSH. FSH rises in both females and males as we age. This turns out to be part of the "gaining weight as we age" issue.

FSH helps younger males produce testosterone. In women, it stimulates the growth and recruitment of immature follicles in the ovary, essential for female fertility. It oversees reproduction on both males and females.

But like most things, FSH has a lot more actions than just reproductive. (Just as we are learning that all sex steroid hormones have a lot more actions than reproductive). A younger, lower level of FSH, is part of staying lean and more youthful. For example, "lower" FSH levels help protect bones in both sexes. While high FSH, independent of sex hormones, stimulates bone destruction.

Although conflicting, studies in rodents and humans during the last decade have provided genetic, pharmacological, and physiological evidence that "elevated" FSH levels that occur in the face of normal or declining estrogen and/or testosterone levels directly regulate bone mass – and adiposity.[63] Keeping FSH lower, in hormonally replaced patients, not only helps how they "feel," but also one's mass. Or…torso size.

Recently, an efficacious blocking polyclonal FSHβ antibody was developed that inhibited ovariectomy-induced bone loss and triggered white-to-brown fat conversion accompanied by mitochondrial biogenesis in mice. ➤

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Moreover, additional nongonadal targets of FSH action have been identified, and these include the female reproductive tract (endometrium and myometrium), the placenta, hepatocytes, and blood vessels. Thus, FSH elevations are endothelial unfriendly – another reason to monitor this in your replaced patients. Both genders.

PS: This info comes from prestigious groups (Division of Reproductive Sciences, University of Colorado Anschutz Medical Campus, Aurora, Colorado; Division of Reproductive Endocrinology & Infertility, University of Colorado Anschutz Medical Campus, Aurora, Colorado; Department of Obstetrics and Gynecology, University of Colorado Anschutz Medical Campus, Aurora, Colorado).

Turns out that there are a number of extragonadal actions of FSH.[64] FSH is now being shown, by the group above, to have "input" into mitochondria of fat cells as well as angiogenic activity on blood vessels.[65]

We know that when women and males get onto HRT, the plasma levels of estradiol and testosterone increase. FSH decreases.

Elevated FSH is being linked to age-related weight gain, bone loss, and even cognitive decline.[66] Pharmaceutical companies are competitively looking for FSH humanized antibodies to follicle-stimulating hormone (FSH) to promote weight loss, bone health, and cognition improvement. This is a very hot area of research. But of course, hormone replacement is the easier and, in my opinion, more natural approach.

Meal Timing. Brigham and Women's Hospital is the second largest teaching hospital of Harvard Medical School. In one of their recent studies,[67] their researchers demonstrated experimental evidence that late eating causes decreased energy expenditure, increased hunger, and epigenetic changes in fat tissue that combined, keeps "love handles" on, no matter your weight loss efforts. Moral of this new research story, avoid regular late-night nibbles while Netflix binging. Late night eating alters fat cells to work against your weight loss efforts.

De-stressing is critical, too. *It's not just what we eat, but how much we eat.* Excessive caloric intake is thought to be sensed by the brain, which then activates thermogenesis as a means of preventing obesity. But if BAT is dysfunctional, this protection mechanism gets thwarted.

Stress does not help. The sympathetic nervous system, through the beta-adrenergic receptor (betaAR)[68,69] action on target tissues, is the efferent arm of this homeostatic mechanism. If the sympathetic nervous system is on overload, it blocks healthy BAT and thermogenesis. You are stressed, you overeat, but you can't induce adequate thermogenesis to right plump wrongs.

A healthy balance between sympathetic and parasympathetic nervous systems is needed to achieve thermogenesis post overeating. Thus, stress plus excessive eating and snacking sets up chubbier and more unhealthy fates.

How to Heal Our Fat Selves

We may need to exercise harder and live smarter to outwit our WAT and the contemporary nasty fat stem cell. I think it's worth it. By the way, when you perform moderately active aerobic exercise, your muscles secrete a fat-fighting hormone called *irisin*, which fights fat with a one-two punch. First, irisin appears to activate genes and a protein that transforms calorie-storing white fat cells into brown fat cells, which continue to burn energy after you finish exercising. Second, irisin appears to inhibit the formation of fatty tissue. So, keep moving. It's the fat-taming mantra.

- Keep moving.
- Detox. Detox. Detox.
- Consume fermented foods daily.
- Take butyrate and resveratrol. Daily.
- Over 40 years of age, consider nitric oxide boosters.
- Consider Receptor Detox and Hormone Balance and Protect.
- Identify subclinical hypothyroidism and treat.
- Get your hormones tested and balanced by hormone replacement if need be.

Test, track FSH. Wow, huh?

Remember, the human body is really all of one thing. Everything affects everything else. We are our own planet.

Mother Earth is all of one thing. Every single thing matters. Even the lowly fat cell.

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Dr. DL Berkson is considered a thought leader in functional medicine. Dr. Berkson has been lecturing for CMEs to MDs, pharmacists, DCS, NDs, and nutritionists for more decades than her ego wants to admit.

Dr Berkson wrote one of the breakthrough books on endocrine disruption. Based on this book, *Hormone Deception* (McGraw-Hill 2000 Awakened Medicine Press 2016) she was invited to be a distinguished scholar at an estrogen think tank at Tulane University (Center for Bioenvironmental Research) where she studied with the scientists that discovered the first two estrogen receptors and launched the EDC field.

Her book *Healthy Digestion the Natural Way* (Wiley 2002) was the first gut, nutrition, spirituality digestion book and a long-time best seller. Its sequel is a breakthrough book creating a new field – *Nutritional Gastroenterology*. Her latest book, *Sexy Brain*, warns of environmental castration and how sex steroid hormones rule the brain.

Dr. B presently works at the *Naples' Center for Functional Medicine* (Dr. David Perlmutter's old clinic) where she initiated the first functional renal program and adjunctive nutritional/pharmaceutical/hormonal support program for breast cancer survivors.

Berkson hosts the *Dr. Berkson Best Health Radio Show* (soon to be called *Agile Answers),* and launched a membership for practitioners - *Smart + Heart* during the pandemic. She writes for substacks.com under Agile Thinking.

References are available online at www.townsendletter.com.

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Insulin Potentiation Therapy (IPT) for All Chronic Disease: Can Old Cranky Physicians Try New Approaches?

16th International Academy IPT Conference in Mexico

by Simon Yu, MD

Let me reintroduce an old forgotten and neglected medical therapy called Insulin Potentiation Therapy (IPT) developed by Mexican military surgeon, Donato Perez Garcia, Sr., MD, in 1932. He was able to cure many medical conditions from asthma, psoriasis, migraine headache, neuro-syphilis, lupus, multiple sclerosis and even some cancers. *Time* magazine covered Dr. Garcia's therapy as insulin shock therapy in 1944. Despite media coverage, his ideas were never fully accepted in the United States. I previously wrote, "Insulin Therapy for Other than Diabetes**,"** and another article, "IPT as an Immune Support Therapy: Scientific Basis of Fudge Factors Needs New Calculation**."** IPT simply targets deep hidden infection and inflammation by using fast-acting insulin.

Most young physicians follow prevailing medical policy and guidelines. There is too much risk to lose everything and their livelihoods. Is there room for older, independent, solo-practice established physicians who refuse to accept insurance-driven models so they can apply their experience in clinical decisions – rather than using cookie cutter insurance, pharma, and algorithm driven protocols? They can be uncompromising contrarians, raising hell for their patients' welfare, truly a rare, dying breed of independent, cranky old practitioners. The crankier the better. These physicians are far less likely burned out and depressed than those employed by a hospital or large healthcare organization. I try not to be too cranky; my goal is searching for and spreading old and new neglected, innovative treatments.

Consider all the modern chronic diseases such as cardiovascular disease, hypertension, diabetes, Lyme, obesity, neurologic disorders, Alzheimer's disease, many forms of cancer, and more. These chronic diseases have become a very promising growth industry for the medical-industrial complex, bigger than the military-industrial complex. I forgot to mention other competing medical industries such as kidney, liver, lung, hormone, anti-aging, sexual dysfunction, regenerative medicine, etc. Follow the money as the global population is aging with multiple ailments and medical diagnoses.

Medical science, Pharma, and Big Money investors are betting on advances in molecular and gene therapy, CRISPR technology, and artificial intelligence (AI) for breakthroughs in managing chronic diseases – not necessarily in finding the cures. The magic word is disease management, not cure. IPT may change the playing field from managing diseases to the possibility of cures if you incorporate dental, fungal, and parasite infections as an integral part of medical therapy – three commonly overlooked underlying causes.

Most chronic diseases are not driven by genetics but by epigenetic changes resulting from underlying infections, environmental toxins and endotoxins, nutritional deficiencies, excessive calories, and overloading our main detox organ systems. Our current medical model rarely addresses dental-related medical issues and parasite infestations. We are blessed with an abundance of fake data, fudge factors, and dogma in medical science. How can we seek out what is real and what is just more false, compromised data? Ask old timer physicians who do not take insurance, are independent, and not employed by hospitals. They will tell you how our medical system has become compromised, suppressed, rigged and controlled by you know who. One of the neglected therapies is IPT.

IPT was brought to the United States by a Canadian-American physician, Steven Ayer, MD, in collaboration with Donato Perez Garcia, MD, grandson of original inventor of IPT. IPT has been

combined with low dose chemotherapy (typically 10% of the standard dose) for cancer treatment as a safer, cheaper alternative to high dose chemotherapy. IPT can be also used as an independent immune support therapy without using low-dose chemo by adding antiviral, antibacterial, antifungal, and antiprotozoal medications, and anti-inflammatory agents, to reduce the total body burden of infection loads and reduce inflammation.

I presented at the International Academy for Insulin Potentiation Therapy in 2017 in Munich, Germany, on "Fungus, Parasites, Dental and Energy Medicine," and how to detect problems based on acupuncture meridian assessment (AMA). You can read more in my article, "Medical Heretics in Munich for Insulin Potentiation Therapy/Low Dose Conference." Some of the cases presented included stage 4 multiple myeloma, lung cancer, squamous cell cancer of head and neck, and ALS neurological disorder. I have been successfully treating these patients by adding IPT as an adjunct therapy to reduce the total body burden of infections and inflammation.

For those interested in IPT, come to the 16th International IPT Conference in Mexico City on February 15-19th, 2023. Featured speakers include Akbar Khan, MD, from Canada, Frank Shallenberger, MD, HMD, ABAAM, and Paul Anderson, NMD, who will lecture on, "Stories of Cancer Survivorship: Integrative Physicians Share What Worked and Why." I will give a one-day workshop on "Acupuncture Meridian Assessment (AMA) to Detect Hidden Parasites and Dental Problems: How to Use Parasite Medications for Cancerous Conditions." There will also be a training on new uses of IPT by Donato Perez Garcia, MD, himself, the great-grandson of the inventor of legacy Insulin Potentiation Therapy.

This International IPT Conference will gather medical heretics in Mexico. They will come from around the world and open the doors to new ways of diagnosing and treating patients. For more information, contact the International Academy of IPT, and let other physicians – young or old, cranky or idealistic – know about this important organization offering a patient-centered, root cause, integrative health approach. Even if you are a cranky old physician, you can learn and try a new option, the healing power of Insulin Potentiation Therapy (IPT).

Dr. Simon Yu, MD, is a board-certified internist. He practices internal medicine with an emphasis on Integrative Medicine to use the best each has to offer. For more articles and information about integrative medicine, patient success stories, and Dr. Yu's latest book, *AcciDental Blow Up in Medicine: Battle Plan for Your Life,* visit his website at www.preventionandhealing.com or call Prevention and Healing, Inc., 314-432-7802. You can also attend a free monthly presentation and discussion on Integrative Medicine at his office on the second Tuesday each month at 6:30 pm. Call to verify the date. Seating is limited, arrive early.

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Monkeypox and Natural Therapies

by Ronald Steriti, ND, PhD©

Monkeypox

Monkeypox is a zoonotic disease caused by an orthopoxvirus that is found mostly in areas of Africa but has been seen in other areas of the world.[1]

Symptoms. Monkeypox causes flu-like symptoms such as fever and chills, a rash appearing 1-3 weeks after the onset of fever, and lymphadenopathy that can take weeks to clear. Lymph node enlargement occurs early, often at the onset of fever. The infection can last up to 4 weeks until the lesion desquamate.[2]

Transmission. Monkeypox can spread through close, personal, often skin-to-skin contact; touching objects, fabrics (clothing, bedding, or towels), and surfaces; and contact with respiratory secretions from someone that has monkeypox.[3,4]

A person with monkeypox can spread it to others from the time symptoms start until the rash has fully healed and a fresh layer of skin has formed. The illness typically lasts 2-4 weeks. Healthcare-associated transmission of monkeypox has been observed on multiple occasions in areas where the disease is endemic. It is, however, considered low risk.[5,6]

Transmission during Sexual and Intimate Contact. Monkeypox is not a sexually transmitted infection in the typical sense. It can, however, be easily transmitted during sexual and intimate contact. The majority of reported cases have no travel-related link to an endemic country, and most cases have been among men who have sex with men.[7,8]

A review article found 98% of the persons with infection were gay or bisexual men. Transmission was suspected to have occurred through sexual activity in 95%. Seventy-five percent were White with a median age of 38 years. Forty-one percent had human immunodeficiency virus infection.[9]

Clinical Suspicion. When there is clinical suspicion for monkeypox, clinicians should ask about travel and sexual history and about any close contacts with people with a similar rash or suspected or confirmed monkeypox infection. Behaviors associated with close contact include sleeping in the same room, drinking or eating from the same container, living in the same residence, etc.[1,10]

Diagnosis. Monkeypox infection can be confirmed via isolation in viral culture or PCR for monkeypox DNA from a patient specimen.[11]

Conventional Treatments

Currently, there are no specific clinically proven treatments for monkeypox infection. As with most viral illnesses, the treatment is supportive symptom management.[11]

While most cases of monkeypox will have mild and self-limited disease, with supportive care being typically sufficient, antivirals (e.g. tecovirimat, brincidofovir, cidofovir) and vaccinia immune globulin intravenous (VIGIV) are available as treatments.

Antivirals can be considered in severe disease, immunocompromised patients, pediatrics, pregnant and breastfeeding women, complicated lesions, and when lesions appear near the mouth, eyes, and genitals.[12-15]

Natural Therapies

Sarracenia purpurea. In the nineteenth century, smallpox ravaged through the United States and Canada. At this time, a botanical preparation, derived from the carnivorous plant *Sarracenia purpurea* (also known as a pitcher plant), was proclaimed as being a successful therapy for smallpox infections.

A study characterized the anti-poxvirus activity of *Sarracenia purpurea* extract against vaccinia virus, monkeypox virus, and variola virus, the causative agent of smallpox. *Sarracenia purpurea* was shown to be an effective inhibitor of poxvirus replication at the level of early viral transcription.

Sarracenia purpurea may act as another defensive measure against orthopoxvirus infections.[16]

S. purpurea extracts have broad anti-viral activity against both pox and herpes viruses.[17]

The Mi'kmaq and Wolastoqiyik (Maliseet) peoples of Eastern Canada have traditionally used infusions of *S. purpurea* for the treatment of tuberculosis-like symptoms. Betulinaldehyde, betulinic acid, and ursolic acid were identified as the principal constituents responsible for the antimycobacterial activity of *S. purpurea*.[18]

Conclusion

The appearance and rapid spread of monkeypox has raised alarms, and it is important to keep abreast of its clinical signs, conventional treatments, and natural therapies.

About The Author

Ronald Steriti, ND, PhD, is a researcher and writer of books and continuing education courses for medical professionals. He is Dr. Wright's researcher at the Tahoma Clinic. PDF copies of three of his books on COVID are available on his web site (https://naturdoctor.com/): *COVID Research Review - Conventional Medicine, COVID Research Review - Alternative Medicine and Natural Therapies*, and *Post-Acute COVID Research Review*.

References

1. Bunge, EM, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. *PLoS Negl Trop Dis*. 2022;16 (2), e0010141. PubMed: 35148313
2. Sklenovská, N and M Van Ranst. Emergence of Monkeypox as the Most Important Orthopoxvirus Infection in Humans. *Front Public Health*. 2018; 6 241. PubMed: 30234087
3. Vivancos, R, et al. Community transmission of monkeypox in the United Kingdom, April to May 2022. *Euro Surveill*. 2022; 27 (22), PubMed: 35656834
4. Kmiec, D and F Kirchhoff. Monkeypox: A New Threat. *Int J Mol Sci*. 2022; 23 (14); 7866. PubMed: 35887214
5. Petersen, BW, et al. Vaccinating against monkeypox in the Democratic Republic of the Congo. *Antiviral Res*. 2019; 162 171-77. PubMed: 30445121
6. Zachary, KC and ES Shenoy. Monkeypox transmission following exposure in healthcare facilities in nonendemic settings: Low risk but limited literature. *Infect Control Hosp Epidemiol*. 2022; 43 (7): 920-24. PubMed: 35676244
7. Bragazzi, NL, et al. Epidemiological trends and clinical features of the ongoing monkeypox epidemic: A preliminary pooled data analysis and literature review. *J Med Virol*. 2022. PubMed: 35692117
8. Guarner J, Del Rio C, Malani PN. Monkeypox in 2022-What Clinicians Need to Know.', *JAMA*. 2022; 328 (2): 139-40. PubMed: 35696257
9. Thornhill, JP, et al. Monkeypox Virus Infection in Humans across 16 Countries – April-June 2022. *N Engl J Med*. 2022. PubMed: 35866746
10. Titanji, BK, et al. Monkeypox: A Contemporary Review for Healthcare Professionals. *Open Forum Infect Dis*. 2022; 9 (7): ofac310. PubMed: 35891689
11. Moore, M and F Zahra. Monkeypox. *StatPearls*. 2022. PubMed: 34662033
12. Rizk, JG, et al. Prevention and Treatment of Monkeypox. *Drugs*. 2022;82 (9): 957-63. PubMed: 35763248
13. Grosenbach, DW, et al. Oral Tecovirimat for the Treatment of Smallpox. *N Engl J Med*. 2018; 379 (1): 44-53. PubMed: 29972742
14. Berhanu, A, et al. Treatment with the smallpox antiviral tecovirimat (ST-246) alone or in combination with ACAM2000 vaccination is effective as a postsymptomatic therapy for monkeypox virus infection. *Antimicrob Agents Chemother*. 2015; 59 (7): 4296-300. PubMed: 25896687
15. De Clercq, E. Cidofovir in the treatment of poxvirus infections. *Antiviral Res*. 2002;55 (1): 1-13. PubMed: 12076747
16. Arndt, W, et al. In vitro characterization of a nineteenth-century therapy for smallpox. *PLoS One*. 2012; 7 (3): e32610. PubMed: 22427855
17. Kannan, L, et al. Anti-herpes virus activity of the carnivorous botanical, Sarracenia purpurea. *Sci Rep*. 202; 10 (1): 18953. PubMed: 33144625
18. Morrison, SA, et al. Antimycobacterial triterpenes from the Canadian medicinal plant Sarracenia purpurea. *J Ethnopharmacol*. 2016; 188 200-3. PubMed: 27174081

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Letter to the Editor

Long Covid and Enzyme Overdrive

Early analysis of an ongoing study of long covid patients done in cooperation with BiomeSight, a UK microbiome testing company has some very surprising results with z-scores often over 10.

At present we have 1037 heterogeneous reference samples with 154 samples from long covid patients. A variety of analysis methods were done, but one method not only had extremely strong statistical significance but also hints of the process behind long covid. This method is not usually done with the microbiome. Each microbiome was processed with data derived from the Kyoto Encyclopedia of Gene and Genomes to estimate the quantity of various enzymes in each sample.

The results were a large number of enzymes found to be much higher with long covid than with the reference population:281 enzymes had a z-score of 5 or higher. Dihydrourocanate:acceptor oxidoreductase (1.3.99.33) had the highest z-score of 18.2 and with the estimate for long covid being 2.5x higher than that of the reference.

A tentative hypothesis is that the covid infection puts enzyme production into overdrive to deal with the active covid infection. Once the infection was eliminated, this overdrive did not shut down. This concept is very similar to the *occult infection* concept advocated by the Pasteur Institute for Tropical Medicine in the 1950s.

Long covid is so devastating to so many individuals, that we thought that we should share these early findings to help researchers. A blog post giving some more details is at http://blog.microbiomeprescription.com/2022/07/02/long-covid-microbiome-scents-we-smell-a-skunk/.

Kenneth Lassesen, MSc
Microbiome Prescription - A microbiome analysis company
https://microbiomeprescription.com/

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Health Statistics and Study Design for the Rest of Us

by Michael Passwater

Orthomolecular Medicine News Service

Given the flood of health information in the news, the increase in the number of health and medical journals and journal publications, blogs, social media posts, websites, and opinions of family and friends, this brief overview is an attempt to help the reader evaluate headlines and discoveries related to human health. Reading newsfeeds today, one can feel surrounded by data in an information desert.

Determining whether two things among many are merely associated, coincidentally seen together like two strangers passing in a crowded city coffee house, or truly causal, with one reliably following the other in a consistent, predictable pattern, is difficult. The human body contains 60 thousand miles of blood vessels and over 37 trillion cells. It is estimated that each of these cells has approximately one billion chemical reactions per second. Essential nutrients are biochemicals and minerals required by the body for constructing its extensive structure and performing its sophisticated functions. Further, human behavior interacting with the environment is complex and affects the body in a myriad of ways. Therefore, a relevant question is how can a study of one or two variables in a complex biochemical network reliably determine a causal relationship with a specific outcome – in other words, how can it differentiate a mirage from an oasis? A closer look at study design and analysis can improve evaluation of the meaningfulness of past assumptions and the latest health news.

Study Design

A basic goal of scientific inquiry in the health sciences field is to isolate a variable and study the impact of changing this variable. In this context, a variable is a characteristic that differs from one person or group to another, or that may change over time within a given person, and can be measured or categorized. By studying changes to the one variable while keeping everything else constant, each specific outcome can be attributed to the change that caused it. In simple systems this works well. For instance, plants from the same batch of seeds can be divided into different groups, and each group of plants can be exposed to equal amounts of a different wavelength of light. Outcomes such as growth of the plants can be measured, and the connection between changes in the variable (light wavelength) and the outcome (growth) can be evaluated.

However, as the system of interest to study becomes more complex, isolating a single variable becomes more challenging. In a complex system, it is often difficult to discover the optimal variable change for discovering what causes a condition or disease. The human body is an extremely complex network of sophisticated physical, chemical, mental, and emotional systems. Finding large groups of humans that are truly identical is impossible. Many human characteristics interact with one another causing a single variable change to have many unintended consequences (which may be unmeasured within a given study). A change to a single variable may fail to trigger important synergistic benefits that would occur if the full set of relevant variables were optimized rather than just one element of the set.

Nutrient synergy is important in human wellness because nutrients work together to support a healthy body. Leaving one or more nutrients in a deficient state while testing the effect of a single other nutrient is a poor approach. For example, vitamin D, selenocysteine, and magnesium have strong co-dependencies in biochemical pathways, with each being a rate limiting factor for the other. Studying the effect of varying one without ensuring adequate levels of the others may produce misleading results. Vitamin K2 is also an important partner to vitamin D. However, measuring and matching the full set of essential nutrients for all participants in a study is resource intensive and difficult.

For those conducting and reviewing nutrient research, Box 1 and Box 2 contain "rules" published by Robert P. Heaney in his landmark article "Guidelines for optimizing design and analysis of clinical studies of nutrient effects."[1]

Blinding

In addition to isolating variables of interest, and controlling for other variables, there are many other aspects of study design. *Blinding* refers to whether or not the study participants and the observers are aware of which treatment has been given to which person or group. A *single blinded* study typically means the subjects are unaware of which treatment is given, but the observers are aware. A *double blinded* study indicates that neither the subjects nor the observers are aware of which treatment is given. Blinding is an attempt to eliminate bias. Observers excited about a new intervention are more likely to see positive effects in people receiving it – and less likely to see benefits when an intervention they are not excited about is used. And a person's thoughts, behaviors, and perceptions are influenced when they know they are receiving a test intervention or a control placebo. Keeping the study subjects and the study observers "blinded" to who

is getting what intervention helps to minimize perception bias.

Group Selection

Another important aspect of study design is randomization. A *randomized trial* means that people are assigned to the study's groups in a random, impartial manner. Inclusion and exclusion criteria are another important aspect of study design. Does the study only enroll patients on Tuesday when Dr. X is in the clinic? Are there so many exclusions restricting entry to the study that the results are unlikely to be generalizable to a real-world population? Are there not enough exclusions causing the overall study results to miss a subpopulation that benefitted from the treatment?

Sample Size

A large sample size is desirable to increase the ability of the study to detect a difference between the test and control group, and to minimize the risk of the study results being due to chance. A large sample size is also thought to minimize the impact of unmeasured factors (confounding variables), although the only way to truly control for a variable is to measure it in the test and control study participants. Sample size is also important. Several online aides for determining appropriate sample sizes are available; two examples are included in the references.[2,3]

Retrospective and Prospective

Whether a study is retrospective (looking back upon) or prospective (planning ahead and observing outcomes as they happen) is another important aspect of studies. Generally, a planned prospective study offers the opportunity to match variables in test and control groups, and to standardize interventions more thoroughly than a retrospective study.

Traditional evidence-based medicine and public health ranks the quality of study designs as follows:[4]

1. **Randomized, double-blind, placebo controlled interventional study.**
2. **Cohort study** – people with a certain health condition are selected. Subgroups with one outcome (e.g hospitalization, death, pneumonia) are compared with those within the group (cohort) who did not have the outcome to see if there is a difference in a variable of interest between the two subgroups. For instance, in a cohort of people with angina, did those admitted to a hospital for a cardiac event have lower levels of omega-3 and vitamin K2 than those who were not admitted to a hospital for a cardiac event. A cohort study may be prospective or retrospective. A prospective cohort study is preferred because it minimizes selection bias, and measuring variables as well as performing interventions can be standardized.
3. **Case-control study** – people with a health condition are compared to people who do not have the condition. For example, people in a nursing home who developed pneumonia might be compared to people in a nursing home who did not have pneumonia to see if they had a difference in vitamin D levels or other variables. Improved propensity score matching allows well designed prospective case-control studies to achieve credibility more comparable to a randomized controlled trial.[5] Propensity score matching refers to the evaluation and comparison of each person's baseline characteristics (e.g. the vitamin D level) to minimize confounding variables.

Interventional vs. Observational Studies

An observational study is one that does not intervene with a treatment – it merely observes outcomes and associates them with different conditions or treatments. An interventional trial gives an active treatment to one group and may also give a null treatment (placebo) to another. While there are merits to randomized double-blind, placebo-controlled trials, the notion that it is unsafe to put an intervention into practice without such a trial is unsound. Much wisdom can be gleaned from retrospective observational studies. For example, there are no prospective double-blind placebo-controlled trials to support the use of parachutes when jumping from airplanes,[6] or for performing cardiopulmonary resuscitation (CPR). Call it recklessness, but I support the performance of these procedures when necessary.

The Placebo

A placebo is an inert intervention given to the "control group" of a study. Its purpose is to make sure the test intervention effects are real, and not just the perception of the patients or observers. However, in an attempt to mimic the test intervention as closely as possible, the placebo may not be

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Box 1. Rules for individual clinical studies of nutrient effects.

1. Basal nutrient status must be measured, used as an inclusion criterion for entry into study, and recorded in the report of the trial.
2. The intervention (i.e., change in nutrient exposure or intake) must be large enough to change nutrient status and must be quantified by suitable analyses.
3. The change in nutrient status produced in those enrolled in the trials must be measured and recorded in the report of the trial.
4. The hypothesis to be tested must be that a change in nutrient status (not just a change in diet) produces the sought-for effect.
5. Co-nutrient status must be optimized in order to ensure that the test nutrient is the only nutrition related, limiting factor in the response.

Box 2. Rules for study inclusion in systematic reviews and meta-analysis.

1. The individual studies selected for review for meta-analysis must themselves have met the criteria listed in Box 1 for nutrient trials.
2. All included studies must have started from the same or similar basal nutrient status values.
3. All included studies must use the same or closely similar doses.
4. All included studies must have used the same chemical form of the nutrient and, if foods are used as the vehicle for the test nutrient, all studies must have employed the same food matrix.
5. All included studies must have the same co-nutrient status.
6. All included studies must have had approximately equal periods of exposure to the altered intake.

Other excellent articles specific to nutrition research design include the following:

- Robert G. Smith (2022) "Vitamins and Minerals for Lowering Risk of Disease: Adding to the Evidence." Orthomolecular Medicine News Service. http://orthomolecular.org/resources/omns/v17n10.shtml
- Richard Z. Cheng (2020) "Covid-19 Highlights the Shortcomings of Evidence-based Medicine". *J Orthomol Med*. 35:1-7. https://isom.ca/article/covid-19-highlights-the-shortcomings-of-evidence-based-medicine

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truly inert as intended. For instance, even a classic "sugar pill" placebo is not inert when studying diabetes. Olive oil and IV multivitamins have been used as placebos in large studies published within the past year.[7,8] Use of anti-inflammatory olive oil as a control in a study evaluating inflammation may obscure benefits of the test intervention since both the test and control arm may have reduced inflammation compared to a group receiving a true placebo. A caustic placebo may make a test drug appear more effective. Similarly, a non-inert placebo may blunt the recognition of side effects in the test intervention if, for instance, it contains nut products or other common allergens that may inflate the rate of reactions in the control group. The administration vehicle for the test substance may impact outcomes as well. A vitamin D study in Brazil used peanut oil to administer the single dose vitamin D intervention, and, sure enough, some people had strong reactions (the projectile vomiting also likely prevented vitamin D from reaching the circulation of those unfortunate patients).[9]

Two fundamental questions for evaluating health research are is the outcome statistically significant and is the outcome meaningful?

Is the outcome statistically significant? Statistical significance is an expression of the likelihood that the results of study happened by chance rather than being the result of the study intervention (behavior, diet, nutrient(s), drug(s) studied). For example, the likelihood (probability) of flipping 4 coins and having them all come up "heads" is 1 in 16 ($1/(2^4)$ or a 6.25% chance). If a study of coin flipping achieves an outcome of 4 of 4 coins landing heads up on the first try, there may be an inclination to announce to the world that all coins land heads up and further research should be conducted to explore the physical forces that pull or push the "tails" side of the coin to the ground rather then the "heads" side. Why would a critic suggest that investing in such further research would be a bad idea? Well, the chance of 4 of 4 coins landing heads up is 1 in 16. So every 16 times this study is performed, one would expect to achieve the outcomes noted, and different results would be expected the other 15 times. Therefore, the critic may repeat the study and find results that disprove the hasty announcement to the world that all coins land heads up.

Statistics such as p-values, odds ratios, and confidence intervals give a sense of whether or not study results were due to chance, or due to a reliable connection between the intervention and the outcome. Study size is a big factor. Were enough coins flipped to even have an opinion on how coins land? Were enough variables examined to be sure the studied variable led to the outcome? ("true-true-unrelated" associations are abundant in our complex world). In general, the larger the study size, and the more variables that are examined, the higher the quality of the study. However, regardless of the study size, associating a single non-biological variable, such as who people voted for or what state people live in, with a serious human health outcome without age adjusting the populations is unlikely to enlighten a hypothesis about causation.

Is the outcome meaningful? Not everything that is statistically significant is meaningful. In a very large study comparing antipyretic (fever-reducing) Drug X and Herb Y, very convincing data may result showing that Drug X consistently reduces a person's fever by 0.1°F more than Herb Y with an impressive 95% confidence interval and p-value. The temperature difference is significant from a statistical perspective, but not from a clinical perspective. The difference is real, but unimportant.

Additional Items to Consider When Reviewing a Study

- Are the results, conclusion, and title consistent? Surprisingly, even major journals occasionally publish articles with conclusions that are inconsistent with the study results.
- Did the study test the right dose, for the right duration (fast enough and for long enough), and with adequate cofactors to optimize the intervention? A CPR study that only allowed 4 chest compressions, or that waited two hours before beginning chest compressions, would likely conclude that CPR is worthless – a fictitious example. However, in the real-world, IVC (intravenous vitamin C) studies have used doses ≤3 g, not permitted use after 96 hours, and included treatment start times as late as 18 hours after arrival for critically ill patients.[10] Consequently, those studies failed to show a beneficial effect of IVC. The advice of Dr. Fred Klenner to increase the dose and frequency of vitamin C administration until the patient recovers, and Dr. Andrew W. Saul to "Take enough C to be symptom free, whatever the amount may be" applies.[11,12]
- Did the study use the best nutrient form and route of administration? It may seem obvious that intravenous (IV) administration differs from oral administration, yet this detail has been confused in studies of important topics such as cancer and vitamin C. Oral iron options such as ferrous sulfate and iron bisglycinate differ in bioavailability, and IV iron dextran has a higher rate of adverse reactions than ferumoxytol and ferric caroxymaltose.[13] Magnesium oxide (an inorganic salt) is a great laxative but poorly absorbed, while magnesium citrate (a chelated organic salt) is generally well absorbed.[14,15] Vitamin D2 (ergocalciferol) differs from D3 (cholecalciferol) in absorption, biochemistry, and epigenetic influences.[16] Selenomethionine differs from the more readily bioavailable methyl-selenocysteine, gamma-glutamyl-Se-methylselenocysteine, and yeast-bound or injected selenite.[17] Niacinamide and niacin have important differences in the setting of cancer.[18] "Vitamin E" was once regarded as a single entity. However, it is now known to be a mixture of 8 different molecules (4 tocopherols and 4 tocotrienols), each with unique as well as overlapping biochemical properties.[19] Generalizing study outcomes achieved with a specific form or route of a nutrient to all forms and routes of the nutrient is a common mistake.

Statistics and Study Jargon

> *No statistic is perfect, but some are less imperfect than others. Good or bad, every statistic reflects its creators' choices….Being Critical requires more thought, but failing to adopt a Critical mind-set makes us powerless to evaluate what others tell us. When we fail to think critically, the statistics we hear might as well be magical.* – Joel Best[20]

Hypothesis – an educated guess at a relationship between a treatment and an outcome. For example, a researcher might speculate based on the results of a previous study that people taking a gram of vitamin C with each meal and a good multivitamin once a day will have fewer unplanned absences from work than those who don't. Or that women with a vitamin D level >40 ng/mL are less likely to have a preterm child than those with a vitamin D level <30 ng/mL.

Null Hypothesis – the assumption that there is no relationship between the test intervention and desired outcome. The null hypothesis basically states that the hypothesis is wrong. Technically, statistics evaluate whether or not the null hypothesis is correct rather than the hypothesis. If the null hypothesis is correct, then there is no relationship between the test variable and the outcome, and the hypothesis is incorrect. If the null hypothesis is proven to be incorrect, then the study results support the hypothesis. Technically, the hypothesis can be proven wrong, but not proven right. If not proven wrong, the hypothesis remains viable and subject to further evaluation. There is no definitive number of studies that will guarantee acceptance of an hypothesis.

P value – an expression of the probability that the results of an experiment testing a hypothesis are due to chance. Generally speaking, the lower the p value, the higher the reliability of the data. A p value below 0.05 is generally required to declare results "statistically significant" (the study outcomes are unlikely to be due to chance). A p value below 0.01 is more convincing.

Odds Ratio[21,22] – measures the relative effect of the study intervention. The odds ratio is the outcome of the test group divided by the outcome of the control group. If the outcome is a rate such as the risk of having a stroke, then it may be called a Risk Ratio or Hazard Ratio.

If the odds ratio=1 this means the outcomes in the test and control group are the same

If the odds ratio is >1 this means the outcome occurred more often in the test group than in the control group

If the odds ratio is <1 this means the outcome occurred more often in the control group than in the test group

Confidence Interval – reflects the certainty of the odds ratio. Because samples of a population are studied rather than the entire population, the study results are an estimate of what the results may be for the full population of interest. A 95% confidence interval (95%CI) shows the range of values within which we can be 95% certain that the odds ratio is contained for the population. If the 95%CI crosses one (e.g. 95%CI = 0.95 – 1.05), the results are not statistically significant because one cannot be certain that the test intervention produced outcomes that differed from the control group.

Critical thinking, developing and testing ideas, and keeping an open mind are challenging yet essential.

Incidence – the number of new cases of a disease, event, or health-state; typically reported as the number of new cases per period of time, which may be called an incidence rate.

Prevalence – the total proportion of a population with a particular condition. Prevalence differs from incidence in that it is not restricted to new cases. For example, the annual incidence of rheumatoid arthritis in the USA is estimated to be 132,000 cases, while the prevalence of rheumatoid arthritis in the USA is estimated to be 3 million cases.[23-25]

Age adjustment – the rate that would have resulted if the population of interest had the same age distribution as a reference standard. Age adjustment is a critical step in population studies (epidemiology). The number of people over 84 years old in Florida is 331,287 (2.1% of the Florida population). The number of people over 84 years old in Utah is 28,951 (1.1% of the Utah population). If more people in Florida are dying from or being diagnosed with a certain condition than in Utah, what does it mean? The populations of each state must be adjusted to a common standard population such as the 2020 USA census to allow an "apples-to-apples" comparison. Without adjusting for the age of the different populations being compared, the data has little meaning and may be harmfully misleading.

Confounding variables – variables other than the intervention being studied may influence these outcome(s) measured and confuse the interpretation of the study results. Do ice cream sales cause crime? Lots of data can be assembled to make the case that it does. However, other variables associated with warmer weather are more likely involved than the sale of ice cream. While it is true that ice cream sales increase in warmer weather, and it true that crime increases in warmer weather, the connection between them is coincidental. Such "true-true-unrelated" associations are abundant in our complex world. As another example, studying disease outcomes and vaccination rates without realizing that a much larger percentage of vaccinated people in the study had vitamin D levels >40 ng/mL, selenoprotein P levels between 3.0-4.5 mg/L, and took one or more grams of vitamin C per day may lead to a false conclusion as to what caused the observed outcomes. Measuring as many variables as possible in a study is important, but resource limitations force investigators to choose the measurements they believe will be the most important.

Controlling for confounding variables can also be misapplied. Interestingly, a major journal published a study last year that used conditions known to be associated with vitamin D deficiencies as variables that then canceled out the test variable of vitamin D as impacting the outcome – essentially saying that low vitamin D is not associated with the disease because conditions with low vitamin D also had the same disease association. Be wary of studies that mix biochemical health markers with non-biochemical health markers. Actual measurements of nutrients within appropriate timeframes in study subjects is critical for evaluating the effects of nutrients. If a vitamin has a half-life of 20 minutes or even 12 weeks in the human body, using a measure of the vitamin in a study subject from 10 years ago to evaluate a current disease is curious, yet publishable.

"Confounding by indication" is a serious challenge in healthcare studies, especially for retrospective observational studies. People receiving blood transfusions are more likely to be bleeding than people not receiving blood transfusions. However, it is not wise to suggest that blood transfusions cause people to bleed to death. In this

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example, the indication (bleeding) for the intervention (blood transfusion) confuses or confounds the association between the intervention (transfusion) and the measured outcome (death). Careful attention to control populations and the "baseline state" of study subjects is important when conducting studies.

Testing New Ideas

Critical thinking, developing and testing ideas, and keeping an open mind are challenging yet essential to gain a deeper and more accurate understanding of ourselves and our relationships with our surroundings.[27] I once thought all creatures eating carotenoid-rich algae and brine shrimp were pink flamingos. Then I observed a pink bird with a white head and neck, and a beak that resembled a wooden spoon eating shrimp. Instead of rejecting the observation, I modified my original hypothesis. The association between eating shrimp and being a pink bird was now stronger, but I recognized two possible outcomes: either being a pink flamingo or a roseate spoonbill. I ate shrimp, and to my disappointment, I did not turn into either of these beautiful pink birds. It turns out more variables were involved in achieving the desired outcome. By prospectively planning a study with an expanded selection criteria allowing a representative sample of all shrimp-eating creatures, and evaluating many more characteristics of each creature in the study, it became apparent that only white feathered birds with very large carotenoid intake and the proper liver enzymes were able to display pink feathers.

Concluding Remarks

"If we all worked on the assumption that what is accepted as true is really true, there would be little hope of advance." – Orville Wright (1871 – 1948)[26]

Humans and their interactions with the environment are highly complex.[27] Nutrition studies are difficult because they require measuring the baseline level of several synergistic nutrients which cannot be easily done with retrospective studies. However, observational studies often contribute important evidence about the outcome of dietary deficiencies, that can be further tested with prospective interventional studies. Persistent inquiry, carefully designed studies, detailed observations – including timely measurement of nutrients – along with rigorous analysis and critical review help us better understand how to more reliably prevent, manage, and cure diseases and lead our best lives.

References

1. Heaney, RP (2014) Guidelines for optimizing design and analysis of clinical studies of nutrient effects Nutrition Reviews 72:48-54. https://pubmed.ncbi.nlm.nih.gov/24330136
2. ClinCalc Sample Size Calculator https://clincalc.com/stats/samplesize.aspx
3. Sample Size Calculators for designing clinical research. UCSF Clinical and Translational Science Institute https://sample-size.net
4. Designing Clinical Research, 4th edition, online companion https://www.dcr-4.net
5. Dahabreh IJ, Sheldrick RC, Paulus JK, et al (2012) Do observational studies using propensity score methods agree with randomized trials? A systematic comparison of studies on acute coronary syndromes. Eur Heart J. 33:1893-1901. https://pubmed.ncbi.nlm.nih.gov/22711757
6. Smith GCS, Pell JP (2003) Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials. BMJ, 327:1459-1461. https://pubmed.ncbi.nlm.nih.gov/14684649
7. Korley FK, Durkalski-Mouldin V, Yeatts SD, et al. (2021) Early Convalescent Plasma for High-Risk Outpatients with Covid-19. NEJM, 385:1951-1960. https://pubmed.ncbi.nlm.nih.gov/34407339
8. Costenbader KH, Hahn J, Cook NR. (2022) Vitamin D and marine omega 3 fatty acid supplementation and incident autoimmune disease: VITAL randomized controlled trial. BMJ 2022;376:e066452. https://pubmed.ncbi.nlm.nih.gov/35082139
9. Murai IH, Fernandes AL, Sales LP, et al. (2020) Effect of Vitamin D3 Supplementation vs Placebo on Hospital Length of Stay in Patients with Severe COVID-19: A Multicenter, Double-blind, Randomized Controlled Trial. https://pubmed.ncbi.nlm.nih.gov/33595634
10. Passwater M (2021) The Victas Trial: Designed to Fail. Orthomolecular Medicine News Service. http://www.orthomolecular.org/resources/omns/v17n08.shtml
11. Klenner FR. (1971) Observations On the Dose and Administration of Ascorbic Acid When Employed Beyond the Range of A Vitamin In Human Pathology. J Applied Nutrit. 23:61-87. http://orthomolecular.org/library/jom/1998/pdf/1998-v13n04-p198.pdf
12. Case HS. (2022) Vitamin C and Infants: Determing dose. Orthomolecular Medicine News Service. http://www.orthomolecular.org/resources/omns/v18n05.shtml
13. Arastu AH, Elstrott BK, Martens KL, et al (2022) Analysis of Adverse Events and Intravenous Iron Infusion Formulations in Adults With and Without Prior Infusion Reactions JAMA Network Open. 5:e224488. https://pubmed.ncbi.nlm.nih.gov/35353168
14. Dean C (2017) The Magnesium Miracle, 2nd Ed. Ballantine Books. ISBN-13 : 978-0399594441
15. Lindberg JS, Zobitz MM, Poindexter JR, Pak CY (1990) Magnesium bioavailability from magnesium citrate and magnesium oxide. J Am Coll Nutr. 1990 9:48-55. https://pubmed.ncbi.nlm.nih.gov/2407766
16. Durrant LR, Bucca G, Hesketh A, et al. (2022) Vitamins D2 and D3 Have Overlapping but Different Effects on the Human Immune System Revealed Through Analysis of the Blood Transcriptome. Front. Immunol. 13:790444. https://pubmed.ncbi.nlm.nih.gov/35281034
17. Rayman MP (2008) Food-chain selenium and human health: emphasis on intake. British Journal of Nutrition, 100:254-268. https://pubmed.ncbi.nlm.nih.gov/18346308
18. Penberthy WT, Saul AW, Smith RG (2021) Niacin and Cancer: How vitamin B-3 protects and even helps repair your DNA. Orthomolecular Medicine News Service. http://www.orthomolecular.org/resources/omns/v17n05.shtml
19. Aggarwal BB, Sundaram C, Prasad S, Kannappan R (2010) Tocotrienols, the Vitamin E of the 21st Century: Its potential against cancer and other chronic diseases. Biochem Pharmacol. 80: 1613-1631. https://pubmed.ncbi.nlm.nih.gov/20696139
20. Best J (2012) Damned Lies and Statistics: Untangling Numbers from the Media, Politicians, and Activists. Berkeley: University of California Press, Updated version, ISBN-13: 9780520274709
21. Hicks T. (2013) A beginner's guide to interpreting odds ratios, confidence intervals, and p-values. August 13, 2013. https://s4be.cochrane.org/blog/2013/08/13/a-beginners-guide-to-interpreting-odds-ratios-confidence-intervals-and-p-values-the-nuts-and-bolts-20-minute-tutorial
22. GraphPad QuickCalcs https://www.graphpad.com/quickcalcs
23. Myasoedova E, Crowson CS, Kremers HM, et al. (2010) Is the incidence of rheumatoid arthritis rising?: results from Olmsted County, Minnesota, 1955-2007. Arthritis Rheum, 62:1576-1582. https://pubmed.ncbi.nlm.nih.gov/20191579
24. Hunter TM, Boytsov NN, Zhang X, et al. (2017) Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014. Rheumatol Int,37:1551-1557. https://pubmed.ncbi.nlm.nih.gov/28455559
25. Eriksson JK, Neovius M, Ernestam S, et al. (2013) Incidence of rheumatoid arthritis in Sweden: a nationwide population-based assessment of incidence, its determinants, and treatment penetration. Arthritis Care Res (Hoboken), 65:870-878. https://pubmed.ncbi.nlm.nih.gov/23281173
26. Orville Wright Quotes. Quotes.net.STANDS4 LLC, 2022. Web. 1 Apr. 2022. https://www.quotes.net/quote/19271
27. Best J. (2021) Is That True? Critical Thinking for Sociologists. University of California Press. ISBN-13: 9780520381407

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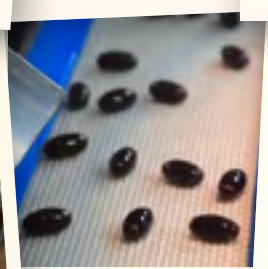

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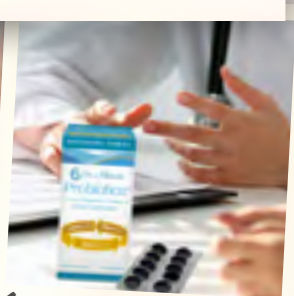

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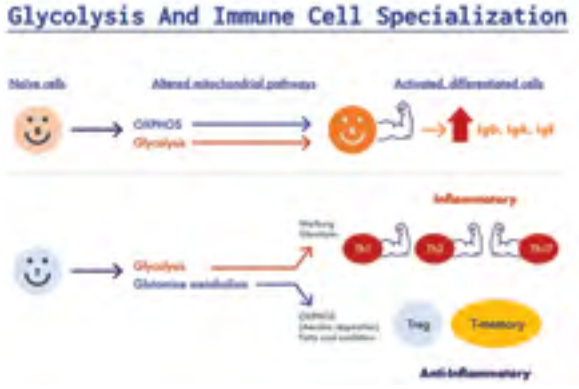
Improving Fibromyalgia Evaluation and Outcomes

by Andrea Gruszecki, ND

Figure 1. Distinguishing characteristics and common symptoms of CFS, FbM, and MCS.

Figure 2. There is a strong association between trauma (physical or psychological) and the development of fibromyalgia.

Figure 3. Aerobic mitochondrial respiration maintains tolerance and homeostasis. Inflammation, toxic exposure, and caloric or glucose excess may dysregulate mitochondrial respiration, causing pro-inflammatory changes in immune cells.



Many patients suffer from chronic pain, fatigue, and inflammation due to disorders such as fibromyalgia (FbM), chronic fatigue syndrome (CFS or myalgic encephalomyelitis), or multiple chemical sensitivity (MCS or environmental sensitivity). Common symptoms to all three disorders include fatigue, pain, sleep disruption, and neurocognitive changes (Figure 1).[1] Fibromyalgia involves a constellation of symptoms, including persistent pain, non-pain-related symptoms, comorbid disorders such as autoimmunity, and psychological distress. The presence of widespread musculoskeletal pain and trigger points is considered specific to the diagnosis of fibromyalgia.[2]

These patients receive little relief from their primary care providers, and up to 73% of patients meeting fibromyalgia diagnostic criteria may be misdiagnosed.[3] Of note, studies reveal that, in the United States, a fibromyalgia diagnosis is often incorrectly assigned to white married women with higher rates of poly-symptoms (somatization) but lower pain and/or trigger point scores. Seeking relief, patients often turn to functional, naturopathic, or other forms of alternative medicine care in search of answers and support.[4]

Identifying Fibromyalgia

The use of available diagnostic tools such as the Polysymptomatic Distress Scale and the Fibromyalgia Survey Questionnaire may improve diagnosis; further discussion of these documents is beyond the scope of this article.[5,6] Since diagnostic criteria are still being refined, an awareness of the known risk factors for fibromyalgia may also be useful for clinicians.[2,3,7] Asian ancestry is protective; the risk of FbM is spread equally over all other ethnic populations. Expect a higher incidence of fibromyalgia if the patient has the following:

- Female gender
- US citizenship
- Social/economic disadvantage
- Western diet and lifestyle
- Lower education level
- Obesity
- Smoker
- Divorced or separated
- Midwest zip code

Comorbid conditions are common with fibromyalgia; however, the presence of a comorbid disorder does not contraindicate a diagnosis of fibromyalgia when it is appropriate.[2,8,9] Co-morbid conditions may include:

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Figure 4. Dried urine organic acids results indicate mitochondrial and primary biochemical pathway disruptions, many of which can be corrected with nutritional support and dietary or other lifestyle changes.

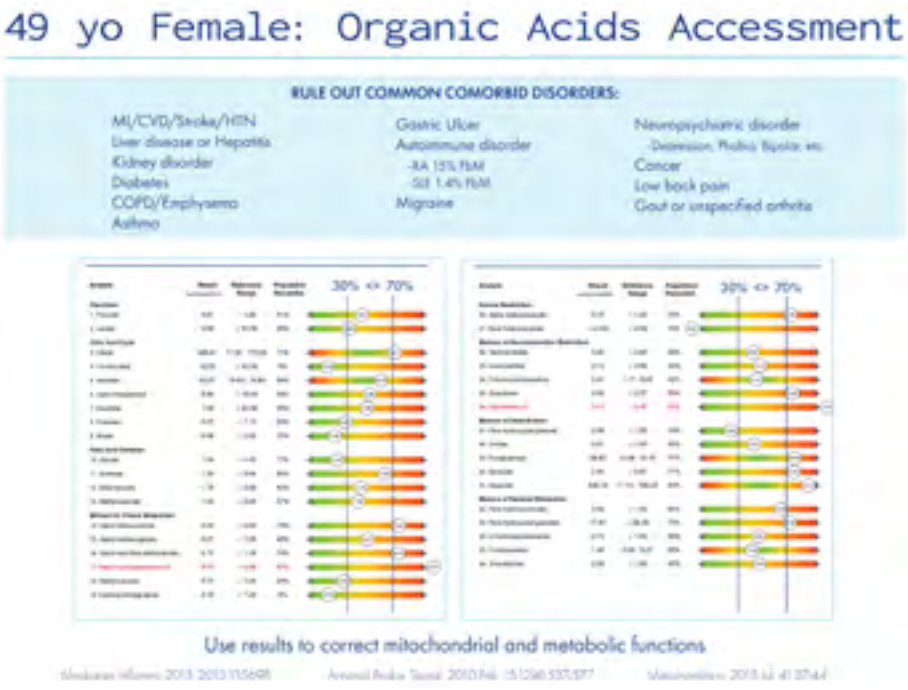
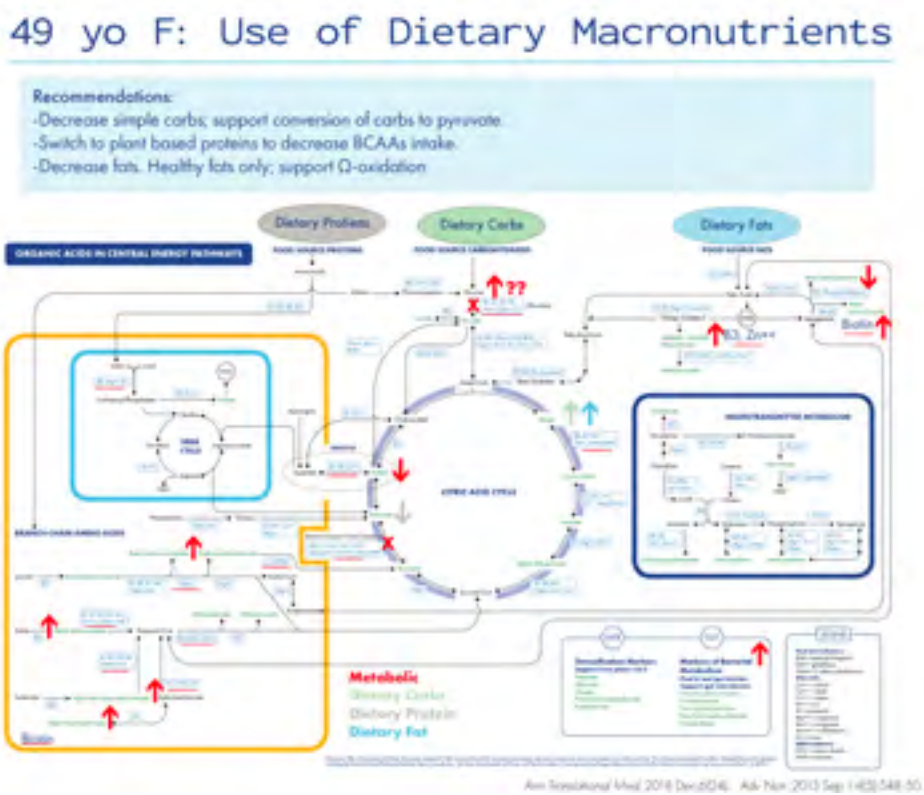


Figure 5. Dried urine organic acids results indicate the specific effects of the current diet and needed nutritional supports.



- Cardiovascular disease or hypertension
- Liver disease or hepatitis
- Kidney disorders
- Diabetes
- COPD/Emphysema
- Asthma
- Gastric ulcer
- Autoimmune disorders: RA 15% FbM; SLE 1.4% FbM
- Migraines
- Neuropsychiatric disorder
- Depression, phobia, bipolar, etc.
- Cancer
- Low back pain
- Gout or unspecified arthritis

Particularly strong co-associations may be seen with insomnia, cognitive decline, fatigue, anxiety, depression, or post-traumatic stress disorder because there is a strong association between trauma (physical or psychological) and the development of fibromyalgia (Figure 2).[4,10,11] There is also a growing association between fibromyalgia and type II diabetes.[12]

Fibromyalgia and Inflammation

The known associations between fibromyalgia, autoimmunity, and Western lifestyle indicate that the assessment and management of inflammation may have profound effects in reducing the chronic symptoms of fibromyalgia and its co-morbid inflammatory disorders.[13-15] The chronic inflammation associated with FbM may originate in either immune system or mitochondrial dysregulation.[16] Mitochondrial function plays a role in the body's innate immune responses, and in the body's recovery from stress or injury-altered mitochondrial function.[17,18] Mitochondrial dysfunction reduces aerobic mitochondrial respiration and dysregulates fatty acid oxidation. The loss of aerobic cellular respiration (OXPHOS) shrinks the thymus gland and reduces its ability to produce tolerant T-helper and T-regulatory immune cells that reduce inflammation (Figure 3).[19, 20]

The chronic inflammation that dysregulates mitochondrial function and fatty acid oxidation pathways, whether from a comorbid disorder

or environmental exposures, can be evaluated using a dried urine organic acids test (Figure 4).[21-24]

Organic Acids Testing for Fibromyalgia

Organic acids results provide information on glucose regulation, antioxidant status, mitochondrial function, use of dietary nutrients, liver detoxification, and digestive functions. This broad overview allows clinicians to personalize results to support specific biochemical or mitochondrial enzymes and functions with diet and nutrient cofactors.[25,26] Enzyme dysregulation occurs for a variety of reasons, including genetic and environmental epigenetic influences such as toxic exposures, nutritional deficiency, or overnutrition or lifestyle choices.[21, 27-30]

Supporting enzymes and pathways with the appropriate personalized cofactors, and removing toxic exposures, food allergies and sensitivities may help to decrease inflammation and provide significant symptom relief for fibromyalgia sufferers and other inflamed (Figure 5).[14,16,25,26] The organic acids test can be repeated after a few months to monitor the effects of the nutritional protocol and lifestyle changes – improvements on the test usually reflect improvements in the patient.[22] The organic acids test may also indicate the need for additional testing, for example stool tests, toxic metals, or toxic chemical screenings.

Case Study

The dried urine organic acids results and energy pathway seen in Figures 4 and 5 are from a 49-year-old, female, fibromyalgia patient. This patient had suffered from fatigue and pain for over 10 years without resolution. She improved under the care of a licensed naturopathic physician, who started the patient's recovery with food sensitivity testing, cranial-sacral therapy, and basic nutritional supports (Figure 6).[19,25,31-34]

Even with the improvements, however, the patient reported a need for vigilance about her energy use and conservation. After five months of care with no additional improvement, the ND ordered a dried urine organic acids profile (see Figures 4 and 5) and a screening test for common environmental chemicals (Figure 7).[24,30,35,36]

Based on the results of the organic acids profile, the patient received an individualized protocol to support her mitochondrial function and biochemistry.[27,26,34] The environmental pollutants screen identified several chemicals in the patient's environment. Once the chemical exposures were stopped and a gentle detoxification protocol, supported by the nutrients indicated in the organic acids results, was added, the patient began to improve.[14,30,37] The patient was functioning well enough by 2022 to weather a significant personal loss of a family member and a Covid-19 infection with only minor setbacks to her energy and health. The patient currently ➤

Figure 6. Food allergy or sensitivity may be a hidden source of inflammation.

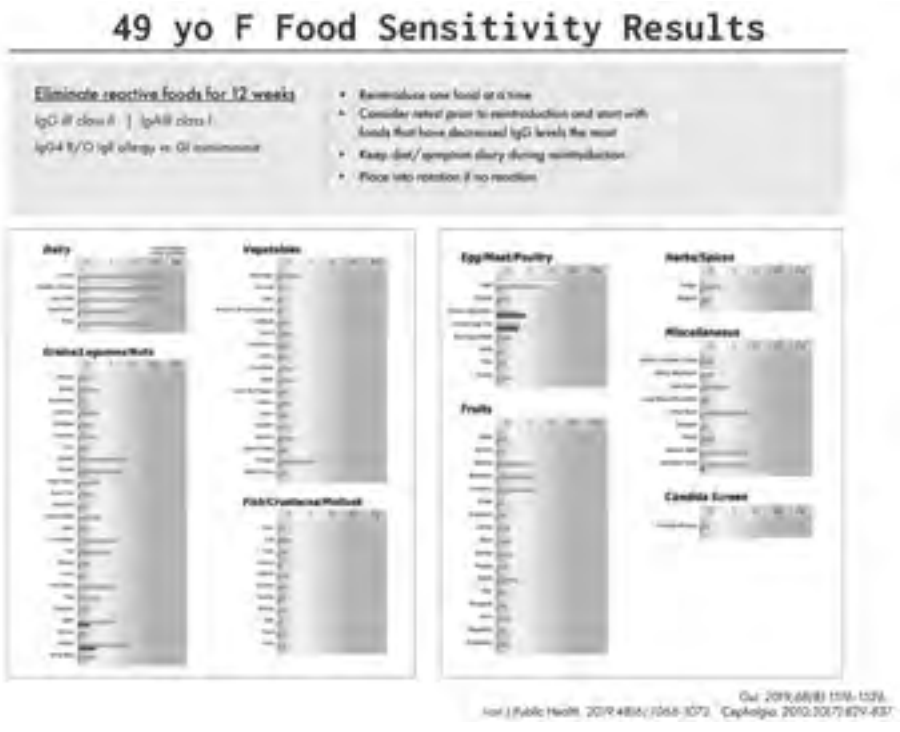
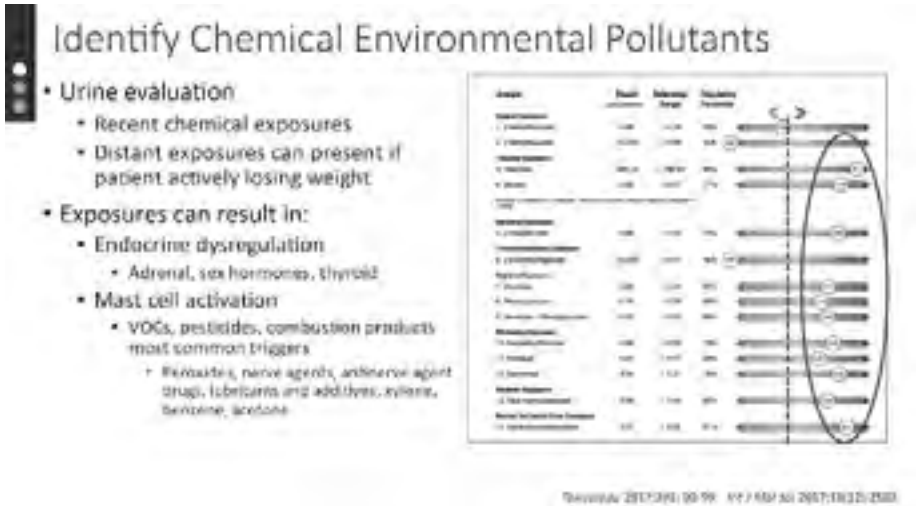


Figure 7. Environmental pollutants such as chemicals or metals can disrupt immune responses and mitochondrial function.



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reports no fibromyalgia flares and is walking 10-11,000 steps daily without exertional fatigue.

Conclusion

The treatment of fibromyalgia depends on the proper diagnosis of the condition, the recognition of risk factors and other contributing factors, an understanding that fibromyalgia is usually a comorbid disorder, and strategies to reduce the underlying inflammation driving the symptoms.

A dried urine organic acids profile, screening for environmental pollutants such as chemicals or metals, and the elimination of allergy or sensitivity exposures can all be used in the assessment and treatment of fibromyalgia and other inflammatory disorders.

References

1. Hu H, Baines C. Recent insights into 3 underrecognized conditions: Myalgic encephalomyelitis-chronic fatigue syndrome, fibromyalgia, and environmental sensitivities-multiple chemical sensitivity. *Can Fam Physician*. 2018 Jun;64(6):413-415.
2. Walitt B, Nahin RL, Katz RS, Bergman MJ, Wolfe F. The Prevalence and Characteristics of Fibromyalgia in the 2012 National Health Interview Survey. *PLoS One*. 2015 Sep 17;10(9):e0138024.
3. Goldenberg DL. Diagnosing Fibromyalgia as a Disease, an Illness, a State, or a Trait? *Arthritis Care Res* (Hoboken). 2019 Mar;71(3):334-336.
4. Pfalzgraf AR, Lobo CP, Giannetti V, Jones KD. Use of Complementary and Alternative Medicine in Fibromyalgia: Results of an Online Survey. *Pain Manag Nurs*. 2020 Dec;21(6):516-522.
5. Wolfe F, Walitt BT, Rasker JJ, Katz RS, Häuser W. The Polysymptomatic Distress Scale Is Simple, Useful, and Effective in Clinical Care and Clinical and Epidemiology Studies. *J Rheumatol*. 2016 Feb;43(2):454.
6. Häuser W, Jung E, Erbslöh-Möller B, Gesmann M, Kühn-Becker H, Petermann F, Langhorst J, Weiss T, Winkelmann A, Wolfe F. Validation of the Fibromyalgia Survey Questionnaire within a cross-sectional survey. *PLoS One*. 2012;7(5):e37504.
7. Choi HJ, Han JY, Seo MR, Ryu HJ, Baek HJ. Fibromyalgia with chronic rheumatic diseases in South Korea: a comparison of clinical and American College of Rheumatology criteria. *Int J Rheum Dis*. 2017 Dec;20(12):1922-1926.
8. Dansie EJ, Furberg H, Afari N, Buchwald D, Edwards K, Goldberg J, Schur E, Sullivan PF. Conditions comorbid with chronic fatigue in a population-based sample. *Psychosomatics*. 2012 Jan-Feb;53(1):44-50.

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

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

9. Wolfe F, Brähler E, Hinz A, Häuser W. Fibromyalgia prevalence, somatic symptom reporting, and the dimensionality of polysymptomatic distress: results from a survey of the general population. *Arthritis Care Res* (Hoboken). 2013 May;65(5):777-85.
10. Lehmann ML, Weigel TK, Cooper HA, Elkahloun AG, Kigar SL, Herkenham M. Decoding microglia responses to psychosocial stress reveals blood-brain barrier breakdown that may drive stress susceptibility. *Sci Rep*. 2018 Jul 26;8(1):11240.
11. Picard M, McEwen BS. Psychological Stress and Mitochondria: A Systematic Review. *Psychosom Med*. 2018 Feb/Mar;80(2):141-153.
12. Pappolla MA, Manchikanti L, Candido KD, Grieg N, Seffinger M, Ahmed F, Fang X, Andersen C, Trescot AM. Insulin Resistance is Associated with Central Pain in Patients with Fibromyalgia. *Pain Physician*. 2021 Mar;24(2):175-184.
13. De Luca C, Scordo G, Cesareo E, Raskovic D, Genovesi G, Korkina L. Idiopathic environmental intolerances (IEI): from molecular epidemiology to molecular medicine. *Indian J Exp Biol*. 2010 Jul;48(7):625-35.
14. Genuis SJ, Tymchak MG. Approach to patients with unexplained multimorbidity with sensitivities. *Can Fam Physician*. 2014 Jun;60(6):533-8.
15. Storino V, Muñoz-Ortiz J, Villabona-Martinez V, Villamizar-Sanjuán JD, Rojas-Carabali W, de-la-Torre A. An Unusual Case of Multiple Food Allergies Comorbid with Multiple Chemical Sensitivity: A Case Report. *J Asthma Allergy*. 2021 Mar 31;14:317-323.
16. Ramírez-Tejero JA, Martínez-Lara E, Rus A, Camacho MV, Del Moral ML, Siles E. Insight into the biological pathways underlying fibromyalgia by a proteomic approach. J *Proteomics*. 2018 Aug 30;186:47-55.
17. Breda CNS, Davanzo GG, Basso PJ, Saraiva Câmara NO, Moraes-Vieira PMM. Mitochondria as central hub of the immune system. *Redox Biol*. 2019 Sep;26:101255.
18. Naviaux RK. Metabolic features and regulation of the healing cycle-A new model for chronic disease pathogenesis and treatment. *Mitochondrion*. 2019 May;46:278-297.
19. Alwarawrah Y, Kiernan K, MacIver NJ. Changes in Nutritional Status Impact Immune Cell Metabolism and Function. *Front Immunol*. 2018 May 16;9:1055.
20. Cunningham CA, Hoppins S, Fink PJ. Cutting Edge: Glycolytic Metabolism and Mitochondrial Metabolism Are Uncoupled in Antigen-Activated CD8+ Recent Thymic Emigrants. *J Immunol*. 2018 Sep 15;201(6):1627-1632.
21. Dela Cruz CS, Kang MJ. Mitochondrial dysfunction and damage associated molecular patterns (DAMPs) in chronic inflammatory diseases. *Mitochondrion*. 2018 Jul;41:37-44.
22. Gruszecki A. (2021) *Organic Acids Profile and Environmental Pollutants Interpretation Guide*. Published by US BioTek, Shoreline, WA.
23. Kumps A, Duez P, Mardens Y. Metabolic, nutritional, iatrogenic, and artifactual sources of urinary organic acids: a comprehensive table. *Clin Chem*. 2002 May;48(5):708-17.
24. Tsoukalas D, Alegakis A, Fragkiadaki P, Papakonstantinou E, Nikitovic D, Karataraki A, Nosyrev AE, Papadakis EG, Spandidos DA, Drakoulis N, Tsatsakis AM. Application of metabolomics: Focus on the quantification of organic acids in healthy adults. *Int J Mol Med*. 2017 Jul;40(1):112-120.
25. Azzolino D, Arosio B, Marzetti E, Calvani R, Cesari M. Nutritional Status as a Mediator of Fatigue and Its Underlying Mechanisms in Older People. *Nutrients*. 2020 Feb 10;12(2):444.
26. Nicolson GL. Mitochondrial dysfunction and chronic disease: treatment with natural supplements. *Altern Ther Health Med*. 2014 Winter;20 Suppl 1:18-25.
27. Godfrey WH, Kornberg MD. The Role of Metabolic Enzymes in the Regulation of Inflammation. *Metabolites*. 2020 Oct 26;10(11):426.
28. Qiu H, Schlegel V. Impact of nutrient overload on metabolic homeostasis. *Nutr Rev*. 2018 Sep 1;76(9):693-707.
29. Sivitz WI, Yorek MA. Mitochondrial dysfunction in diabetes: from molecular mechanisms to functional significance and therapeutic opportunities. *Antioxid Redox Signal*. 2010 Apr;12(4):537-77.
30. Zolkipli-Cunningham Z, Falk MJ. Clinical effects of chemical exposures on mitochondrial function. *Toxicology*. 2017 Nov 1;391:90-99.
31. Karsten CM, Köhl J. The immunoglobulin, IgG Fc receptor and complement triangle in autoimmune diseases. *Immunobiology*. 2012 Nov;217(11):1067-79.
32. Virdee K, Musset J, Baral M, Cronin C, Langland J. Food-specific IgG Antibody-guided Elimination Diets Followed by Resolution of Asthma Symptoms and Reduction in Pharmacological Interventions in Two Patients: A Case Report. *Glob Adv Health Med*. 2015 Jan;4(1):62-6.
33. Xiao N, Liu F, Zhou G, Sun M, Ai F, Liu Z. Food-specific IgGs Are Highly Increased in the Sera of Patients with Inflammatory Bowel Disease and Are Clinically Relevant to the Pathogenesis. *Intern Med*. 2018 Oct 1;57(19):2787-2798.
34. Maggini S, Wintergerst ES, Beveridge S, Hornig DH. Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. *Br J Nutr*. 2007 Oct;98 Suppl 1:S29-35.
35. Guerrero RB, Salazar D, Tanpaiboon P. Laboratory diagnostic approaches in metabolic disorders. *Ann Transl Med*. 2018 Dec;6(24):470.
36. Meyer JN, Chan SSL. Sources, mechanisms, and consequences of chemical-induced mitochondrial toxicity. *Toxicology*. 2017 Nov 1;391:2-4.
37. Hodges RE, Minich DM. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *J Nutr Metab*. 2015;2015:760689.

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On the Cover

The Lobay Viewpoint

by Douglas Lobay, BSc, ND
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The Last Ember

There is something magical and inherently healing about the heat and the light of fire from a wood stove. Our wood stove was located in the basement of our house on the outskirts of our small town. My father fabricated our wood stove from a large hollow steel cylinder welded together with pieces of metal, a door, a damper and a large triangular flume with piping that attach to our brick fireplace. During the cold and harsh winter months, our woodstove would be lit, burning wood fuel and warming our house. The fire would burn all night and supply all our heating needs. The last ember would burn out by the early morning.

Marion was my mother, and she was generally a kind soul with a loving heart. She was a traditional homemaker who grew her own garden and made wonderful and nourishing meals from scratch. She canned her own food and made her own bread. She also knitted and crocheted sweaters, socks, mittens and blankets. She could also have a temper and she could verbalize her displeasure to a person or circumstance she didn't like. She experienced her share of loss and tragedy. Her first husband passed away suddenly from drowning. Her second child died from crib death when only a few weeks old. Her first born and eldest passed away in a car accident when only eighteen years old. She turned to religion to seek answers to the pain and loss she experienced. She studied with several different Christian groups but never really committed to one faith. She chose instead to read the Bible daily. Her favorite book in the Bible was the poetic book of Psalms.

At the beginning there were subtle signs. She would often forget places and names. She would get dates, time and numbers confused. She misplaced things and couldn't remember where she left them. She would brush off these momentary lapses and make whimsical excuses. She would then accuse her husband of not listening to her and following instructions. After he suddenly passed away, her symptoms worsened. Stories became more convoluted and a mix of reality and memories of the past. One moment she would talking totally cogent and logical and then drift off into something that bordered fantasy. Her short-term memory faded, but she could still remember vivid details of her distant childhood and early adulthood. She was diagnosed with vascular dementia.

Dementia, whether formally diagnosed as Alzheimer's disease, vascular dementia or some other cause, is a scourge of a disease. It is insidious and progressive and robs a person of their so-called twilight of their life or golden years. As her memory deteriorated, she was placed in a bright and beautiful but somewhat sterile care home with other similar aged infirm and decrepit individuals. She seemed to adjust to her new living arrangements fairly nicely. As she grew older, she became frail and weaker, lost her appetite and ability to walk unaided. One nurse told us she would often wake up in the middle of the night while still dark outside and sing songs from her past. She passed away peacefully in the early morning one day in January after they couldn't wake her to give her medicine.

I am going to miss our telephone calls. I could often remember phoning my mom from anywhere and anytime and talking to her and asking her advice. When I moved away to college and university, I could phone when I was down or despondent and say "Hi Mom…." When I graduated and went to naturopathic school in Seattle, I could always phone home and have her answer. As I travelled to different places around the world, I could still phone home and talk. After I got married and lived in a different city than my parents, I could still phone

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home and talk to Mom. As her illness progressed, the phone calls dwindled. She would often have trouble hearing me, would get me confused with someone else, or inadvertently hang up on me. She talked about the incidences that happened long ago to people who have long since passed. And then the phone calls stopped.

Spouses, children, and caregivers of patients suffering from dementia and other neuro-degenerative diseases are exposed to a variety of stressors.[1-3] They experience a range of emotions ranging from confusion, grief, fear, sadness, anxiety, depression, embarrassment, loss, rejection and guilt. More than anything, I felt a certain amount of guilt and powerlessness to do anything. I am forever grateful to my younger sister who was my mother's primary caregiver during this time. I moved away to go to school when I was young and practiced naturopathic medicine in a different city. I was busy with work, my wife and raising a family. I didn't see my mother as often as I would like. Yes, there were phone calls, but she was not tech savvy and we couldn't have virtual visits. During the Covid pandemic, the care home was under strict lockdown for months. I only had a few brief visits outside her window. My last visit was just after Christmas when I was able to visit her in person. She was confined to her medical bed. We talked about things that were both real and imaginary and punctuated by brief smiles and laughter. I held her hand, told her I loved her, gave her a kiss on her forehead, and that was the last time I saw her.

As I sit back and reflect on my mother's life, I try to think about what legacy she left behind. Like everybody she had her share of good and bad, ups and downs, tragedy, and triumphs. She had good qualities and some not so good qualities. Her relationship with my father was punctuated with episodes of acrimonious discourse. At times he drank too much, and she didn't like that. Despite their shortcomings they still had a half decent relationship. After he passed away, she would always say that she missed and loved him. We had a fairly good middle class up bringing. My mom was a stay-at-home mother, and my father was a shop foreman at the Ministry of Highways. We lived in a sprawling rancher home on one acre of land with a big organic garden. We had all sorts of toys, including motorcycles, go-karts, and snowmobiles. We were involved in many sports, including hockey, baseball, soccer, and skiing. We grew up in a time of black and white television and just five original channels. We grew up in era before electronic gaming and cell phones. We had the freedom of the hills and roamed outside over mountains, hills, ponds, and meadows. I know I was blessed to have a happy and caring childhood.

In naturopathic school I befriended another student whose childhood in Idaho was marred by a strict and seemingly callous upbringing. He told me that his father used to punish him mercilessly and his mother never told him she loved him. He was scarred from his childhood. His relationships were difficult and tenuous. He couldn't believe the relationship I had with my mother and how loving and caring she was. After pondering on the matter, I came to the conclusion that the single most important legacy I got from my mother was "unconditional love."

Unconditional love is loosely defined as a love or deep concern for another without any attachments or boundaries.[4] A true mother's love to a child is epitomized as an unconditional love. I know that my mother's love for me was an example of unconditional love. To a point I knew she would love me no matter what I did, wherever I was or whoever I was with. I know she could be harsh and discipline me at times, but I still knew above all else she truly loved and cared for me. I am forever grateful for friendship, guidance and love she gave and showed me.

Many studies show that children shown unconditional love are better adapted, healthier and have superior stress resolve. It is critical for the personal development of self-esteem. Children not shown unconditional love tend to show more helplessness, anger, and resentment. Children shown unconditional love are generally happier and more fulfilled. They have better interpersonal relationship on many levels. The expression of unconditional love is a template for emotional, physical and spiritual growth later in life.

One book I found helpful was called *On Death and Dying* by Elizabeth Kubler-Ross. She was a Swiss-American psychiatrist who wrote a watershed book about pain and loss of a loved one in 1969. She suggested a five-stage model of grieving experienced by family members and care givers that included the sequential emotions of denial, anger, bargaining, depression, and acceptance. At first there is denial or refusal to deal with the inevitablity of fate of someone's life. Then there is an anger or a strong feeling of dissatisfaction with the realization of this end. Then there is bargaining and glimmers of hope. After hope fades and reality endures, then there is a general feeling of despondency and dejection. After this, there is general acceptance of the inevitability of fate and the reality of destiny.[5]

Betty was smartly dressed as she came to my office to discuss the results of her heavy metal test. She wore brown shoes, white slacks, and a tan blazer. Around her neck was a chiffon scarf embroidered with spring flowers. She wore dark gloves and black horn-rimmed glasses. She was tall and slim and had a short, cute haircut. Her husband of 61 years led her by the hand as she shuffled down the hallway. Betty suffered from dementia, probably Alzheimer's disease, and couldn't

tell me what time and day it was, didn't know what she ate for breakfast or where she was exactly. Her condition had deteriorated somewhat since I last saw her – or she was just having a bad day. She mumbled her words and vacillated in and out of consciousness during our visit. Her test was quite good, and her levels of toxic metals was low. I was at a loss as to what to suggest that might help her. I casually suggested that we could contact the local health unit and arrange for a nurse or home care to deliver some at-home services. I suggested that if Betty's dementia progressed, we could think about placing her in a nursing home for care. Walter scolded me for using the word dementia and said he was still perfectly able to care of her at home. And besides their daughter would come over frequently, help out and give him some respite. He said with a glimmer in his eye that there was always hope, maybe she would get some better and maybe the nutritional supplements would help more. After concluding our visit Walter struggled to put Betty's blazer back on and then they both shuffled down the hall and left. I smiled. He was very tender with her and he dressed her very nice.[6]

References

1. Lindren CL et al. Grief in spouse and children caregivers of dementia patients. *West J Nurs Res*. 1999 Aug;21(4) 521-37.
2. Moyle W et al. Living with loss: dementia and the family caregiver. *Aust J Adv Nurs*. Mar-May 2002;19(3):25-31.
3. Etters L et al. Caregiver burden among dementia patient caregivers: a review of the literatrure. *J Am Acad Nurse Pract*. 2008 Aug;20(8):423-8.
4. Hofmann SG et al. Loving-kindness and compassion meditation: Potential for psychological interventions. *Clinical Psychology Review*. November 2011;31(7):1126-1132.
5. Kubler-Ross E. *On Death and Dying*. Scribner Publishing. Scribner Reissue edition. New York, NY. August 2014.
6. Duggleby W et al. Renewing everyday hope: the hope experience of family caregivers of persons with dementia. *Issues Ment Health Nurs*. 2009 Aug;30(8):514-21.

Douglas G. Lobay is a practicing naturopathic physician in Kelowna, British Columbia. Dr. Lobay graduated with a Bachelor of Science degree from the University of British Columbia in 1987. He then attended Bastyr College of Health Sciences in Seattle, Washington, and graduated with a Doctorate of Naturopathic Medicine in 1991. While attending Bastyr College, he began to research the scientific basis of natural medicine. He was surprised to find that many of the current medical journals abounded with scientific information on the use of diet, nutrition, vitamins, and botanical medicines. Besides practicing naturopathic medicine Dr. Lobay enjoys research, writing and teaching others about the virtues of good health and nutrition. He has authored several books, numerous articles, and papers and has taught many courses at seminars and colleges throughout his career. He is married to Natalie and has two daughters, Rachel and Jessica. He also enjoys hiking, hockey, skiing, tennis, travelling and playing his guitar.

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Townsend Letter: Moving On

by Jule Klotter

"There is nothing permanent except change," said the Greek philosopher Heraclitus; and *Townsend Letter* has dealt with multiple changes over the past 40 years, including its name! It began as *Townsend Letter for Doctors* (*TLfD),* in 1983, expanded to *Townsend Letter for Doctors and Patients* (reflecting the number of educated laypeople who subscribed) in 2004, and then settled on its current name *Townsend Letter – The Examiner of Alternative Medicine.* As Jonathan Collin mentioned in "Letter from the Publisher" (page 6), this issue is the last edition of *Townsend Letter.*

What began as an "informal newsletter for doctors communicating to doctors," early in 1983, matured into a magazine with an international reputation for presenting the clinical experiences of alternative/integrative doctors and practitioners. Unlike professional journals that specialize in one branch of medicine, *Townsend Letter* has always embraced multiple schools of medical practice, including nutritional, orthomolecular, functional, homeopathic, naturopathic, chiropractic, botanical, anti-aging, energy modalities, acupuncture, massage therapy, and applied kinesiology. And the magazine has always welcomed real-world clinical observations and viewed such empirical evidence as being the first step in medical research. As Jonathan Collin wrote in the January 1994 issue, "… providing to professionals and public the thoughts and practices of an alternative practitioner is *invaluable*. It is only when such thoughts have public expression that peer review begins to take place."

Collin, who has had a lifelong interest in publishing, wanted to provide an outlet for doctors who thought and worked outside the medical status quo. He envisioned the publication as "a bulletin board for doctors to share their pet therapies and mad-scientist ideas." And in the first decade or so – before the widespread use of blogs and social media – the magazine was filled with letters-to-the-editor, sharing clinical observations, debating the pros and cons of diverse alternative practices, and more.

Inside the August/September 1988 issue (#61/62), for example, a robust "Letters to the Editor" section debated the possible toxicity of *Streptococcus faecium* used in some probiotic products. In other letters, Warren M. Levin, MD, suggested applying a nitroglycerine patch to acupuncture point Pericardium 6. Bernard Rimland, PhD, asked for scientific references that support kinesiology. Serafina Corsello, MD, responded to an earlier writer's criticism of the 'interventive naturopathic approach.' Sherry A. Rogers, MD, notified doctors of a recent paper that explained how to test for environmental chemical reactions, at a time when sick building syndrome and multiple chemical sensitivities were just beginning to be acknowledged. *TLfD* had become the 'bulletin board,' the forum for questioning and discussion as physicians and patients sought answers to recognized illnesses and to new syndromes that failed to respond to conventional therapies.

While mainstream press assured readers that the new disease AIDS was "incurable and almost always fatal," *TLfD* reprinted an article by Robert F. Cathcart III, MD, describing his clinical use of large doses of ascorbic acid (vitamin C) and other nutrients along with a clean diet to lessen symptoms. While conventional medicine and the chemical lobby maintained that people with a bewildering array of symptoms were delusional, *TLfD* gave people with chemical sensitivity and environmental illness a place to voice their experiences and gave practitioners a venue for sharing their clinical insights. AIDS, attention deficit/hyperactivity disorder, chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivities, chronic Lyme, Gulf War syndrome, autism – a profusion of new diseases and syndromes erupted in the 1980s and 1990s, conditions that affected mind and body and could not be cured with a simple procedure or magic pill. Interest in complementary and alternative medicine surged. By 2003, the *Townsend Letter,* which started as an eight-page newsletter, was publishing a magazine with over 160 pages, 10 times a year.

As the magazine grew, Collin recruited doctors, practitioners, and healthcare journalists to write columns related to their field. Alan R. Gaby, MD, an expert in nutritional medicine and author of the "Literature Review and Commentary" column, began writing for *TL* in late 1985. He had written for the Northwest Academy of Preventive Medicine newsletter when Collin was editor. "I was impressed with his open-mindedness and his interest in nutritional medicine," Dr. Gaby told me by e-mail when I wrote about *Townsend's* 30th "birthday" for the February/March 2013 issue. "When he founded the *Townsend Letter* and asked me to be a writer, I was happy to be a part of his new endeavor."

Naturopathic physicians Judyth Reichenberg-Ullman and Robert Ullman began their "Healing with Homeopathy" column in 1990, a column that Dr. Judyth has continued to write on her own after her husband retired. After they read *TL* for the first time, Dr. Judyth remembers thinking, "Holistic medicine is well represented, but why isn't anyone writing about homeopathy in the *Townsend Letter*? All it took was a call to Jonathan…."

Tori Hudson, ND, a recognized expert in women's health, began "Women's Health Update" in 1992. She told me, "*TLfD* was one of the very few publications at the time that I started, that offered a resource for clinicians in a wide range of topics. The articles were topical, controversial, informative and, yes, even the 'out there' articles were important to me. I always liked that the *TLfD* editor and staff include columns and articles that were left brain and right brain, mainstream evidence-based natural medicine as well as the progressive, theoretical, unproven, and even edgy."

Many other columns have appeared in this magazine over the years. Dr. Melvyn R. Werbach's "Nutritional Influences on Illness," which became a mainstay for almost two decades. Sherry A. Rogers, MD, wrote a column on environmental medicine, a topic now covered by Marianne Marchese, ND. Anna MacIntosh, PhD, ND, reviewed research studies related to exercise and physical activity. Robert A. Anderson, MD, presented research on the connection between mind, emotions, and physiology in "Psychoneuroimmunoendocrinology Review and Commentary." Tim Batchelder took on medical issues from an anthropological view. John Weeks discussed the business side of alternative medicine. Paul Yanick wrote about quantum healing and functional medicine. Bob Flaws covered Chinese herbal medicine and acupuncture. Kerry Bone, Donald Brown, and Andrew Gaeddert shared research about botanicals and phytotherapy.

Collin began testing the idea of having a theme for each issue in August/September 1999; the first topic was lupus and autoimmune disease. That issue contained lupus patient Henrietta Aladjem's perspective and a review of her book. Practitioners such as the late Abram Hoffer, MD, PhD, provided their perspectives as well. He and Melvyn Werback, MD, reported that food sensitivities contributed to autoimmune disease. Environmental risk factors linked to lupus were discussed by Rose Marie Williams in her "Health Risks & Environmental Issues" column. A few months later, *Townsend Letter* looked at the "Best & Worst of Alternative Medicine" (February/March 2000). Contributors included many notable names in the world of complementary and alternative medicine: Jeffrey S. Bland, PhD; Joseph E. Pizzorno Jr., ND; Abram Hoffer, MD, PhD; Richard Kunin, MD; Joseph M. Mercola, DO; and more.

Since those first theme issues, *Townsend Letter* has sought to focus the diverse views of its contributing writers on topics such as Lyme disease, chronic fatigue, chemical sensitivity, cardiovascular health, allergies, respiratory health, cancer, women's health, men's health, the brain and mental health, inflammation, and alternative laboratory tests. Some of the "Best Reads" that have appeared in *TL*'s pages are available on our website: www.townsendletter.com.

In addition to complementary and alternative healthcare practices, health freedom and informed choice have been major topics of interest. In headline articles on the front of the 36-page June 1986 issue, Bruce Halstead related his dealings with the California State Board of Medical Quality that resulted in a truly "draconian sentence" of four years in state prison, $10,000 fine, delicensure, and court orders to "desist from all professional activity in the health care field." What terrible actions had led to this sentence? Halstead had recommended a homeopathic herbal preparation to patients in the hope of enhancing their immune function. He neither manufactured the product nor profited from its sale.

Dr. Halstead was just one of numerous physicians being prosecuted in the US for advocating alternative therapies at that time. More recently, *Townsend Letter* has been covering doctors who are facing the threat of delicensure because they have not succumbed to the official narratives around covid or vaccines. Medical freedom, as well as improvements in medical care, needs practitioners who can think outside the one-size-fits-all box and communicate their views. Without doctors free of coercion and threat, patients lack information to make an informed choice.

Townsend Letter has been at the forefront of innovative, holistic healthcare for 40 years, and its legacy as "the examiner of alternative medicine" will continue on the web.

Punitive medical boards have not been the only threats to medical freedom. The November 1991 issue reflected the turmoil surrounding the FDA's attempts to regulate dietary supplements as if they were drugs. *TLfD* contained testimonies, written by Jeffrey S. Bland, PhD, and Kirkpatrick W. Dilling, that were submitted to the FDA Dietary Supplement Task Force. FDA agents had shut down several clinics and supplement manufacturers and suppliers over the years, restricting access and consumer choice.

The FDA's actions gained widespread notoriety in May 1992, when armed police and FDA agents raided Dr. Jonathan V. Wight's Tahoma Clinic in Kent, Washington. What "illegal" substance instigated the raid? B vitamins. The police thought that they would find narcotics. Dr. Wright fought a hard legal battle for almost four years until the FDA finally dropped the charges in 1995. The highly publicized

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raid generated more urgency to pass the federal Dietary Supplement Health and Education Act (DSHEA). The legislation, which was an ongoing topic in *TLfD* for several years, asserted consumers' right to have access to safe dietary supplements. It was finally signed into law in 1994. DSHEA grandfathered in any supplement that was on the market before 1995.

When FDA tried to restrict access to N-acetyl-L-cysteine (NAC) in 2021, *Townsend* staff was able to find 13 advertisements in pre-1994 issues showing NAC had been sold in supplements before DSHEA went into effect. On April 20, 2022, FDA announced an unpublished (not finalized) decision that the supplement NAC, which was to be restricted to drug use only, was restored to food supplement use. The FDA did note in its memorandum that NAC has been used as a supplement for more than 30 years.

NAC is by no means the only product, used by integrative practitioners, to attract FDA's heavy hand. Bioidentical hormones (see www.townsendletter.com), homeopathy, and compounding pharmacies have all been threatened. *Townsend Letter* continues to follow these issues and others that threaten access to non-pharmaceutical treatments/products.

In October 2008, the American College for the Advancement in Medicine (ACAM) presented Jonathan Collin with its Legacy Media Award. The award honored *Townsend Letter* then in its 25th year of publication, for its contribution to the field of alternative and integrative medicine. The award is well deserved. With an extraordinary open-mindedness, Jonathan Collin has created a unique forum for the sharing and discussion of nonconventional viewpoints. Over the years, *Townsend Letter* has published information that has later (often years later) been verified by mainstream researchers. Suicide ideation caused by SSRIs, dangers of Vioxx, the benefits of IV vitamin C in cancer, and the importance of beneficial bacteria and probiotics are just a few of the topics that appeared in *TL*'s pages long before scientific verification and mainstream coverage. I cannot help but wonder what other topics will eventually be accepted by the wider medical community. Will it be Dr. Alan McDaniel's view on hypothyroidism (See May-June 2021 issues or www.townsendletter.com)? Will doctors use functional medicine to reverse ailing kidneys, like Dr. Devaki Lindsey Berkson hopes (June 2021)? Will Dr. Garth L. Nicolson's research into restoring cellular membrane function become standard for people with chronic illnesses, like Gulf War syndrome (November 2022)? Who knows what seeds are being planted by these *Townsend* articles?

Like other publications, *Townsend Letter* has been affected by the economic decline that began with the dot.com/technology bubble bust in 2000, and major changes in the publishing and advertising industries. Although Collin moved to a new printer Dartmouth Printing Company (Hanover, New Hampshire) in the summer of 2011 issue to ease financial stress, current economics have forced another change. Instead of producing a magazine, *Townsend Letter* will continue to publish articles of interest on its website and in the weekly e-newsletter.

Along with its many informative contributors, *Townsend Letter* has been blessed with a committed and creative staff. Barbara Smith has been the magazine's managing editor since 1995. She has been responsible for the magazine's layout and design since the mid-1980s. From 1995-2010, she worked in the office. Now, more times than not, she performs layout on the road as she and her husband, Larry, travel in their RV to visit friends and family, harvest beets in the Fall, and sell Christmas trees in Texas in December.

Sisters Joy Reuther-Costa and Julie Reuther maintain the office these days. The *Townsend Letter* office consists of the dining and a small bedroom in a small, two-story house, which also holds Dr. Collin's Olympic Peninsula medical practice, in uptown Port Townsend, Washington. Joy started as circulation assistant in the 1980s, under her mother JoAnn, who was *Townsend*'s circulation manager until her death in 1994. Today, Joy is circulation manager and webmaster for the magazine. Julie started working as a teen on *Townsend*'s mail crew in its early years. Ten times each year, the mail crew – a group of adults and teens – took over the living-dining room of Dr. Collin's clinic to address, add inserts, and organize according to zipcode and post office regulations the boxes of finished issues, trucked from Printery Communications down the street. Today, Julie is managing assistant; she takes care of day-to-day office activities and helps Dr. Collin keep track of manuscripts and advertisers.

Compared to the other three, I (Jule Klotter) was a latecomer. I was initially hired as a temporary editor in 1990. But when *Townsend*'s editor, Irene Alleger returned from her sabbatical, Dr. Collin hired me to develop an index of the magazine's authors and article keywords. Later, he asked me to compile events for the calendar, write book reviews that provided information for busy doctors, and abstract articles for "Shorts." I became *Townsend Letter*'s editor near the end of 2016.

Townsend Letter has been at the forefront of innovative, holistic healthcare for 40 years, and its legacy as "the examiner of alternative medicine" will continue on the web. If you want to subscribe to the e-newsletter, go to the website www.townsendletter.com and submit your email address. You can also send a request – and a few kind words about your experience with the magazine – to info@townsendletter.com.

To quote our Editor-in-Chief, thank you, thank you, thank you.

Thank you!

Healing with Homeopathy

by Judyth Reichenberg-Ullman, ND, MSW
www.healthyhomeopathy.com

The Homeopathic Lion's Milk: *Lac Leoninum*

The Original Big Five

I just returned from a month in Kenya... my first journey to Africa, though I wish I had accepted an invitation to go with a group of homeopaths twenty years ago or so. I am a huge animal lover; my very favorite is the elephant. The term "Big Five" originally referred to these five large African mammals who were known to be potentially dangerous, when encountered by humans: lion, elephant, leopard, rhinoceros, and Cape buffalo. It was considered a feat by trophy hunters (perish the thought) to slaughter them, stuff them, and hang them proudly on the walls of their dens (ironic name) or living/game rooms. Now, fortunately, these amazing animals are largely protected in game parks and reserves in Africa. Poaching, however, threatens to decimate them, as well as climate change.

I cannot communicate sufficiently how remarkable it was to see these amazing animals in the wild, often from very close distances. A friend and I were fortunate enough to spend nearly three weeks in the Masai Mara Game Reserve, Lake Naivasha, Nakuru National Park, Samburu National Game Reserve, Ol Pejeta Conservancy, Amboseli National Park, and Tsavo West National Park. During the last two days before returning, we did another three-hour game drive at the Nairobi National Safari Park as well as visiting the Sheldrick Elephant Orphanage (the highlight of the entire trip for me) and the Giraffe Center. In the 150-square mile Amboseli, (southern Kenya), due to the worst drought in 70 years, their precious water holes were dried up, resulting in many carcasses of zebra and wildebeest readily visible from our safari vehicle. Cheetahs were elusive, despite our visit to many game parks, and we saw only one leopard, lounged in a tree with its impala prey.

During the last decade, nearly 10,000 African rhinos have been lost to poach. It was estimated, three years ago, that 350,000 elephants remained in Africa. Ten to fifteen thousand are killed each year by poachers. Since 2008, 11,000 rhinos have been poached, slaughtered for ivory, meat, and body parts. Ivory, thankfully, is now illegal on the world market, yet poaching is still rampant. In South Africa, for example, 451 rhinos were killed in South Africa alone, the first time in six years that the country recorded an increase. Between slaughter by humans and global warming, it is largely up to organizations such as the *Sheldrick Foundation* in Kenya, *Save The Rhino International*, and other similar groups to save these remarkable creatures from extinction. It was truly remarkable for me to finally be so close to these magnificent, remarkable beings. Do not wait, however, to go.

Homeopathic remedies are prepared from animal substances, as well as mineral and plant. I thought it would be fascinating to share a bit about the use of these "big five" as remedies. One of my favorite remedies is *Lac leoninum* (lion's milk). There are also remedies made from elephant's milk (*Lac loxodonta Africana*). The big five remedies have the following characteristics:

- strong issues of survival
- competition
- struggles between victim and aggressor
- predator vs. prey
- sexuality
- camouflage
- conflict/a split
- contradiction
- a feeling of being dirty, disgusting
- attractiveness
- liveliness

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Humans needing remedies made from mammals demonstrate the following characteristics:

- highly evolved, intelligent
- a strong maternal instinct and family connection
- nourish their young with milk
- sexuality
- competition
- highly adaptable
- able to communicate among their own species
- strong issues of sexuality

Of the "big five," my clinical experience is with *Lac leoninum* (lion's milk). It is important to mention that whenever a homeopathic medicine is prepared from a mammal, it is done so humanely, generally from a tiny amount of blood or milk.

Lion's Milk

I first learned about this remedy from the wonderful book of a colleague, Nancy Herrick, *Provings of Eight New Animal Remedies* (1998). I had a wonderful case of a 13-year-old young man with quite the temper. His mother brought him to me for help with oppositional-defiant disorder. He had quite a swagger and pushed his weight around at every opportunity. This young man's mother was beside herself because he was so difficult to be around. Extremely selfish with a ravenous appetite, he would finish his own food, then reach for whatever else was on the table, oblivious to the desires of other family members. He pushed others out of his way, was territorial and invasive, and his temper was frightening.

I prescribed *Lac leoninum* 1M for this young man, Daniel, and his temper diminished considerably. Daniel became bearable to family members, though his nature continued to be pushy and selfish. During the first appointment, his mom shared that the first sound out of his mouth after birth was a loud roar. (I promise I am not making this up!) At one of his follow-up appointments, his mom quoted him, "I am nursing my wounds... I am at the top of the food chain." Sounds uncanny, but it is true. He was simply expressing his inner nature. I treated him for a year or two.

I am currently treating a second young man, Connor, fifteen years old with *Lac leoninum*. As an infant, he would wake five to ten times a night. His mom had to pin him down to nurse because he was always fighting with her, grabbing her nose or face. "A rule breaker from the very beginning." Connor's parents would put him to bed, and he'd be up two minutes later. Strong-willed, defiant, he refused to eat. Even as a toddler, he bit and scratched other kids. If someone took his toy at school, he'd bite, scratch, push, and pull their hair. The teachers accused the parents of letting Connor watch violent TV, but it was not the case. "Your son's hands are always on others." Connor almost got kicked out of school many times. Connor was incredibly intelligent, but lazy. If he didn't want to do chores, he simply wouldn't. Nor his homework. Connor failed every class, despite counselors and tutoring.

The youngster's room was a complete disaster. "He leaves a trail. Very disorganized. We have to remind him, step by step. Every day. We are so tired of being mad at him. Now he is in high school and has to smell good, so he can't walk around in dirty clothes. Connor changes his outfits three times a day. He wants a wardrobe stage. He was a dress-up kid with costumes till he turned 9. He's a big boy: 6'3" and nearly 210 pounds.

"When Connor was little, if I didn't play with him, he'd come over and bite my big toe. He has always been the class clown. He likes to be the center of attention. But, if he makes a mistake, he shuts down and gives up. We'd buy him a brand-new toy and, ten minutes later, he broke it. At age three, I gave him a cordless drill. He took our vacuum cleaner apart in five minutes... Connor is like a locomotive. It's hard to get him moving but, once he is, it's hard to stop him. He would break his crayons at school, cut his clothes all the time until third grade.

"Connor is very good at listening and gathering intelligence. He eavesdrops on our adult conversations. But he won't complete a chore. He is a debater. Constantly makes up clever puns. Connor talked early and has a great sense of humor. He is quite the storyteller, and his timing is comedic. Connor is a debater. When it comes to disciplining him, he is not bothered by threats or spankings. He always has a game plan, but it is very self-serving. His pediatrician described Connor as 'high-spirited.'"

From Connor's father: "Connor is not motivated. He quits when things are hard. Overdramatizes every little injury. Just wants to do what he wants. Connor decided he wouldn't play soccer and just sat on the field. He has a hard time falling in line and has been defiant Connor since day one. He avoids responsibility and will try to prove his lies. He does not want to lose face. Connor is constantly covering up. He is willing to die on the hill because he is so obstinate."

I asked whether Connor could be cruel. "Definitely. He taught his little brother to pull the tails off of lizards. He's got an aggressive streak, but he is tender when he wants to be. He can get highly explosive, punches his bed when he is mad, and has broken door handles off multiple times. When he gets mad, he goes 'grrrr' and shakes them till they break."

Further information from Connor's mom, which clearly confirmed the prescription of *Lac leoninum*: "Chores are a fight, battle. He doesn't want to do what he doesn't want to do. Then it turns more aggressive, ugly. He might push his brother out of the way. I call it manhandling. He'll grab my face, tries to hug me, trap me, throws a fit, breaks things. I found a picture that he ripped into a million pieces. We have a

very large dog. If she barks, Connor will come running out, grab her aggressively, and try to force her onto her bed.... Connor definitely likes meat. He is never satisfied with vegetables. The minute there is meat, he pounces on it. Connor is always asking for more meat. If we take him to a restaurant, he orders a big hamburger. Connor wants to win every situation, battle to the death." I prescribed a single dose of *Lac leoninum* 1M for Connor.

After the Remedy

Six Weeks: From his mom: "Connor's grades are the best they've ever been. Last quarter he got an F, 2 Ds, and some A's, B's one C. This time, before finals, he got 2 As and 2 Bs. He's doing a lot more of the work autonomously. He's a bit more affectionate and his behavior is a little better. Connor is still a touchy guy, but he's been a lot more gentle since the remedy. When I asked him to talk about his feelings towards his grandpa, who is dying, he got snarly and hissy."

Twelve Weeks: "We applied for a school scholarship. He buckled down and got some of the better grades ever. He got the scholarship. More As and Bs this quarter. The principal and vice principal unanimously wanted to support him. He has skin in the game. We've been giving him *Lac leoninum* 1M every week. He comes home from school fairly happy. He likes his down time... extra sleep. Connor is in a growth spurt. He tells me, 'I need more food!' He continued the *Lac leoninum* up to once a week."

Sixteen Weeks: "He's reverting back to some of his old behaviors. When he walks past you, he nicks you. Back to being aggressive and the beast mode. He hugs me, grabs my face, pushes my body away, moves my arms. He wants what he wants. When he gets it, he can be mean, physical. He was doing really well. He's manhandling again. Pushes you out of the way." I prescribed a dose of *Lac Leoninum* 10M and sent another dose to have on hand.

Eighteen Weeks: Mom: "Connor rarely goes out of his way for anyone, but he is doing much better again. His little brother was having trouble putting on his belt. Connor stood on his brother's bed to help him. It was very tender and loving. Over the weekend he pulled out his little brother's loose tooth for him. He decided all by himself to write a paper. We still have little blips here and there, but he is getting a bit more mature... He is back to coming up to me and telling me he loves me. Initiating hugs. That is the Connor that I used to love. He is even playing video games with his little brother. There's a little bit of a sassy mouth, but it has gotten better. Much less manhandling. Now he giggles and banters. If I tickle him. Before he would get angry and move you out of the way. Or avoid you. He hasn't been in beast mode since we gave him the new dose. His principal says he's doing pretty well."

Connor should continue to improve over time. I find this to be a fascinating case and remedy. It is remarkable to me how often his mom, who has a totally different nature, uses lion-like words to describe her son. I like to call this phenomenon "Speaking from Source," where the patient or family member uses the very words from the natural substance, in this case the lion. I look forward to continuing to follow Connor over time and expect him to continue to mature in a more balanced, more human, so to speak, way.

Let me end by saying that, if you have any desire to experience the remarkable wild animals in Africa, do not wait. Go! With climate change, poaching, and pandemics, who knows how much longer such an opportunity will be possible!

Some Fabulous Opportunities to Experience Kenya From Afar

My favorite lodging was the Kilaguni Serena Safari Lodge in Tsavo West National Park. The lodge supplies its own watering hole, which attracts many families of elephants, zebras, and Cape Buffalo, as well as hyenas and other animals. During our stay they were installing a webcam, which I find thrilling. You, too, can access it at https://webcams.aeroclubea.com/TsavoChyulu/tsavo_chyulu_Tsavo_KilaguniN.html.

The highlight of my entire trip was the visit to the Elephant Orphanage run by the Sheldrick Wildlife Trust in Nairobi https://www.sheldrickwildlifetrust.org. I adopted two of the most precious baby elephants, Nyambeni and Mzinga. One was rescued from a well/ditch and the other abandoned. Both were airlifted by helicopter (no small feat), and both are now thriving and just adorable. One can adopt them for as little as $50/year.

You may have heard of the remarkable interspecies animal communicator and tracker, Anna Breytenbach. I originally saw her on YouTube, having been able to miraculously communicate with the ferocious black leopard, Diabolo. Since that time, I have watched a couple of amazing videos and webinar during the pandemic: "The Incredible Story of How Diabolo Became Spirit" (https://www.youtube.com/watch?v=gvwHHMEDdT0) is the original video and https://www.youtube.com/watch?v=apN1UhDn4WE is a YouTube interview with her by Andrew Newman, author of the children's book, *How Diablo Became Spirit.*

Dr. Judyth Reichenberg-Ullman is the author of *Whole Woman Homeopathy*, and co-author, with Dr. Robert Ullman, of other books on homeopathy: *Ritalin-Free Kids, Homeopathic Self Care, The Savvy Traveler's Guide to Homeopathy and Natural Medicine*, *A Drug-Free Approach to Asperger Syndrome and Autism, The Homeopathic Treatment of Depression, Anxiety, and Bipolar Disorder,* and *Rage-Free Kids*, as well as *Mystics, Masters, Saints and Sages – Stories of Enlightenment*. She has been a columnist for the *Townsend Letter* since the early 90s, and has taught internationally. Judyth and Bob live on Whidbey Island Washington, with their golden retriever, Rosie Posie, and in Pucón, Chile with a menagerie of farm animals.

Please visit www.healthyhomeopathy.com (where you will find a wealth of articles, blogs, and more) and Facebook at Healthy Homeopathy. Dr. Reichenberg-Ullman can be reached at drreichenberg@gmail.com or by calling 360-322-4996.

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Curmudgeon's Corner

by Jacob Schor, ND, FABNO
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Vitamin C and Mortality

I debate whether to send this article to our good Dr. Collin, publisher of the *Townsend.* My hesitation is not because the data in this study suggests a key belief of ours may be wrong, but rather because the results are still hard for me to accept. Curmudgeon I may be, but even so, I feel hesitant to write this article.

I think it needs to be considered nevertheless as the findings may be important to our clinical practices. This information will either be later disproven, or perhaps this study will be considered the turning point when we began to rethink how vitamins should be dosed. This could be the study we will reference in years to come.

The study I want to write about is by Tian et al, published September 2022 in the journal *Nutrition* and describes a non-linear association between serum vitamin C and all-cause or cause-specific mortality.[1]

The results suggest that vitamin C may not be as benign as we have believed, and doses we have thought safe to recommend patients may be increasing their risk of dying.

This was not a clinical trial but simply a careful analysis of data already collected as part of the National Health and Nutrition Examination Survey (NHANES 2003-2006), specifically the two NHANES cycles (2003-2004 and 2005-2006) in which serum vitamin C concentration levels were measured in participants. Multivariable Cox proportional hazards models were used to show the risk for all-cause or cause-specific death according to baseline serum vitamin C levels in this cohort. Of the initial 20,470 participants, about half were excluded, mostly because of missing vitamin C data. In the end, 9902 participants were included in the analysis of data that was collected up until 2015. Their mean age was 45.6 years and 51.6% were female.

Serum vitamin C level (mg/dL) detected using isocratic high-performance liquid chromatography was the primary variable of interest. The researchers felt this was a more accurate measure of vitamin C in comparison to earlier studies that estimated vitamin C status from food frequency questionnaires. NHANES data was matched with national death index records allowing for accurate assessment of which participants died and the cause.

Earlier studies had suggested that the dose response to vitamin C might not be linear; in other words, higher doses might not have the same benefits as low doses. This study was designed to specifically examine such a possibility.

During a median follow-up of 10.6 years, there were 1558 all-cause deaths, including 320 from cancer, 374 from cardiovascular disease (CVD), and 120 from respiratory diseases.

Serum vitamin C levels exhibited a statistically significant U-shaped relationship with all-cause and CVD-associated mortality. That is, very low vitamin C levels raised risk of dying but again, so did high levels. As vitamin C levels increased above the mean, risk of dying again increased. Graphically with risk of dying on the vertical axis, this dose response looks like a big U.

While the association between vitamin C and death from cancer or respiratory disease did not reach statistical significance, there were trends in the data suggestive of a possible positive association for these conditions as well.

Perhaps the biggest weakness of this study was that the researchers didn't know what they were looking for aside from greater risk of mortality. Not knowing what diseases would be influenced by high vitamin C, they used data from relatively young cohort. Participants had only to be older than 18 for their data to be included. An older cohort may provide more definitive data.

Nevertheless, if the findings reported in this study are valid, we should be questioning our assumptions about the safety of vitamin C.

This study isn't the first to suggest that higher vitamin C status might have a detrimental effect on life expectancy. Earlier studies have reported similar results and Tian's study was designed specifically to examine this.

In 2016, Cadeau et al reported that vitamin C intake had a similar non-linear effect on breast cancer risk. Risk was highest in women with either very low or very high vitamin C status. Cadeau compared vitamin C intake among the 2482 cases of invasive breast cancer that had occurred among the 57,403 postmenopausal women in a French prospective cohort using food frequency questionnaires to estimate vitamin C intake. They reported

that, "…vitamin C supplement use was associated with increased postmenopausal breast cancer risk in women with high vitamin C intake from foods. Our data suggest a potential U- or J-shaped relation between total vitamin C intake and postmenopausal breast cancer risk that deserves further investigation."[2]

In 2018, a large review and meta-analysis by Jayedi et al, which examined "Dietary Antioxidants, Circulating Antioxidant Concentrations, Total Antioxidant Capacity, and Risk of All-Cause Mortality," reported that most antioxidants were associated with lower risk of dying, but they also described a U-shaped relationship between vitamin C and mortality.[3]

Obviously, these results come from epidemiological data and not from a randomized clinical trial. We generally put greater faith in results from clinical trials than from epidemiologic data, yet NHANES is one of the most trusted cohorts from which to mine data. These results should leave us questioning whether to even run high-dose long-term clinical trials using vitamin C out of ethical concerns.

Confounding variables often receive the blame when unwanted associations are found in epidemiologic data. In Tian's cohort the known lifestyle factors associated with lower mortality risk were consistently seen in those with the highest vitamin C levels. Comparing study participants based on vitamin C concentrations, those in quintile 5, the participants in the top 20% of C levels, were more likely to be White, better educated, more physically active, more affluent, and to eat more fruits and vegetables than those with lower levels of C. They were also less likely to smoke, have diabetes, or be overweight (lowest mean BMI of all quintiles). Those in Quintile 5 also had the lowest mean homocysteine and C-RP of all participants. These characteristics would lead one to predict that these people would have the lowest risk of dying during the study period but instead they were 77% more likely to die than those in Quintile-3 whose vitamin C levels were at or near the mean of all participants. (HR 1.77 1.51-2.09) when the unadjusted data were examined.

How could we miss this? Earlier studies focused on comparing inadequate versus adequate levels, never suspecting the possibility of a non-linear relationship and that at higher doses the relationship might shift. It's always easier to spot what you are looking for than something you aren't. Especially when it comes to vitamin C. We've justified use of high dose C not so much on data but on the gorilla business. Most animals, including fish, birds, and mammals synthesize vitamin C in their bodies. Humans are among the rare exceptions to this rule. So too are gorillas. It is assumed that "species which have lost the capacity to synthesize vitamin C have a vitamin C-rich diet…. This explanation is consistent with the fact that wild anthropoid primates (unable to synthesize vitamin C) consume much more vitamin C than the recommended daily allowance for adult humans in the USA, about 1 mg/kg/day. For example, gorillas (*Gorilla gorilla*) consume 20-30 mg/kg/day…."[4] Thus, we have concluded that humans should supplement their diet with additional vitamin C to attain levels similar to what other primates consume. It makes sense, but no one seems to have checked if this makes us live longer.

In recent years, U-shaped dose responses have been reported for several other vitamins that we'd previously been unconcerned about. In early 2022, Xu et al reported that high serum folate might raise risk of CVD in some populations. A few months earlier, in September 2021, vitamin B-12's association with all-cause mortality was also reported to be U-shaped, and again at higher serum levels risk of dying increased.[5] Also in 2021, Zhang reported that slightly higher levels of dietary niacin may increase risk of hypertension.[6]

While each of these relationships will need to be studied individually in far greater depth before we can confirm or deny their validity, their collective publication in such a short period leaves this reader wondering if we are seeing this new pattern now only because researchers have only recently started looking for it or simply feel safe to report on what they observe in their data.

The idea that varying doses of a substance might have strikingly different effects on biological systems hearkens back to the Arndt-Schulz Law that described such biphasic dose-responses. Unfortunately, this concept was deeply 'marginalized' for many years as it was closely associated with homeopathy. Using the proper term hormesis to describe biphasic dose responses hindered publication. In recent years, it has become acceptable in scientific publications to describe hormetic dose responses simply as U-shaped or J-shaped curves while omitting the term hormesis entirely from the discussion. This recent 'acceptability' seems to have allowed publication of a rapidly growing number of papers describing dose responses that clearly fit the definition of hormesis even if describing them simply as U-shaped curves.

This recent paper by Tian et al, should leave us questioning whether many of our patients are doing themselves long-term harm by taking daily doses of vitamin C and maintaining more than adequate serum levels of vitamin C. Past efforts at investigating vitamin C focused on benefits gained from reducing damage associated with deficiency and then, have sought long term benefits against a variety of diseases. This study may be among the first to purposefully look for long-term harm associated with use.

Perhaps we should use Tian's data and say that without specific indications for need, our goal should be to keep serum vitamin C at close to 1.06 mg/dL or alternatively use the daily dosage of 125 mg/day suggested by Jayedi et al in their meta-analysis. I write 'perhaps' because such suggestions may seem strikingly low to both patients and practitioners alike and would require abandonment of long held assumptions.

The current excitement on the potential benefits of intravenous high dose vitamin C (IVC) for treating cancer may drown out the cautionary message Tian's data may have revealed. How do we equate these two seemingly opposing effects? Think of IVC as having a pharmaceutical oxidative impact, similar to chemotherapy, and it makes sense that we might want to be cautious with vitamin C. Few healthy people would want to take chemotherapy drugs over the long term, even at low doses.

References

1. Tian T, et al. Association of serum vitamin C with all-cause and cause-specific death: Data from National Health and Nutrition Examination Survey (NHANES 2003-2006). *Nutrition*. 2022 Sep;101:111696.
2. Cadeau C, et al. Vitamin C supplement intake and postmenopausal breast cancer risk: interaction with dietary vitamin C. *Am J Clin Nutr*. 2016 Jul;104(1):228-34.
3. Jayedi A, et al. Dietary Antioxidants, Circulating Antioxidant Concentrations, Total Antioxidant Capacity, and Risk of All-Cause Mortality: A Systematic Review and Dose-Response Meta-Analysis of Prospective Observational Studies. *Adv Nutr*. 2018 Nov 1;9(6):701-716.
4. Drouin G, Godin JR, Pagé B. The genetics of vitamin C loss in vertebrates. *Curr Genomics*. 2011 Aug;12(5):371-8.
5. Xu K, et al. Association between serum vitamin B12 and risk of all-cause mortality in elderly adults: a prospective cohort study. *BMC Geriatr*. 2021 Sep 16;21(1):497.
6. Zhang Z, et al. Evaluation of Dietary Niacin and New-Onset Hypertension Among Chinese Adults. *JAMA Netw Open*. 2021 Jan 4;4(1):e2031669

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The Townsend e-Letter

Fibromyalgia

From the Latin:
"fibro" (fibrous tissues)
"my" (muscles), and
"algia" (pain)

Worldwide, it affects hundreds of millions of people. Nobody knows who it will hit, or when it will start, although studies show that it usually starts between the ages of 25-55, and generally affects women more than men. Fibromyalgia is said to affect from 2% to 6% of the population, depending on where you find your statistics, but that's still a large number – if we go with 4%, that adds up to roughly 320 million people.

- It was named in 1976, although it had been around as a collection of symptoms for many decades longer.
- Symptoms can come and go, and move around the body, affecting different areas at different times.
- Fibromyalgia does not damage joints or muscles.
- You are at higher risk of a fibromyalgia diagnosis, however, if you have a rheumatic disease, which affects the muscles, joints, and bones.
- Fibromyalgia, medically, is considered a 'benign' illness because it does not cause major disease, deformity, or direct death, but it is still serious.
- Fibromyalgia patients often turn to suicide, feeling like they have no quality of life, and will never improve.
- It may surprise you to learn that 'non-pharmaceutical' options for treating fibromyalgia have not really been tested, and proven in studies; but these treatments, such as acupuncture, chiropractic and massage therapy, have been found helpful by many patients and practitioners, in practice, in the real world.

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➤ *continued from page 72*

more regulations and unnecessary restrictions on dietary supplements. While it is important for the public to be informed about natural remedies that are truly dangerous, promulgating false claims about toxicity is not in the public interest. It is therefore incumbent on the Sacramento County coroner to reopen the McClintock case, in order to determine if there is more convincing evidence that white mulberry leaf contributed to her death. If the coroner is not able to provide such evidence, she should reclassify the cause of death as "unknown."

Going back to the nursery rhyme that I recited at the beginning of this editorial (which ends with "Pop! goes the weasel"), I am slightly more embarrassed to try to connect it to the McClintock case. But here it goes: One of the definitions of "weasel" is an untrustworthy person. And one of the definitions of "to pop" (or more accurately, to "pop off") is to talk thoughtlessly. It would be unfair to label the coroner in this case as untrustworthy because I do not know what led her to conclude that white mulberry leaf was a killer herb. However, unless additional information is provided, it would be reasonable to suggest that the coroner's *diagnosis* cannot be trusted, and I would feel justified in amusing myself by labeling her pronouncement (as the title of this editorial suggests) a mulberry bush-league diagnosis.

Alan R. Gaby, MD

References

1. https://www.cbsnews.com/news/experts-question-white-mulberry-death-of-lori-mcclintock-congressmans-wife/
2. Li Y, et al. Safety evaluation of mulberry leaf extract: Acute, subacute toxicity and genotoxicity studies. *Regul Toxicol Pharmacol*. 2018;95:220-226.

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CALENDAR

JANUARY 25-28: AMERICAN CHIROPRACTIC ASSOCIATION CONFERENCE in Washington, DC. CONTACT: https://www.acatoday.org/education-events/aca-engage-2023/

JANUARY 26-29: 18th ANNUAL NATURAL SUPPLEMENTS – An Evidence Based Update in San Diego, California. CONTACT: https://www.acatoday.org/education-events/aca-engage-2023/

JANUARY 28-29: INTERNATIONAL CONFERENCE ON TRADITIONAL MEDICINE AND HERBS in New York City, New York. CONTACT: https://waset.org/traditional-medicine-and-herbs-conference-in-january-2023-in-new-york

FEBRUARY 15-19: 16th ANNUAL INTERNATIONAL INSULIN POTENTIATION THERAPY CONFERENCE in Mexico. CONTACT: https://www.eventbrite.com/e/16th-international-ipt-conference-tickets-404946615227

FEBRUARY 23-25: INTEGRATIVE HEALTHCARE SYMPOSIUM in New York City, New York. CONTACT: https://www.ihsymposium.com/

FEBRUARY 27-MARCH 3: INTEGRATIVE MEDICINE AND HEALTH SYMPOSIUM in Chicago, Illinois. CONTACT: https://www.consortiummeeting.org/#home

MARCH 3-5: EXPLORING COMPLEX, CHRONIC ILLNESS THROUGH THE LENS OF TRUE HEALING online. CONTACT: https://forumforintegrativemedicine.org/

MARCH 24-26: JOINT AMERICAN HOMEOPATHY CONFERENCE in San Antonio, Texas. CONTACT: https://www.jahc.info/

APRIL 24-25: INTERNATIONAL CONFERENCE ON INTEGRATIVE MEDICINE AND NUTRITION in New York City, New York. CONTACT: https://waset.org/integrative-medicine-and-nutrition-conference-in-april-2023-in-new-york

APRIL 26-30: 34th CLINICAL APPLICATIONS FOR AGE MANAGEMENT MEDICAL CONFERENCE in Miami, Florida. CONTACT: https://agemed.org/cme-conferences/

APRIL 27-30: ACUPUNCTURE MERIDIAN ASSESSMENT FOR DOCTORS, DENTISTS, AND HEALTH PROFESSIONALS in St. Louis, Missouri. Detecting parasites, dental & fungal problems with Simon Yu, MD. CONTACT: https://preventionandhealing.com/training/

APRIL 28-30: CNDA ANNUAL CONFERENCE – Naturopathic Approaches to Complex Chronic Diseases in Santa Rosa, California. CONTACT: https://www.calnd.org/ce-events

MAY 4-7: NATIONAL ASSOCIATION OF NUTRITION PROFESSIONALS HEAL CON in Bellevue, Washington. CONTACT: https://healcon.org/

MAY 18-20: A4M 31st ANNUAL SPRING CONGRESS – INFLAMMATION: THE COMMON PATHWAY TO DISEASE in Orlando, Florida. CONTACT: https://www.a4m.com/the-fire-inside-2023.html

JUNE 1-3: INSTITUTE FOR FUNCTIONAL MEDICINE ANNUAL INTERNATIONAL CONGRESS in Orlando, Florida. CONTACT: https://discover.ifm.org/aic-2023

JUNE 2-4: SASKATCHEWAN ASSOCIATION OF NATUROPATHIC DOCTORS HEALING SKIES CONFERENCE in Saskatoon, Saskatchewan, Canada. CONTACT: http://www.sasknds.com/healing-skies-conference.html

JUNE 16-18: 5th INTERNATIONAL HOMEOPATHY RESEARCH in London, United Kingdom. CONTACT: https://www.hri-research.org/2022/07/hri-london-2023-save-the-date/

JULY 20-22: AMERICAN ASSOCIATION OF NATUROPATHIC PHYSICIANS CONVENTION in Phoenix, Arizona. CONTACT: https://naturopathic.org/

AUGUST 24-27: ACUPUNCTURE MERIDIAN ASSESSMENT FOR DOCTORS, DENTISTS, AND HEALTH PROFESSIONALS in St. Louis, Missouri. Detecting parasites, dental & fungal problems with Simon Yu, MD. CONTACT: https://preventionandhealing.com/training/

OCTOBER 19-22: 24th ANNUAL ILADS SCIENTIFIC CONFERENCE in Boston, Massachusetts. CONTACT: https://www.ilads.org/ilads-events/

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All Around the Mulberry Bush-League Diagnosis

I am only slightly embarrassed to admit that what I have written below reminded me of an old nursery rhyme, which went:

All around the mulberry bush
The monkey chased the weasel.
The monkey thought it was all in fun
Pop! goes the weasel.

In December 2021, Lori McClintock, wife of Tom McClintock, who is a member of the US House of Representatives from California, died suddenly and unexpectedly. Mrs. McClintock had apparently been healthy and had just joined a gym. In August 2022 the report issued by the Sacramento County coroner, Kimberly Gin, was released to the public. According to the report, the cause of death was dehydration due to gastroenteritis and due to the adverse effects of white mulberry leaf ingestion. It appears that the entire basis for concluding that white mulberry leaf was a cause of death was that a partially digested white mulberry leaf was found in Mrs. McClintock's stomach. Gin's conclusion is even more remarkable, considering that her herbal consultant wrote in a letter to the coroner's office that white mulberry leaf is nontoxic.[1]

This case was widely reported in the media, in part because McClintock was the wife of a public figure and also because, for some reason, it is considered newsworthy when a nutrient or herb gets blamed for causing someone's death. In contrast, the media rarely reports on the tens of thousands, if not hundreds of thousands of deaths that are caused each year by prescription drugs. McClintock's case also stirred interest because of the immediate pushback that came from many scientists, herbalists, and pathologists, who argued that there was no evidence to support the coroner's conclusion that white mulberry leaf was a cause of death.

The leaves of the white mulberry tree have been used for medicinal purposes in China for hundreds of years, and the whole leaf or extracts from the leaf are currently being used in many countries. White mulberry leaf is widely considered a nontoxic herb. In acute toxicity studies in rats, no adverse effects were seen after oral administration of 15 g of the leaf per kg of body weight. In subacute toxicity tests, no adverse effects were seen with a dose of 7.5 g per kg per day.[2]

According to Bill Gurley, from the University of Mississippi's National Center for Natural Products Research, "It would take literally bushel baskets of white mulberry leaves to cause some type of untoward effect. And even then, you don't see anything lethal." Dr. Gregory Davis, who is the director of the forensic division of the University of Alabama-Birmingham's Department of Pathology and chief coroner and medical examiner for Jefferson County, Alabama, stated that white mulberry leaf is considered nontoxic, and that he is not convinced it played a role in McClintock's death. And Dr. James Gill, chairman of the College of American Pathologists' Forensic Pathology Committee and chief medical examiner of Connecticut, stated that he would have concluded that McClintock's death was a natural death due to unknown causes.[1]

Mainstream medicine has a long history of uncritically accepting weak evidence regarding alleged toxicity of natural medicines. Such evidence is sometimes exploited to try to convince the public that natural medicine is dangerous and to provide ammunition for those who want to place

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