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Diego Saporta, MD

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

Clinical Study #2 (2007)

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

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

Clinical Study #3 (2014)

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

Clinical Study #4 (2016)

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

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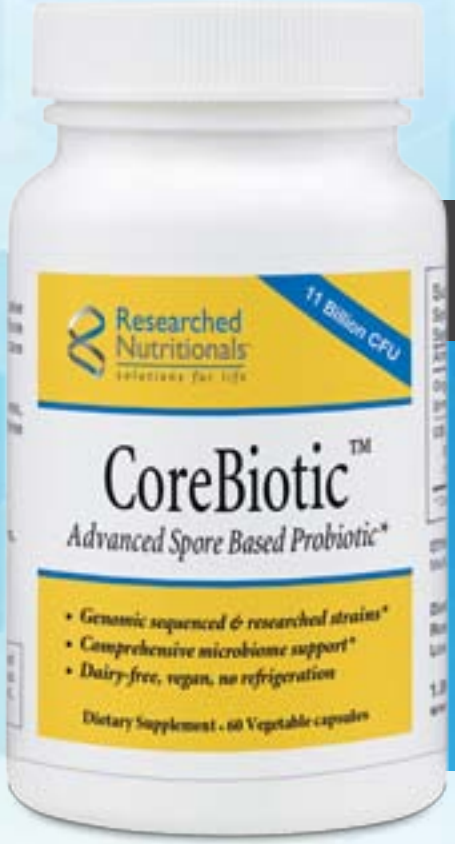

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From the Publisher

Britt Hermes – Naturopathic Turncoat

Britt Hermes, a graduate of Bastyr University, has joined the ranks of skeptics who publicly decry naturopathic and alternative medicine. Hermes makes the case that naturopathy is not scientific, based on her experiencing the four-year naturopathic educational program of Bastyr and later entering a "rigorous" master-of-science-degree program at a German university. In an interview, "From Zero to Hero" on YouTube, she claims that the naturopathic medicine lacks a scientific basis despite the fact that the educational program "emulates" a medical school curriculum. Hermes makes the distinction that evidence-based medicine is not science-based medicine, although her explanation of this did not make sense. Hermes apparently has become a dandy for the naysayers who want an insider to poke the eyes of naturopathic physicians.

Hermes at one point after completing her ND degree and undertaking a residency in pediatrics joined a naturopathic clinic that was offering cancer care. The clinic had been using an imported alternative cancer treatment, "Ukrain," which caused Hermes to freak out that an illegal drug was being used for which she could be held responsible. She then questioned not just the legitimacy of alternative cancer care but also the entire scientific basic of naturopathic medicine. Rereading a textbook of naturopathic medicine, she surmised that none of the information had a scientific basis. Her justification for disdaining it was the fact that the Bastyr curriculum included three courses in homeopathy which she dismissed as physically impossible, and, therefore, not

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From the Publisher

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science-based. Her wholesale criticism of naturopathy is based on naturopath dependence on asking patients to follow unproven diets and use supplements of dubious manufacturing standards that have not undergone rigorous clinical trials.

Much of the antagonism that Hermes holds against naturopathic medicine derives from the fact that she paid $180,000 for her ND education funded through loans that she must continue to pay off. She is now pursuing a PhD degree in genome research but keeps up her hobby of denigrating naturopathy through blogging. Like most skeptics, Hermes ignores the entire notion that healing is not a scientific process. Patients do not seek the care of a physician to undergo scientific medicine; they see a physician because they are ill and they wish to get better. Of course, some conventional physicians and most skeptics think that if scientific medicine is unable to cure the illness, oh well, that is all that medicine offers. It would be unconscionable for these individuals to offer a treatment that wasn't proven, even if it were likely to heal the patient.

Britt Hermes

Hermes' crusade against naturopathic medicine, like most skeptics' criticisms, is wrong-headed and a public disservice. If we could heal our illnesses purely through biology, chemistry, and physics, we wouldn't see the ravages of addiction and mental illness, cancer and neurologic disease, chronic fatigue and fibromyalgia. Genomic and metabolic research as well as new drug design offer tools for diagnosing and treating patients but are not the end-all for healing. Where conventional medicine has largely abandoned natural healing approaches to restoring health, naturopathic medicine embraces them. Hermes dismisses all healing approaches that naturopathic physicians offer as either common sense recommendations or placebo-based treatment. While common sense and placebo are important for the healing process, naturopathic medicine offers much that conventional medicine ignores.

Britt Hermes' "Zero to Hero" is a zero.

Vaccination's Dilemma: Unsafe at Any Dose

Much like the arguments employed by Hermes, concern about vaccine safety by individuals and physicians is considered sacrilege. The medical community is incensed that an increasing number of parents are opting to not vaccinate their children. Public health administrators consider that society as a whole is threatened when the entire "herd" of humans are not immunized; that individuals without vaccination benefit indirectly by their vaccinated neighbors preventing an outbreak. The science of vaccination is considered fully proven and the risk from receiving a vaccine is considered so minimal that there is no acceptable excuse for opting not to

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From the Publisher

➤ *continued from page 8*

vaccinate. Because ongoing campaigns seek to ensure that all children are vaccinated, there is no scientific discussion or opinion that is acceptable either in medical journals or the media to question the safety of vaccines. Medicine largely denies that any adverse effect or condition that develops post-vaccination is related to the vaccine. When an adverse effect and/or condition does appear to be directly the result of a vaccine, acknowledgement and compensation for it is only secured through litigation. The media and journals will not report incidents of vaccine injury.

In this issue of the *Townsend Letter,* Richard Gale and Gary Null examine what makes vaccines inherently unsafe and unproven. As NYU professor of law, Mary Holland, has explained, "the CDC can't have it both ways. Vaccines cannot be simultaneously safe and unsafe." It is bizarre that it is only through a 2011 Supreme Court legal decision in the Bruesewitz vs Wyeth case that vaccines have been acknowledged to be "unavoidably unsafe." As Gale and Null discuss, we know that the vaccine ingredients, mercury and aluminum, categorically cause toxicity. While the CDC claims that thimerosal, the primary mercury adjuvant in vaccines has been eliminated, aluminum continues to be included in most vaccines. What remains most concerning is that vaccine manufacturers do not disclose what the other ingredients are in each vaccine. Gale and Null note that these do not just include "polysorbate 80, formaldehyde, and other additives." Additionally, "vaccine technology makes it impossible to filter out all genetic contamination and DNA debris from vaccine preparations" permitting inclusion of "prions, viral oncogenes, and other viral variants." The worry is these foreign genetic contaminants can and would alter us epigenetically. Gale and Null worry that vaccine authorities ignore these concerns, blithely telling the public that vaccines are safe.

The recent examination of a new syndrome, "autoimmune/inflammatory syndrome induced by adjuvants" (ASIA) is characterized by various conditions thought to be induced by adjuvants in treatment. An adjuvant is defined as a biologic or chemical that induces an enhanced immune response. What has gone largely unrecognized is that increased immune response can serve as a trigger for developing an autoimmune disease. The fact that most vaccines contain adjuvants has led to examination by researchers of evidence for ASIA brought about by vaccines. While most studies have not demonstrated significant increase in relative risk (RR) of vaccines leading to autoimmune disease, a 2017 study in *Autoimmune Review* suggested that vaccines are related to increased risks for systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).[1]

Given the increasing incidence of autoimmune disease, parents and doctors have a right to question the safety of vaccines and should not be belittled for engaging in such discussion. The dictates of medical authorities and trolls on the internet to shut down dialogue has led to an underground community of anti-vaccination individuals who do not comply with public health demands. The *Townsend Letter* welcomes scientific discussion on the safety or non-safety of vaccines.

Managing Eye Disorders with Natural Therapies by Chris Meletis, ND

Patients are thrilled with their new vision after undergoing cataract surgery. But if they develop glaucoma, they are obligated to life-long treatment with one or more eye medications. Worse, if they develop macular degeneration, there is very little the ophthalmologist can offer to reverse deteriorated vision. Chris Meletis, ND and Kimberly Wilkes examine, in this issue, common eye conditions and offer natural remedies that support restoration of eye health and improvement in vision. Not surprisingly, macular degeneration is worsened by staring at the computer screen, TV, and cell phone. Meletis and Wilkes suggest that we filter the blue light that we are exposed to while using these devices. Lowering elevated homocysteine levels, eating a low-glycemic diet, and supplementation with lutein may prevent development of macular degeneration.

While surgery offers a miraculous restoration of vision for patients with cataracts, an eye lubricant with N-acetylcarnosine may prevent the early cataract from advancing. Eyedrops with the herb, Coleus forskohlii, may be very helpful for glaucoma. Forskolin in combination with B vitamins, taurine, and carnosine were remarkably helpful in reducing intraocular pressure. Meletis and Wilkes also discuss how eye disease often reflects body health in general. Supplements for eye health are helpful in preventing neurologic and cardiovascular disease. As practitioners, we should reconsider our patient's eye concerns and advise nutritional supplementation as an adjunct to drug treatments.

Allergy and Immunotherapy by Diego Saporta, MD – Our Cover Story

The TV ads tell us to use Claritin® to experience relief from our allergy symptoms. Anti-histamines and medications are effective in reducing symptoms of rhinitis and asthma. Of course, naturopathic physicians would prefer prescribing natural medicines, herbs and nutraceuticals, like stinging nettles and quercetin, magnesium and Vitamin C. However, neither the pharmaceutical medications nor the natural medicines are likely to eliminate inhalant allergies. And if the patient is not eliminating food allergens and sensitivities, it is very unlikely that the rhinitis symptoms will abate with medication. When allergy symptoms remain severe, the patient is referred to the allergist who will advise skin prick testing for allergy diagnosis and subcutaneous injection immunotherapy to desensitize the allergens.

Diego Saporta, MD and David Hurst, MD, PhD argue that skin prick testing fails to determine many important allergens that would be more easily diagnosed by intradermal testing. Treatment of the "total allergenic load" is more effective in reducing rhinitis symptoms than treatment of only the most important allergens. Furthermore, intradermal testing permits the practitioner to use a very, very low-dose allergen dose to minimize the risk of a severe reaction. A treatment mixture can be prepared with a myriad of different allergens at varying dilutions as determined by intradermal testing. The allergen mixture can be injected in the office; but more conveniently, it can be prepared for sublingual administration that can be done at home.

Saporta and Hurst's paper in this issue is part one of their report on management of the allergic patient. Part two will appear in the May issue. For those who would like to read more of Saporta's work, see his "Allergy and Immunotherapy" article in the April 2016 issue:

http://www.townsendletter.com/April2016/allergy0416.html.

Jonathan Collin, MD

1. Wang, B et al. Vaccinations and risk of systemic lupus erythematosus and rheumatoid arthritis: A systematic review and meta-analysis. *Autoimmune Rev*. 2017: July 16(7), 756-765.

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"Ahh-portunity" in Crossing the Dental-Medical Divide

Introduction

In December 1776, George Washington assessed the unmet needs of a beleaguered Continental Army and made a brilliant tactical decision, a new approach timelessly memorialized as Crossing the Delaware. Let's rally around that bold crossing. After this President's Day, imagine Port Townsend, Washington, as the launch point for crossing the Dental-Medical Divide. This column provides four Durham boats, ways health practitioners can work together to resupply their patients with health. I named this column "Ahh-portunity" since embarking involves the simple maneuver, "Open wide."

Trench Warfare

Treat periodontal disease to reduce systemic inflammation. At age 67, George Washington died suddenly from infection in the oral cavity. Whether it was strep throat, quinsy (peritonsillar abscess) or bacterial epiglottitis, the microbial battle began years earlier in the gingival crevices, before he became edentulous. A look at George Washington's ivory (not wooden!) dentures on my son's school field trip to Mount Vernon, Virginia, prompted me to explore the story.

My research was illuminated in my forthcoming textbook, by chapter author David Kennedy, DDS. He explains that gingival crevices are a battleground of dysbiosis, inflammation, and resulting obesity. Microbes in the mouth depend on the gingival crevices, where they secrete chemicals to make an environment that gives them the survival advantage. Oral flora differs from the intestinal microbiome in that it doesn't colonize until six months of age when the first teeth erupt and form gingival crevices.

Today we have antibiotics that would have cured George Washington. Why do most people have gingivitis? For one, antibiotics barely get into the crevices, making them poor performers in the mouth's trench warfare. Secondly, antibiotics potentially worsen gingivitis by giving offending fungi, protozoa, and parasites a survival advantage over bacteria. In the setting of a poor diet and sugar, infections are jumpstarted. Once infections are hunkered in their trenches, improving diet isn't sufficient to remedy gingivitis. Rooting out the offending organisms necessitates a dental and medical alliance.

Teeth (or at least one tooth) Are Sensory

Encourage patients to use their junk-food-free sense of taste to guide beverage selection. When our sense of taste is not overridden by added sugar, it can guide us to the minerals we need. Pedialyte© with its fortified zinc tastes good one time, and a few hours later it tastes awful once zinc needs are restored. A breakthrough non-caloric beverage called Good Idea© contains chromium to promote glucose control, and the chromium enhances the taste when body stores are inadequate. Similarly, water rich in iron tastes good to iron-deficient children, a longstanding observation called pica. Zinc, chromium and iron bind to and activate enzymes called metalloproteins, but how taste is messaged regarding total-body mineral status remains elusive.

Ancient Eastern medicine developed diagrams of postulated pathways of communication from the body's extremities to the teeth. Could these vague neural pathways be involved in communicating the body's mineral needs? I doubted so, until I met fellow explorer, Martin Nweeia, DMD, DDS. Dr. Nweeia became fascinated with the narwhal. This marine mammal's "tusk" was historically called the horn of the mythical unicorn. In actuality, it is neither tusk nor horn. It is a tooth!

Curiosity nudged Dr. Nweeia until he reasoned, "I'm a dentist and this is a tooth. Maybe I'm the one for the job." He crossed waters colder than Washington's Delaware for his comparative dentistry research. There, he discovered that the narwhal tooth has sensory functions. It can measure gradients such as temperature, electrolytes, and mineral concentrations. Living on land, we bring mineral water to us, but marine mammals go to the source of minerals, guided perhaps by their tooth. If

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humans also have sensory teeth, there is yet another reason to eat nutritiously – keeping a keen sense of mineral tastes.

Teledontics

Add a third dimension to metabolic pathways in order to assess patients' oxygen intake. *Washington Crossing the Delaware* is an 1851 commemorative painting famous for its three-dimensional as-if-I'm-there quality. Like painters, dentists work with a *palate* and skillfully make flat metabolic pathways jump out of the page, especially for supply of the most vital nutrient, oxygen!

My own dentist Kevin Fielding, DDS, explained the approach of the Pankey Institute. When he mentioned Mallampati score, the dental chair suddenly got uncomfortable. In medicine we are taught that Mallampati scores are important to assess for intubation, since it records clearance between the base of the tongue and the soft palate. Dentists appreciate the broader significance for assessing risk of upper airway obstruction and sleep apnea caused by a narrowed palate and oral cavity, even when tonsils and adenoids are not enlarged.

Teeth respond to the forces from neighboring muscles and soft tissue, a concept which forms the basis for orthodontics. My textbook chapter author Joseph Yousefian, DDS, explains another way teeth and oropharyngeal cavity communicate back and forth systemically, by responding to signals from the metabolic and epigenetic pathways, in "teledontic model." The orthodontic approach of utilization of headgear, functional appliances to improve the overbite, or extracting teeth to alleviate crowding can have a teledontic downside. They can prevent the pharyngorofacial complex forming the upper airway from attaining its full size, proper shape, and ability to take in oxygen.

Teledontics is very practical. For one, it adds physiologic perspective to the photos Weston Price, DDS, published in the 1930s, contrasting the faces of children who ate an ancestral diet with those who adopted a Western diet. The diet-dental connection is an important one.

Oxygen is an important and apparently overlooked nutrient. Now my screening for sleep apnea includes a brief "ahh-peration" for detection of clenching, small jaws, narrowed and crowded dental arches, and a high Mallampati score. Clenching is sometimes a physiologic adaptation to increase airway muscle tone and patency in order to obtain oxygen. Teledontic treatment to expand the upper airway can resolve clenching and its inherent side effects of damaging the temporomandibular joints, and developing small jaws and narrow upper airway. It also treats obstructive sleep apnea and its comorbidities. In sum, any clinical signs of oxygen deficiency, including frostbite,

pulmonary hypertension, peripheral vascular disease, obesity, excessive daytime sleepiness and fatigue are now my clinical ahh-portunities.

Opioid-Sparing Pain Control

Diversion Control is the name of the Drug Enforcement Agency's office that authorizes doctors and dentists to prescribe narcotic pain medications. Notice the word "*diversion*" which means routing something from its usual course. Now that our beleaguered healthcare system faces not mere diversion ditches but floodwaters, the government has enlisted its healthcare professionals to address the opioid crisis. Dentists and doctors alike are to grab oars and get patients to safe shores. But if not opioids, what should we use for pain management? Again, I turned to dentists.

I visited the large open-space dental operatory at University Padjadjaran in Bandung, Indonesia. Our group was amazed by the tranquility among the pediatric patients. "What type of anesthesia do you use?" I asked faculty member Helena Runkat, DDS. "Very little!" The approach to pain management was indeed opioid-sparing with acculturation that dentistry is a privilege and that the dentist is a friend, entertaining distraction, meditation, aromatherapy, hypnosis, and ways to relax the jaw. My favorite technique is an Eastern Medicine technique: Lips together, teeth apart, and tongue to the roof of the mouth.

I first learned about photobiomodulation to treat temporomandibular joint pain from Richard Godine, DVM, past-president of the North American Association for Laser Therapy. He uses 16 types of laser to manage pain in companion animals. Several are used to manage dental pain since the veterinarian profession hasn't erected a Dental-Medical Divide. Impressed with Dr. Godine's outcomes, I reached out to Dr. Michael Hamblin, PhD, principal investigator at the Wellman Center for Photomedicine at Massachusetts General Hospital, who wrote a chapter in my forthcoming medical book detailing the molecular mechanisms by which light of specific wavelengths treats pain.

Collaboration

Together our confident crossing of the Dental-Medical Divide will lead our beleaguered continental healthcare, resupply our patients with health, and bring us professional opportunity.

Lastly, I've credited several of the 35 authors in the forthcoming book *Metabolic Therapies in Orthopedics*, Second Edition. Orthopedic surgeon Kenneth Cintron, MD, and I are its editors, and it is being published in 2018 by CRC Press. Please join us as we seek to continue patient-centered cross-specialty collaborations. BetterOrthopedics.com is a dedicated book-preview website to keep the dialogues going. ◆

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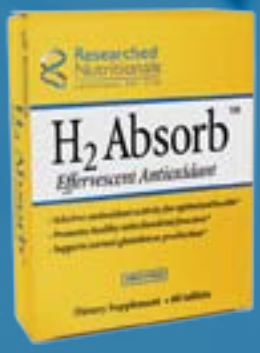

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Coffee: An Emerging Superfood

by Steven M. Helschien, DC

Introduction

In addition to being one of the most popular drinks in the world, recent studies have shown that coffee may also be the world's top superfood. Brewed coffee is one of the world's richest food sources of antioxidants, containing more antioxidants than blueberries, cranberries, and dark chocolate. In the past, it was thought that coffee was unhealthy, but many new studies are proving that coffee has a multitude of health benefits. The American Institute for Cancer Research reports coffee contains hundreds of potentially bioactive compounds, including those with anti-inflammatory, anti-oxidative, and anti-cancer effects.[1] There is new science to prove that coffee is beneficial for health, performance, and longevity. This is the first in a series of articles written to educate the healthcare community about the science behind the healthy benefits of coffee.

Coffee Antioxidants

There are numerous antioxidants in coffee that can reduce inflammation by neutralizing harmful free radicals, as well as decrease the risk of diseases related to inflammation, such as cancer and cardiovascular disease. Some of the powerful antioxidants include the following:

- Chlorogenic Acid – A compound that plays an integral role in antioxidant, anti-inflammatory, and antibacterial activities in the body.
- Quinine – An antioxidant known for its ability to fight diseases. Quinine has positive effects on blood sugar levels and boosts athletic performance.
- Plant Phenols – Similar to the antioxidants found in berries, plant phenols are responsible for protecting the body from cellular damage, certain types of cancer, and cardiovascular disease. They are also known for breaking down lipids and carbohydrates in the body, which helps with weight loss.
- Cafestol – An antioxidant found in decaffeinated coffee, cafestol acts as an anti-inflammatory substance in the brain, and also as a modulator for bile acid in the intestines.
- Melanoidins – These compounds have anti-bacterial as well as anti-inflammatory properties.

The Health Benefits of Coffee

Regular coffee consumption has been shown to have multiple health benefits, including the following:

*Enhancing brain function***.** Coffee helps the brain function more efficiently, including improving focus, concentration, cognitive function, and working memory. Research shows that coffee consumption increases attention span, the ability to reason logically, and dramatically improves reaction time. Focus is heightened when you combine an L-theanine supplement with coffee.[2]

Reducing the risk of Alzheimer's, Parkinson's, and dementia. Those who drink coffee on a daily basis have a 65% less chance of developing Alzheimer's or other dementia as they age. It's also reported that coffee drinkers are also up to 60% less likely to develop Parkinson's due to the caffeine content.[3] Drinking decaf coffee will not lower the risk of Parkinson's.

Increasing energy. Coffee can provide increased energy and potentially improve mental performance.[4]

Protecting the heart and cardiovascular system. An analysis of 36 studies, totaling more than one million study subjects, found those who regularly drank coffee were less likely to develop heart disease.[5] Many heart conditions are caused by inflammation, including atherosclerotic blockages. Antioxidants have been shown to reduce the incidence of death in these cases.

Fighting cancer. According to the American Institute for Cancer Research, the antioxidants, phytochemicals, phenols, and nutrients found in coffee all play an important role in helping reduce the risk of many cancers.[6] These cancers include the following:

- Breast cancer: Helps to reduce the risk or delay onset.
- Oral cancer: Reduces the chance of developing oral cancer as much as 39% according to the American Association for Cancer Research.[7]
- Brain cancer: Both men and women see a 40% reduction in certain forms of brain cancer.[6]
- Colorectal Cancer: Researchers at the University of Southern California Norris Comprehensive Cancer Center of Keck Medicine examined more than 5,100 men and women who were suffering from colorectal cancer plus 4,000 women and men who had never suffered from the disease (control group). Researchers reported that coffee consumption was associated with a lower risk of colorectal cancer, and the more

continued on page 20 ➤

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Coffee

➤ *continued from page 18*

coffee the subjects drank, the lower their risk became.[8]

- Liver Cancer: Studies suggest that people who drink at least one cup of coffee a day have a lower risk of liver cancer compared to those who only indulge occasionally.[9]
- Skin Cancer: Coffee drinkers are less likely to develop melanoma.[10]
- Prostate Cancer: Men who drink coffee regularly appear to lower their risk of prostate cancer, especially the most lethal form, according to researchers at Harvard School of Public Health.[11]
- Uterine Cancer: Researchers from Harvard Medical School found there is an association between drinking coffee and lower endometrial cancer risk. The scientists found that coffee is a protective factor for uterine cancer.[12]

Reducing the risk of type 2 diabetes. Studies have shown that coffee drinkers can reduce their risk of type 2 diabetes by as much as 50%. The research suggests that the main antioxidant in coffee, chlorogenic acid, inhibits the absorption of glucose, thereby stabilizing insulin levels.[13]

Protecting the liver. There are several diseases that affect the liver, including fatty liver disease, and hepatitis. These diseases can result in cirrhosis of the liver. Those who drink coffee every day can protect their liver from cirrhosis, reducing the risk of liver disease.[14]

Promoting weight loss. Coffee promotes weight loss by burning fat, suppressing appetite, and increasing metabolism. A 2015 study that included more than 93,000 subjects, found that those who drank coffee had a lower risk of obesity and type 2 diabetes.[15]

Improving sports performance. Coffee boosts fatty acids within the blood stream, allowing muscle tissue to absorb and burn fats for fuel, enabling the body to save its carb reserves for use later in the workout. The caffeine found in coffee improves muscular contractions and blood flow, allowing for smoother neuro-muscular transitions and increased force of contraction. Coffee also assists with muscle repair and muscle pain after exercise.[16]

Helping to fight depression and enhancing mood. Consumption of coffee increases brain chemicals that promote a sense of wellbeing, allowing one to perform in a state of emotional efficiency.[17]

Reducing the risk of retinal damage. Chlorogenic acid in coffee beans can reduce the risk of retinal damage caused by oxidative stress.[18]

Reducing the risk of multiple sclerosis. The anti-inflammatory properties of coffee are believed to prevent the inflammation that leads to the development of multiple sclerosis.[19]

Suppressing pain. The caffeine in coffee acts as a pain suppressant and anti-inflammatory.

Extending human life. If coffee can reduce the risk of so many diseases, it is logical to extrapolate these results to life extension. Many studies have shown the correlation of coffee drinking and longevity. According to studies from the *Annals of Internal Medicine*, coffee drinking lowers the risk of premature death for women by 26% and for men by 20%.[20]

A new study published in the *Annals of Internal Medicine,* which looked at total and cause-specific mortality, examined the association of consumption of total, caffeinated, and decaffeinated coffee with risk of subsequent total and cause-specific mortality among 74,890 women in the Nurses' Health Study (NHS), 93,054 women in the NHS 2, and 40,557 men in the Health Professionals Follow-up Study. The study concluded, "Higher consumption of total coffee, caffeinated coffee, and decaffeinated coffee was associated with lower risk of total mortality." The study leader hypothesized that the combination of lignans, magnesium, quinines, and other key phytochemicals in coffee worked together to reduce risks for disease and extend lifespan.[21]

Since the benefit of increased lifespan in this study was seen with both caffeinated and decaffeinated varieties, caffeine was not likely to be the source of the increased lifespan. Also noteworthy is that the reduced risk of death was lacking among study subjects who were smokers or former smokers.

Not All Coffees Are Created Equal

The best quality coffee yields the greatest potential health benefits. The way coffee is grown, handled, and roasted has a direct effect on its quality. Where it is grown (high altitudes are best), how it is farmed (whether organic or pesticides are used), and whether mold or mycotoxins (toxins produced by mold) are present, all affect the quality

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

of the coffee. Most conventional coffees test high for pesticides and herbicides, and low-quality coffees may contain up to 50% mold or mycotoxins.

Under-roasting or over-roasting can also have a dramatic effect on the health benefits of coffee. The optimal preparation is a medium roast that preserves high antioxidant compounds to maximize chlorogenic acids and keeps acrylamide levels low. Acrylamide is a toxin that can result from under- and over-roasting.

Conclusion

Many studies have been conducted showing the positive impact of coffee consumption on health. New studies are consistently being added to the already large body of scientific evidence indicating that drinking antioxidant-rich coffee daily has a wide range of diverse health benefits, including disease prevention and, in some cases, disease reversal. The majority of these findings have yet to reach the health community and general public; but as information becomes more available, health professionals are learning that moderate, daily, high-quality coffee consumption can have a variety of health benefits for their patients.

References

1. Giovannucci EL. Coffee doesn't need cancer warning. American Institute for Cancer Research [online]. Available at: http://blog.aicr.org/2018/02/05/coffee-doesnt-need-cancer-warning/. Accessed February 2, 2018.
2. Haskell CF. The effects of L-theanine, caffeine and their combination on cognition and mood. *Biol Psychol*. 2008;77(2):113-22.
3. Ross GW, et al. Association of coffee and caffeine intake with the risk of Parkinson disease. *JAMA*. 2000;283(20):2674-2679.
4. *Harvard Health Letter.* What is it about coffee? Harvard Health [online]. Available at: https://www.health.harvard.edu/staying-healthy/what-is-it-about-coffee. Accessed February 1, 2018.
5. Ding M, et al. Long-term coffee consumption and risk of cardiovascular disease: A systematic review and a dose-response meta-analysis of prospective cohort studies. *Circulation*. 2014;129:643-659.
6. Holick C, et al. Coffee, tea, caffeine intake, and risk of adult glioma in three prospective cohort studies. *Cancer Epidemiology, Biomarkers & Prevention*. January 2010;19(1):39-47.
7. Gapstur S, et al. Associations of coffee drinking and cancer mortality in the cancer prevention study-II [abstract]. *Cancer Epidemiology, Biomarkers & Prevention*. 2017 Oct;26(10):1477-1486.
8. Schmit SL, et al. Coffee consumption and the risk of colorectal cancer. *Cancer Epidemiology, Biomarkers & Prevention*. 2016;25(4):634-639.
9. Petrick JL, et al. Coffee consumption and risk of hepatocellular carcinoma and intrahepatic cholangiocarcinoma by sex: The Liver Cancer Pooling Project. *Cancer Epidemiology, Biomarkers & Prevention.* 2015;24(9):1398-1406.
10. Loftfield E, et al. Coffee drinking and cutaneous melanoma risk in the NIH-AARP Diet and Health Study. *JNCI*. 2015;107(2):dju421.
11. Wilson KM, et al. Coffee consumption and prostate cancer risk and progression in the health professionals follow-up study. *JNCI*. 2011;103(11):876-884.
12. Je Y, Giovannucci E. Coffee consumption and risk of endometrial cancer: Findings from a large up-to-date meta-analysis [abstract]. *International Journal of Cancer.* October 1, 2012;131(7):1700-10.
13. Boggs DA, et al. Coffee, tea, and alcohol intake in relation to risk of type 2 diabetes in African American women. *AJCN* 2010;92(4):960-6.
14. Klatsky A, et al. Coffee, cirrhosis, and transaminase enzymes [abstract]. *Arch Intern Med*. 2006;166(11):1190-1195.
15. Nordestgaard A, Thomsen M, Nordestgaard B. Coffee intake and risk of obesity, metabolic syndrome and type 2 diabetes: a Mendelian randomization study. *Int J Epidemiol*. 2015 Apr;44(2):551-65.
16. Maridakis V, et al. Caffeine attenuates delayed-onset muscle pain and force loss following eccentric exercise. *Journal of Pain*. 2007 March;8(3):237-243.
17. Lucas M, et al. Coffee, caffeine, and risk of depression among women. *Arch Intern Med.* 2011;171(17):1571-1578.
18. Jang H, et al. Chlorogenic acid and coffee prevent hypoxia-induced retinal degeneration. *Journal of Agricultural and Food Chemistry*. 2013 Dec 20;62(1):182-91.
19. Hedström AK, et al. High consumption of coffee is associated with decreased multiple sclerosis risk; results from two independent studies. *J Neurol Neurosurg Psychiatry*. Available at: http://jnnp.bmj.com/content/early/2016/02/03/jnnp-2015-312176. Accessed January 28, 2018.
20. Lopez-Garcia E, et al. The relationship of coffee consumption with mortality. *Annals of Internal Medicine*. 2008 Jun 17;148(12):904-14.
21. Ding M, et al. Association of coffee consumption with total and cause-specific mortality in three large prospective cohorts. *Circulation*. 2015;132:2305-2315.

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FCT® and Dermatology: Are Skin Disorders Just the Tip of the Iceberg for Underlying Chronic Diseases?

by Savely Yurkovsky, MD

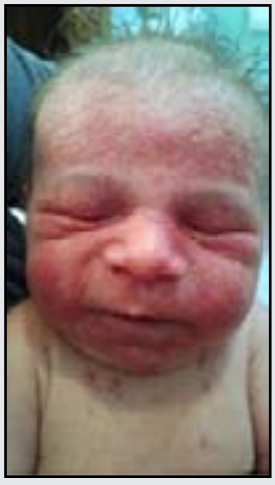
Even though classical homeopathy, for two-and-a-half centuries, and Traditional Chinese Medicine, for five thousand years, have been rendering consistent observations, tying skin conditions to the health of internal organs, the conventional dermatologists still remain in a dangerous, trigger-happy "cortisone mode," concerning the majority of skin problems. "Cortisone mode" and "penicillin mode," initially a seeming panacea for straight-forward acute conditions, have inspired the pharmaceutical industry into a madman transplant of these modes into the extremely complex nature of chronic diseases. The end result of this simplistic and ever-profitable experiment, involving hundreds of drugs and training doctors how to sell them, we all know. Today, the sickest and weakest populations are afflicted with a slew of incurable chronic diseases, starting from early childhood. In 'natural' medicine, "cortisone mode" for skin disorders is widely practiced through its different siblings, tea tree oil, colloidal silver and others.

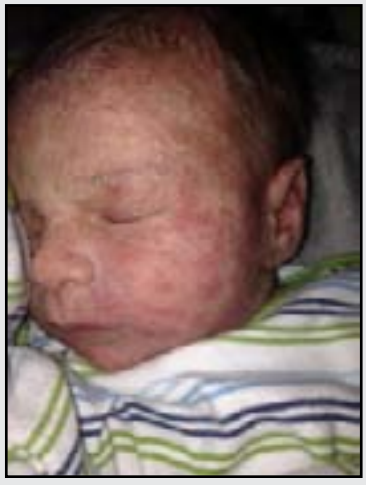
Little heed is paid to the fact that established basic knowledge of conventional medicine, itself, deems skin to be the largest detoxifying area in the body, due to its vast square footage and a number of sweat glands, pores, blood and lymphatic vessels, all of which are supposed to vent out disease-producing elements. Among these are, environmental pollutants, infectious agents, and toxic metabolic products, which the internal organs must reduce in order to stay alive. In addition, medical research has also established that connective tissue, a vast detoxifying and regulatory spider web of the body, connects skin with the DNA and other vital compartments of cells.

Speaking of DNA, while many folks and medical practitioners fall for the misleading sentencing of genetic lab testing deeming inevitability of sickness to genetic defects, such as MTHFR in clearing out toxins as mercury, chemicals, molds, and others, and concoct some interesting vitamin regimens to undo this, science of epigenetics has established that many gene malfunctions have nothing to do with the structural genetic defects. These malfunctions are just functional, due to environmental pollutants, infections, electromagnetic radiation, side effects of drugs and other morbid agents that reside in the cellular structures around genes and confuse their functions.

Case #1:

A bit of an interesting pre-history to these photos. The parents, and particularly the mother, were advised to have several more FCT sessions, in order to assure better health for their future child. While the father, who had extremely low sperm count, had it completely restored on FCT, while fertility 'specialists' were blank concerning its causes, the mom started FCT later, underwent a gradual removal of mercury fillings, and still remained toxic with mercury and rampant candidiasis. However, fertility assembly lines, as all fast-food medicine, do attract by their speedy gratification; and the mom opted for it, out of FCT and in rather bad spirits over my being a messenger with unpleasant-to-the-ear news. However, some time later, I was contacted by her, with the real unhappy message that, unfortunately, the begotten child, through fertility tubes, has been ailing, from, virtually, day one. By the time of his office visit, the boy, of just 14 days old, has already failed on the treatments of his pediatrician and a dermatologist, consisting of cortisone and antifungal and antibiotic ointments, prescribed for his entire body that was covered in a monstrous-looking rash. His general health was just as bad, as he was quite lethargic and anorexic. After bio-resonance testing established severe candida and staphylococcal infections, with the underlying mercury toxicity in his skin and lymphatics, as well as kidneys being clogged by mercury, the appropriate remedies went to work and completely cured him within days' time.





Obviously, whatever leads to preventing cells from venting these toxins out – steroids, antibiotics, ointments or pills, or a fancy laser removing bad looking skin lesions to make it look better – usually makes one's health worse. Certainly, 'rejuvenating' skin creams and cosmetics have not missed out on this profitable paradise. Not to lose out, for this author, on other potential friendships…the result of the blood baths by the "penicillin mode" treatments of chronic Lyme, Strep, PANDAS, acne, Staphylococcal and other chronic infections, many of which present skin lesions, speak for themselves too. There is an emergence of even more aggressive mutated original infections, a whole slew of vicious fungal infections and, overall, damaged health. Among the endless variety of cortisone and penicillin modes are any anti-agents: anti-inflammatory, anti-allergy, anti-histamines, decongestants, anti-acid, antibiotics, (anti-life), anti-cholesterol, and, in the skin family, anti-athlete's foot and anti-toenail fungus. Centuries of observations in classical homeopathy have tied suppressions of any bodily discharges and skin lesions to pathologies of nervous, cardiovascular, respiratory, gastrointestinal and other systems; and we all know today that all of these "anti" treatments have produced their own medical textbooks of chronic diseases, with just the officially known side effects. Just look at the dermatological champion Accutane's black box warning, concerning severe colitis, suicidal depression, and other serious chronic diseases. While all these effects are deemed to be due to purely chemical side effects of drugs, no attention is paid to another powerful mechanism: the blocking of physiological, detoxifying channels. Whether this is done through drugs or 'natural' substances is irrelevant.

Other equally important observations, back in those and more successful times of classical homeopathy, were that, as the chronic diseases were regressing under its treatment, the originally suppressed lesions would return in chronological sequence of those dermatologic 'therapeutic successes,' only to be, finally, prudently resolved. This is logical too, since, according to the well-established conventional medical knowledge, skin, as any organ, is also a part of the gigantic interconnected and interdependent network of all the internal organs and tissues. As a result, its lesions (eczema, diaper rash, acne, psoriasis, warts, athlete's foot, toenail fungus; unhealthy appearance: pale, excessively red, flabby, blotchy, oily, dry, prematurely wrinkled and aged; sensations: itching, burning, or tingling) virtually all represent morbid spillovers from sick internal organs. To mention a few, the gut that does not properly digest and absorb nutrients and spills its toxins into the bloodstream, infected and poisoned lymphatics and capillaries, kidneys and liver that are poisoned and unable to properly excrete and detoxify, malfunctioning thyroid, and other organs in charge of handling and supplying healthy fat, nutrients, and oxygen to the skin, all leave it no chance to look healthy. All in all, and quoting the great Paracelsus, "extinguishing smoke," on the skin's surface, while "leaving the fire inside," only destroys the internal organs more by clogging their venting ability. That is why one of the more zealous teachers of classical homeopathy has kindly suggested

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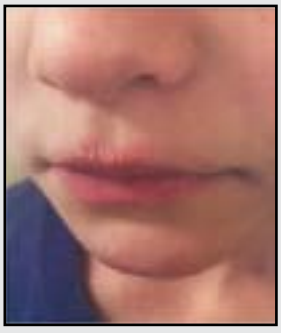
Case #2:
A case of ringworm in an eight-year-old girl disappeared promptly after a remedy prepared off its cause, ringworm, was administered.



Case #3:
In this 12-year-old boy's case, skin rash was primarily due to mercury toxicity and completely cleared on the treatment. As a side bonus, his severe, formally diagnosed PANDAS, with hundreds of tics a day, headaches, fatigue, depression, and fears for years, has been completely healed too. The penicillin mode from the hands of a PANDAS specialist-immunologist, in the way of intravenous and oral antibiotics, had failed prior. The causes for his PANDAS were determined by bio-resonance testing and consisted of mercury, lead, and thallium toxicities, strep, Lyme, worms and candida infections, plus our daily EMFs (electromagnetic fields), all affecting his brain. Just to note, shortly preceding the cure, his originally suppressed diaper rash had returned! And when it did, both the very patient, intelligent parents and I knew that this was the good news of the very last morbid layer in his disease returning to the surface and manifesting true restoration of health, preceding the cure.

Case #4:
As logical as it may sound that autoimmune diseases, such as vitiligo, in this case, are all due to bad genes, this speculation did not hold much weight in this case, either. Bio-resonance testing established mercury and other metal toxicity in this boy's immune organs and skin, with the appropriate remedies successfully addressing these. As a reminder, the science of epigenetics also lists environmental pollutants as triggering autoimmune processes in the absence of autoimmune genes.

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that all dermatologists be thrown down to the bottom of an ocean. However, for humanitarian reasons, I feel that the degree of the immersion should be moderated….

Managing Skin Problems in a Healthier Way

Short of intense symptoms, such as severe itch, burning or pain, which cause significant discomfort, all skin problems must take the back seat in favor of treatment of the exact causes of malfunctions of the internal organs and tissues first. Since there is no other test in all of medicine that can determine these causes and all the malfunctioning internal organs except for bio-resonance testing, that is exactly what I do and teach.

Certainly, it took years of trial and error to sort out and, then, seek only true causes of chronic diseases, instead of the endless red herrings that are present and lead to ineffective treatments. Following the specific data collected, homeopathic-energetic remedies go to work in order to stimulate the release of primary causes of malfunctions of both internal organs and skin (mercury, lead, and other environmental pollutants, infectious agents such as HPV, candidiasis, parasites, molds, bacteria) as well as promoting the repair of the sick organs and skin. Cases 1-4 in the sidebar are a few concrete examples, enacting one of those unofficial laws of nature, where a picture is worth a thousand words. Perhaps, besides conventional dermatological idiocies, these may also address even bigger ones, that "homeopathy is nothing other than over-diluted placebos," and the notorious "snake oil."

Case #5

But if there are still any doubters left out there about whether these children, including a 14-day-old infant, all fell for some black magic spell of a placebo effect, I was advised, years ago, to add D.V.M to my professional titles, by Mr. and Mrs. C, following the FCT cure of their beloved cat, Bumpy, from a severe skin disease.

The good citizen, Bumpy, was suffering from a mysterious condition diagnosed by his DVM as either allergic, neurologic, or psychiatric, or who knows, due to Bumpy pulling out his hair in bunches, making himself look like a moving chessboard. The consistent blasts, by his vet, of prednisone, did little to reduce Bumpy's efforts to sustain such an exotic hairstyle. But after bio-resonance testing indicating that Bumpy's real problem was heavy parasitic infestation of his gut, his enthusiasm as a chess fan has vanquished; and his skin returned to its original respectful look.

A Detailed Conclusion

With the premise that cats don't lie and FCT does work, this presentation concludes itself.

P.S. Our next FCT training event is on May 4th-5th, 2018. Come and learn, you won't regret it. ◆

Savely Yurkovsky, MD, a pediatrician, internist, and cardiologist, has evolved a novel medical model that interfaces important knowledge from biology, medicine, toxicology, and physics. Its primary focus is on the most important aspect of chronic diseases – its causes – along with the most effective diagnostic and therapeutic means to address these. This has transformed the often-imprecise medical interventions into a far more effective, exact, and predictable science. He has founded a teaching organization, "SYY Integrated Health Systems, Ltd.," which provides training in this medical system under the concept of FCT®, Field Control Therapy. This concept as medicine of the future was suggested by Professor Emeritus of Materials Science at Stanford University, William A Tiller, PhD. Dr. Yurkovsky has presented FCT at many professional symposia in both the US and Europe, including the annual Bio-terrorism 2005 conference: "Unified Science & Technology for Reducing Biological Threats & Countering Terrorism" with affiliation to the Homeland Security Office and Harvard Medical School, among others. Dr. Yurkovsky has been nominated for the prestigious Bravewell Leadership Award for "significant contributions to the field of medicine" and "compelling vision for the future of medicine," in 2005. He has authored numerous articles and the book, *The Power of Digital Medicine* that was endorsed by prominent scientists from MIT, Columbia, and Stanford Universities and contributed a chapter on homeopathy to the textbook of *Integrative Gastroenterology* edited by the Chief of Integrative Gastroenterology department at Johns Hopkins University medical school, Gerard Mullin, MD. Dr. Yurkovsky maintains a private practice with a cause-based approach to diseases, covering these from pediatrics to geriatrics, located in Chappaqua, New York.

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Osteopathic Techniques for Open-Angle Glaucoma

Rahul Pandey and Indian colleagues recently conducted a small pilot study to explore the effect of muscle energy technique and myofacial release on primary open-angle glaucoma (POAG). POAG, the most prevalent form of glaucoma, is a major cause of blindness worldwide. A build-up of intraocular pressure (IOP), due to poor aqueous humor outflow, is the primary risk factor for POAG. In patients with POAG, intraocular pressure slowly increases to 20-30 mm Hg, from a normal of 10.5 to 18 mm Hg, damaging the optic nerve and producing peripheral and, eventually, central vision loss. Conventional treatment includes lifelong medication use to control the pressure and surgery.

Pandey et al say that autonomic dysfunction, constriction of the superior and inferior orbital fissure that provides space for blood vessels and nerves, and muscular dysfunction are among the contributors to increased IOP. Contraction of muscles around the eye orbit that govern the eyelid (orbicularis-oculi muscle) is known to raise IOP. A normal blink increases IOP by about 10 mm Hg, and powerful contraction of the muscle can push IOP to 50 mm Hg or higher. Moreover, the authors say, "An imbalance in the ocular muscles tone can cause a movement dysfunction at the sphenoid bone, at the maxilla and at the ocular muscle nerves." In addition to muscle contraction, flexibility between the bones in the eye orbit and skull – particularly the phenopetrosal suture, the occipitomastoid suture, and the lacrimal bone – are key for functional drainage in the head and preventing IOP.

Pandey et al decided to test the effect of two osteopathic techniques to balance extra-ocular muscle tone and improve drainage of aqueous humor – muscle energy technique (MET) and myofascial release (MFR). Nine patients, ages 15 to 30 years old, completed three weeks of MET/MFR treatment, consisting of a 30-minute session, six days per week. Intraocular pressure, measured at baseline and at treatment's end, showed a mean reduction of 3.1±1.9 mm Hg ($p=0.002$). The authors note, "The reduction in each 1 mm Hg of IOP lowers the progression of the risk of disease by approximately 10%." In addition to reducing intraocular pressure, the treatment relieved eye irritation and headache reported by patients.

In addition to small sample size, lack of a control group, and lack of randomization, the authors viewed their failure to document physical activity level and other symptoms as study limitations. More research, of course, is needed to confirm the effects of this treatment and to identify responsive populations.

I found the osteopathic view of muscle tone and bone structure in relation to glaucoma fascinating. It made me wonder if there are exercises that can help prevent the constrictions that contribute to increased intraocular pressure. Do people who habitually contract the orbital eye muscles (when squinting or frowning) increase their risk of open-angle glaucoma? Do the same physiological processes contribute to other forms of glaucoma? Would breathing techniques that balance autonomic function affect IOP? It amazes me how simply looking at a problem from another viewpoint can generate all kinds of possibilities.

Pandey R, et al. Non-pharmacological therapies for primary open angle glaucoma: A quasi-experimental pilot study. *Saudi Journal of Ophthalmology.* 2017;31:95-98.

Nanoparticles and Allergy Response

Over the past decade, manufacturers have increased their use of nano-sized chemical compounds (diameter, 1-100 nm) in commercial products. The Project on Emerging Nanotechnologies (www.nanotechproject.org) lists over 110 nanoparticle-containing foods and cooking supplies. Nano-sized materials are also used as anti-setting agents in cosmetic foundations, for ultraviolet radiation protection in sunscreens, and as antimicrobial agents in clothing, bandages, detergents, and other products that contact the skin. Some researchers, like Kazuma Higashisaka and colleagues at Osaka University (Japan), are concerned that these particles may have unrecognized toxic effects.

Present regulations evaluate safety by the chemical structure: "...if the bulk or submicron-sized material is deemed safe, the nano-sized material is also assumed to be safe." However, nano-sized particles don't act the same as larger materials. Nanoparticles can display unique electrical properties, greater tensile strength, increased liquidity, and greater chemical reactivity. Nano-materials have greater surface area per unit weight than larger amounts of the same material and readily interact with proteins and other biological molecules. In fact, proteins in plasma will surround nanomaterials within 30 seconds of exposure, forming a "protein corona." "The protein corona is thought to confer nanoparticles with a biological identity that determines where they will localize and what biological effects they will have," say Higashisaka et al.

A 2017 review, by Yasuo Yoshioka et al, examined the possibility of allergic responses caused by skin exposure to nanomaterials in commercial products. The authors point out that about 4,000 chemicals are known to sensitize the skin and induce allergic contact dermatitis, but little is known about the effects of nanoparticles on the skin or its microbiota. "Because sensitization to chemicals is sometimes induced at relatively low levels of exposure to that substance via skin exposure," the authors write, "the sensitization potential of nanomaterials might be an important potential nanotoxicity." At this point, researchers are debating whether nanoparticles can penetrate the epidermis and the protective

barriers of healthy, intact skin. Nonetheless, some studies indicate that nanoparticles have immunomodulating effects – "even if they do not penetrate the skin." Nanoparticles may affect antigen-presenting cells in the epidermis (eg, Langerhans cells). They may also reach the dermis and other protective immune cells via hair follicles.

Of course, if the skin is damaged and the barrier is broken, nanoparticles are free to travel into the body. A 2015 study conducted by S. Smulders et al found that titanium levels increased in lymph node cells after topical application of titanium dioxide nanoparticles, along with a skin-sensitizing chemical, to a cut in a mouse ear. Also, mice exposed to the titanium compound – unlike those exposed to silver or silicon dioxide nanoparticles – displayed increased skin sensitization.

In addition to chemical compounds, nanoparticles may increase the body's response to pollen or other antigens on the skin. Because of their greater surface area, nanomaterials can bind more antigen per mass unit. Yoshioka et al write: "...we must not forget that exposure to nanomaterials via skin often occurs simultaneously with exposure to other chemical compounds and allergens, such as foods and pollen and that this interaction might modulate the antigenicity of these compounds. Many recent reports have shown that skin is an important site for the onset of allergy."

The Japanese researchers do not discount the useful and unique properties that nanomaterials bring to commercial products, but they seek ways to use nanomaterials with an eye on safety. "Given that the health effects of exposure to nanoparticles may become evident only after long-term exposure, there is an urgent need to begin collecting information on the health effects of real-world exposure to nanoparticles in humans" say Higashisaka and colleagues. The Osaka researchers are working on the use of biomarkers to predict nanotoxicity during early stages of a product's development – long before a company releases a new product to the market.

Higashisaka K, et al. Nano-Safety Research: Examining the Associations among the Biological Effects of Nanoparticles and Their Physicochemical Properties and Kinetics. *Biol. Pharm. Bull.* 2017;40(3):243-248.

Smulders S, et al. Nano-TiO2 modulates the dermal sensitization potential of dinitrochlorobenzene after topical exposure (abstract). *Br J Dermatol.* 2015;172(2):392-9.

Yoshioka Y et al. Allergic Responses Induced by the Immunomodulatory Effects of Nanomaterials upon Skin Exposure. *Frontiers in Innumology.* February 16, 2017.

Omega-3 Fatty Acids and Dry Eye

"Because omega-3 fatty acids decrease inflammation and promote health, they can provide significant benefits for patients with dry eye – a disease inflammatory in nature," says Julie Poteet, an optometrist and certified nutrition specialist, in a 2017 article. The higher the ratio of omega-6 to omega-3 tear lipids in people with dry eye, the lower the tear volume. While this association does not prove causation, studies have found that omega-3 supplementation decreases dry eye symptoms.

Because the Western diet is high in omega-6 fatty acids, Poteet recommends supplementation with omega-3s. Omega-3 fats, such as EPA and DHA, compete with omega-6 fats for incorporation into cell membranes. Cells use both types of polyunsaturated fats to make signaling molecules. Leukocytes use omega-6 fats, such as arachidonic acid, to make pro-inflammatory cellular mediators, including thromboxanes, prostaglandins, and leukotrienes. Omega-3 fats, however, are used to make resolvins and other molecules that serve as a brake to inflammation. The presence of more omega-3s in the cell membrane limits the amount of pro-inflammatory mediators that cells can make and provides other benefits. In studies of moderate to severe dry eye conditions, omega-3 fats have inhibited several markers of inflammation, including tear inflammatory cytokines and T-cell infiltration. Also, omega-3-derived resolvins have reversed corneal epithelial damage due to dry eye and increased tear flow in animal studies.

Although specific dosing guidelines for dry eye are not yet available, Poteet says that between 1,000 and 2,250 mg of EPA and DHA from fish oil, using a reliable brand, is a "reasonable starting dose." She says that omega-3 alpha-linolenic acid, found in flax oil, does not "reliably or efficiently" convert to EPA and DHA in humans. In addition, Poteet recommends supplementing with 500 mg of gamma-linolenic acid (GLA), an omega-6 fatty acid that can produce anti-inflammatory prostaglandin E1 and has benefits for people with dry eye. GLA is found in evening primrose oil, borage oil, hemp oil, and black currant seed oil.

Supplementation may have some adverse effects. Fish oil can produce unwanted gastrointestinal effects, including "fishy burps" and loose stool or diarrhea. Also, high doses of EPA and DHA increase bleeding risk, so Poteet urges practitioners to ask patients if they are taking drugs or other supplements (eg, garlic, ginkgo, saw palmetto) that have anticoagulant effects. Poteet also mentions the possibility that omega-3 supplementation may have immunosuppressive effects, according to a 2013 study (Fenton JI et al. Immunomodulation by dietary long chain omega 3 fatty acids and the potential for adverse health outcomes. *Prostaglandins, Leukotrienes, and Essential Fatty Acids.* 2013;89(6):279-90). She says, "While it's unclear if these findings translate to impaired immune function in vivo, exercise caution...in individuals with compromised immune systems."

Poteet J. From Alpha to Omega: How Fatty Acids Fight Dry Eye. *Review of Optometry.* May 15, 2017; 78-83.

***Bifidobacterium* Mixture for Seasonal Allergic Rhinitis**

A 2017 Italian study, led by Michele Miraglia Del Giudice, found that a combination of *Bifodobactrium longum BB536, B. infantis M-63, and B. breve M-16V* significantly improved allergic rhinitis symptoms and quality of life in children with pollen-induced rhinitis and intermittent asthma. The unidentified mixture, which is marketed as a medical device I class, has been tested for in vitro compatibility, stability over time, and optimal dosages. In previous research, *B. breve* improved symptoms of atopic dermatitis and restored enteric microbiota after antibiotic use; and *B longum* BB536 significantly reduced nasal symptoms and Th2-polarized immune response in patients with seasonal allergic rhinitis. *B infantis* M-64 is commonly used in probiotic formulas, according to the authors.

The prospective, double-blind, placebo-controlled, randomized study enrolled 40 children (18 males; mean age 9 ± 2.2 years) with a documented allergy to *Parietaria* pollen. One group received sachets that contained the *Bifidobacterium* mixture, and the control received sachets containing an inert excipient placebo. The participants were to dilute the contents of one packet in a little tepid water or milk and drink it in the morning. The treatment continued for eight weeks. The children were evaluated at baseline and at treatment's end. Lung function in the two groups was similar at baseline. At the end of eight weeks, allergic symptoms and quality of life measures significantly improved in children taking the probiotics, while symptoms and quality of life significantly declined in the placebo group.

"The rationale for using probiotics in allergic disorders is robust and is based on the concept that the balance between immunologic tolerance and inflammation is regulated by crosstalk between intestinal microbiota and innate and adaptive immune response," say the authors. Not all bifidobacteria produce the same results; effectiveness and anti-inflammatory actions vary among bacterial strains.

The small number of patients in this study is the main limitation. The authors would like to see this preliminary trial followed by a larger, multicenter study.

Del Gludice MM, et al. *Bifidobacterium* mixture (*B longum* BB536, *B infantis* M-63, *B breve* M-16V) treatment in children with seasonal allergic rhinitis and intermittent asthma. *Italian Journal of Pediatrics.* 2017:43:25.

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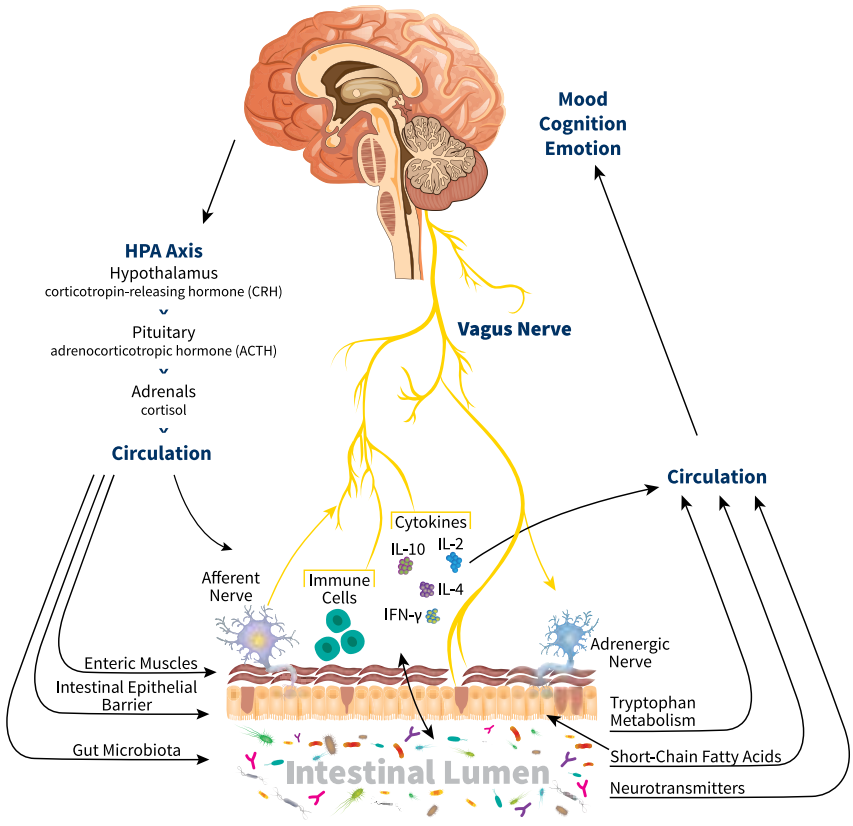
Introduction: the gut-brain axis

The gut-brain axis is a communication network that links the central nervous system (CNS) with the enteric nervous system. The anatomical network includes the brain and spinal cord, autonomic nervous system (ANS), hypothalamic-pituitary-adrenal (HPA) axis, and the innervation of the GI tract, or enteric nervous system.

Both neural and hormonal routes of communication allow the brain to influence intestinal activities, including activity of functional effector cells (i.e., immune cells, epithelial cells, enteric neurons, smooth muscle cells, interstitial cells, etc.). Gut microbiota also influence the CNS both directly and indirectly by supporting epithelial barrier function, modulating immune function, supporting healthy inflammation metabolism, and directly altering circulating neurotransmitter levels.



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Target gb-X research

Target gb-X strains were specifically selected for their pronounced synergistic influence on the gut-brain axis as demonstrated by both human and animal studies.

Clinical findings

Steenbergen and colleagues studied the effects of Ecologic BARRIER in a 2015 randomized, triple-blind, placebo-controlled trial (n=40, non-smoking healthy young adults, mean age 20 years) at a dose of 5 billion CFU per day. Consumption of Ecologic BARRIER significantly reduced overall cognitive reactivity to sad mood, in particular aggressive and ruminative thoughts, as assessed by the Leiden index (LEIDS-R).†[2] Heightened cognitive reactivity to normal, transient changes in sad mood is an established marker of vulnerability to more serious mood alterations in otherwise healthy individuals, and is therefore considered an important target for interventions.

Animal studies

In a 2016 laboratory study, 40 male rats were randomized to either a control or high-fat diet for 10 weeks.[3] After five weeks, the rats received either placebo or the Ecologic BARRIER probiotic blend. Forced swim test results demonstrated, independent of diet, Ecologic BARRIER significantly improved mood in the treatment group by 34%.†[3] In addition, the probiotic group had decreased levels of inflammatory cytokines and increased indole-3-propionic acid, a potential neuroprotective agent.

Conclusion

Target gb-X with Ecologic BARRIER is the first probiotic clinically shown to support healthy mood.† Supplied as convenient, single-serving, shelf stable sachets, Target gb-X is suitable for supporting the gut-brain axis through intestinal barrier integrity and healthy immune/inflammatory response.†

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[1] Van Hemert S, Ormel G. Influence of the multispecies probiotic Ecologic Barrier on parameters of intestinal barrier function. *Food and Nutrition Sciences*. 2014, 5, 1739-1745.
[2] Steenbergen L, et al. A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. *Brain Behav Immun*. 2015 Aug;48:258-64.
[3] Abildgaard A, et al. Probiotic treatment reduced depressive-like behavior in rats independently of diet. *Psychoneuroendocrinology*. 2017 May;79:40-48.

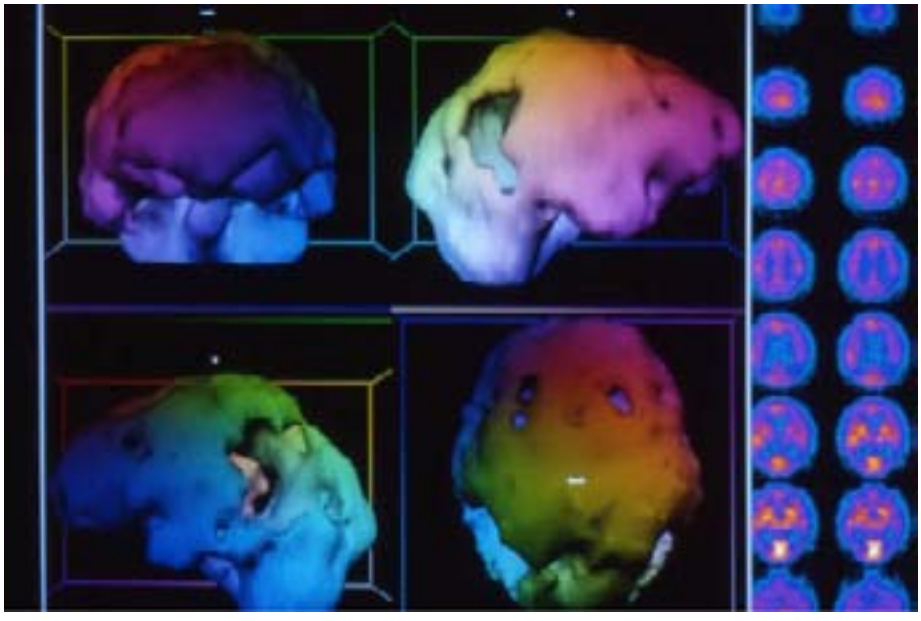
Oxygen and Pressure Epigenetics: Understanding Hyperbaric Oxygen Therapy After 355 Years as the Oldest Gene Therapy Known to Man

by Paul G. Harch, MD

Despite the "Decade of the Brain" from 1990-2000[1] and all the advances of modern medicine, treatment of the most common neurological diseases (traumatic brain injury, stroke, and dementia) has made minimal progress in the last 100 years. In 2017 Alzheimer's Dementia alone accounts for 5.4 million cases in the U.S.[2] Total costs for dementia are estimated to be $259 million this year.[2] The numbers will burgeon in the decades ahead as the Baby Boomers' demographic and the excesses of their earlier years pay a negative dividend.

Imagine for a moment a treatment that generically addresses/treats the underlying pathophysiology of traumatic brain injury (TBI), concussion, stroke, dementia, and many other neurological and systemic diseases, a treatment that not only restores reserve capacity,[3] but stimulates repair and regrowth of tissue, a treatment that gives people back their lives.

Figure 1. Pre-HBOT, SPECT brain blood flow imaging transverse slices and four-view three-dimensional surface reconstruction of 58-year-old male with Alzheimer's disease. Color scheme for slices is white, yellow, orange, purple, blue, and black from highest to lowest blood flow. Color scheme for three-dimensional surface reconstructions is aesthetic. Three-dimensional views are top row, left to right: frontal and right lateral; bottom row, left to right: left lateral and top of head. Defects or holes in the surface represent significant relative reductions in blood flow. Note primary defects in parietal/occipital/temporal watershed regions.



Figures 1-4 feature the SPECT brain blood flow scans of the first Alzheimer's patient treated with oxygen and pressure epigenetics. On a challenge from neurologists at the University of Oklahoma School of Medicine, a 58-year-old man was referred for treatment 5.5 years after the diagnosis of Alzheimer's disease. Having failed multiple treatments and shown minimal symptomatic improvement on rivastigmine, the scans document the typical posterior watershed areas of damage in Alzheimer's and the dramatic improvement in regional brain blood flow after one, 40, and 80 hyperbaric oxygen therapy (HBOT) treatments. Simultaneously, the patient's symptoms, quality of life, and Folstein Mini-Mental Status Exam score improved (from 9 to 13); and formal cognitive memory testing by university neuropsychologists recorded the first improvement in their multi-year testing sequence. The case was reported to the US Congress in 2002, along with 14 other cases of chronic traumatic brain injury, substance abuse, mental retardation, cerebral palsy, stroke, alcoholism, carbon monoxide poisoning, shaken baby, and autism.[4]

Since 2001 this author has treated nearly 1,000 cases of chronic neurological injury spread across 80 or more neurological diagnoses. This

includes eight additional Alzheimer's cases, and over 60 cases of cognitive decline/dementia of a variety of causes, including this author's mother, whose life and quality of life were prolonged six years with oxygen and pressure epigenetic therapy.[5] How can 80 intermittent exposures to increased pressure and hyperoxia improve neurocognitive function in a patient with a terminal neurodegenerative disease? How can 14 other cases with a variety of untreatable chronic neurological diseases respond similarly? The answer to this question begs the question of "What is hyperbaric oxygen therapy?" The answer given to this author by his medical school resident was the answer given to his entire generation of physicians: "… a type of oxygen therapy, it's performed in chambers, and it's worthless, unscientific, been thoroughly disproven, charlatanism, snake oil sales, and fraud."[5] Eight years later in a diving medicine practice, this author found this wasn't true. The correct answer has vexed the medical profession for 355 years, but will only be apparent after a quick review of the most misunderstood therapy in medicine.

Hyperbaric therapy originated in England in 1662[6] and, through the 1930s, consisted exclusively of compressed air. The breadth of its application was reflected in an 1877 review by Arntzenius which featured 300 references.[7] Oxygen was added to air decompression treatment tables by the US Navy in the late 1930s, and Dutch surgeons started using high pressure oxygen for surgeries, infections, and poisonings in the 1950s to spawn the modern era of hyperbaric oxygen therapy.[5] To organize the new field, establish credibility, and gain reimbursement, early hyperbaric physicians identified a list of purportedly scientifically proven diagnoses that were adopted by the FDA (Table 1).[8] The foundation of this list was an arbitrary unscientific definition of HBOT.[9] That definition has confused the scientific community, Food and Drug Administration, Medicare, medical insurance companies, and lay public, and stymied the understanding and advance of the therapy ever since:

> Hyperbaric oxygen (HBO_2) treatment, in which a patient breathes 100% oxygen intermittently while inside a treatment chamber at a pressure higher than sea level pressure (i.e., > 1 atmosphere absolute; atm abs), can be viewed as the new application of an old, established technology to help resolve certain recalcitrant, expensive, or otherwise hopeless medical problems…pressurization should be to 1.4 atm abs or higher.[9]

The definition omitted the 300+ year contribution of pressurized air[6] and lacked any evidence that 1.4 ATA (atmospheres absolute) of pressure was the minimum pressure requirement for HBOT, i.e., 1.399 ATA or less pressure was not. In addition, "certain recalcitrant, expensive, and otherwise hopeless" describes nearly all chronic and most acute medical conditions, yet the list of "certain" diagnoses is 48 in

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Figure 2. After one HBOT, SPECT brain blood flow imaging transverse slices and four-view three-dimensional surface reconstruction of 58-year-old male with Alzheimer's disease.

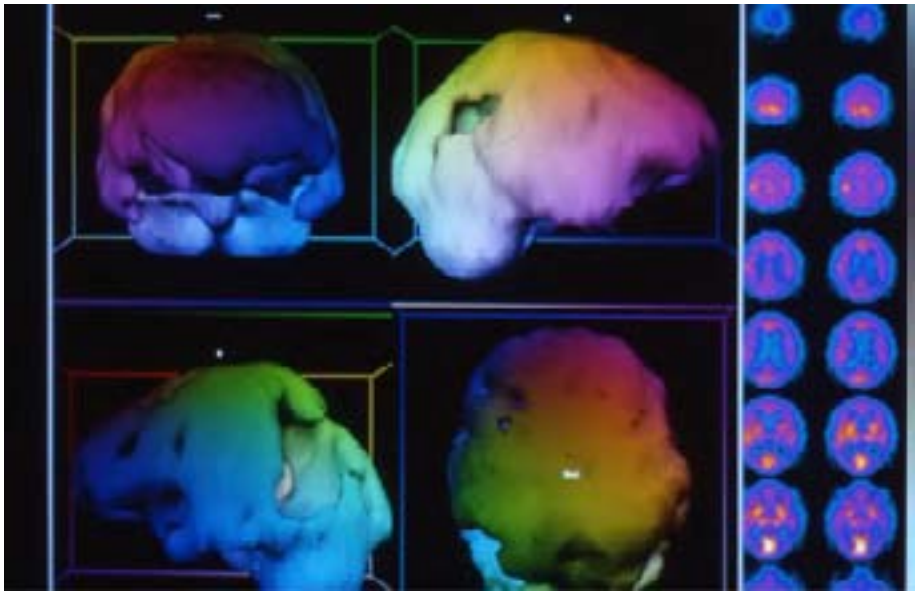
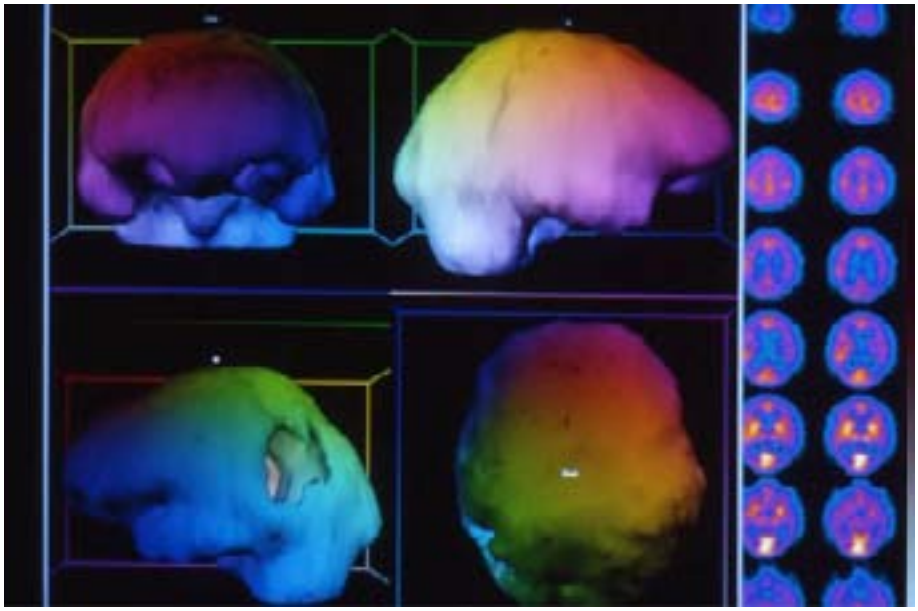


Figure 3. After 40 HBOTs, SPECT brain blood flow imaging transverse slices and four-view three-dimensional surface reconstruction of 58-year-old male with Alzheimer's disease.



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China, and more than 60 in Russia.[10] This definition of HBOT appears to change as it crosses national borders, yet scientific principles don't and shouldn't. Sir Isaac Newton's apple falls the same way in the US as it does in Russia, not the opposite direction.

Table 1. FDA-Cleared Indications for Hyperbaric Oxygen Therapy

1. Air or Gas Embolism
2. Carbon Monoxide Poisoning and Smoke Inhalation, Carbon Monoxide Complicated by Cyanide Poisoning
3. Clostridial Myonecrosis (Gas Gangrene)
4. Crush Injury, Compartment Syndrome, and Other Acute Traumatic Ischemias
5. Decompression Sickness
6. Enhancement of Healing in Selected Problem Wounds
7. Exceptional Blood Loss (Anemia)
8. Intracranial Abscess
9. Necrotizing Soft Tissue Infections (Subcutaneous Tissue, Muscle, Fascia)
10. Osteomyelitis (Refractory)
11. Radiation Tissue Damage (Osteoradionecrosis)
12. Skin Grafts and Flaps (Compromised)
13. Thermal Burns

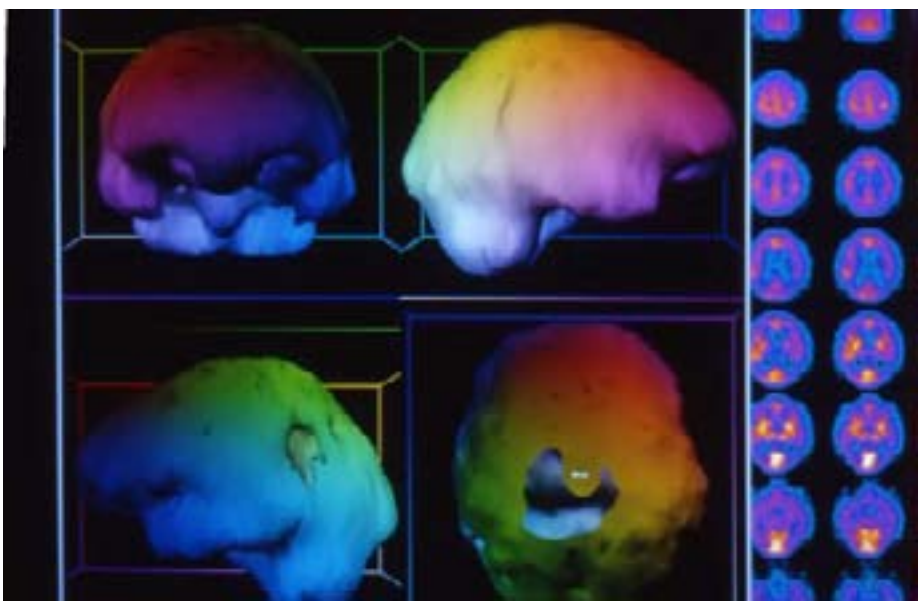
The confusion over this mis-definition and Table 1 is that no physician has been able to connect the dots …until now. In 1999, HBOT was redefined scientifically as "…a medical treatment that uses high pressure oxygen as a drug by fully enclosing a person or animal in a pressure vessel and then adjusting the dose of the drug to treat pathophysiologic processes of the diseases."[11] HBOT had been shown in multiple animal species to have profound effects on acute and chronic disease pathophysiology.[9] It was felt that the intermittent exposure to increased pressure of oxygen acted to ameliorate acute disease pathophysiology and the repetitive application in chronic conditions to have trophic effects, i.e., grow new tissue.

This definition, however, was inadequate. It still did not explain the 300+ years of pressurized air,[6,7] the Russian experience with very low doses of hyperbaric therapy,[12] nor the confusing HBOT cerebral palsy study of 2001 where 1.3 atmospheres absolute of air (9.9 feet of seawater pressure, the depth of a swimming pool) improved children with cerebral palsy (CP).[13] All of these examples feature elevated pressures with minimal elevations in oxygen. The FDA inadvertently clarified the matter in their 2012 response to this author's Investigational New Drug Exemption (IND) application: "… we consider your intervention to be a combination therapy, the constituents of which are hyperbaric treatment and hyperoxic treatment. Each of these constituents has the potential to contribute independently to the overall therapeutic effect…" This suggested for the first time in the modern history of hyperbaric medicine the possible contribution of hydrostatic pressure to the clinical effects of HBOT.

A quick investigation revealed 70 years of published research demonstrating the responsiveness of living organisms to the slightest elevations in atmospheric pressure that began within as little as one minute of pressurization.[14] Somehow, this treasure trove of literature escaped the purview of the entire modern clinical hyperbaric medicine field. Pressures from 1.0015 to 1.26 ATA delivered to human and animal cells for 15 minutes or longer have caused the elaboration of a wide variety of bioactive proteins and stimulated cell proliferation.[15] In other words, hydrostatic pressure effects were an essential component of hyperbaric therapy, and they are elicited by very small increases in pressure.

Acknowledging this wide range of hyperbaric and hyperoxic bioactivity, the controversial applications to CP,[13] autism,[16] mild traumatic brain injury/persistent post-concussion syndrome (PPCS),[17] PPCS with post-traumatic stress disorder,[18] and other diagnoses become understandable as multi-dosing hyperbaric therapy studies have demonstrated effectiveness of some doses of hyperbaric therapy, ineffectiveness of others, and toxicity of others.[15,19] In particular, all of these studies have demonstrated the benefit of hyperbaric therapy in the low pressure/low hyperoxic range. This low-dosing range was reinforced by

Figure 4. After 80 HBOTs, SPECT brain blood flow imaging transverse slices and four-view three-dimensional surface reconstruction of 58-year-old male with Alzheimer's disease. Clear area in top-of-head view in right lower quadrant is artifact due to edge cutoff of camera field of view.



the recent publication of a two-year-old drowned girl who experienced dramatic neurological recovery and global regrowth of brain tissue after three months of normobaric oxygen and hyperbaric oxygen therapy.[20]

The question remained, however, how do repetitive administrations of intermittent increases in pressure and oxygen reverse pathophysiology and stimulate tissue growth? Tissue growth requires replication of DNA. In 1997, Siddiqui et al argued that the oxygen component of HBOT was a DNA signaling agent.[21] Multiple publications confirmed this concept in the next 11 years,[22-30] culminating in the demonstration that a single HBOT at the pressure used for diabetic foot wounds and radiation wounds up- or down-regulated the expression of 8,101[31] of the known 19-20,000[32] protein-coding genes in the human genome. The largest clusters of upregulated genes were the anti-inflammatory genes and those that coded for growth and repair hormone, and the largest clusters of downregulated genes were the pro-inflammatory genes and apoptotic genes. Further work showed the differential gene effects of pressure and oxygen,[33] whereby different and similar clusters of neuronal genes are affected by different pressures and different amounts of hyperoxia.[34] In essence, during hyperbaric therapy physicians are playing a symphony with patients' gene expression, the music of which is determined by the various pressures and amounts of hyperoxia to which the patient is exposed.

Summing up the current understanding of this 355-year-old therapy, HBOT appears to be an epigenetic therapy in the broad sense of the original definition of Waddington: "…the branch of biology which studies all molecular pathways modulating the expression of a genotype into a particular phenotype."[35] The combination of hyperoxia and increased pressure are acting at the epigenetic level to differentially and temporarily alter gene expression and suppression of over 40% of all of our protein-coding genes. The net effects are permanent tropism and tissue repair and temporary and permanent inhibition of inflammation and apoptosis.[9,31,36-8] By mechanisms involving oxygen-sensitive gated membrane ion channels[39] and pressure-induced strain on cell and mitochondrial membranes,[14,40] hyperbaric pressure and hyperoxia are two organically, and naturally, manipulating, ubiquitous natural-occurring agents that effect salutary changes in disease at the epigenetic level. Essentially, this is the oldest, most pervasive and panoramic gene therapy finally known to mankind.

Viewed as a gene therapy, this discussion comes full circle to the constrained list of clinical applications in the United States and begs the question of what other diagnoses may be responsive to oxygen and pressure epigenetics. Controlled trials exist for many diagnoses, including idiopathic sudden sensorineural hearing loss,[41] acute severe traumatic brain injury,[42] acute myocardial ischemia,[43] CP,[13] autism,[16] prevention of post-coronary artery bypass cognitive decline,[44] multiple sclerosis,[45] avascular necrosis,[46] fibromyalgia,[47] complex regional pain syndrome,[48] and vascular dementia.[49] This last study is most exciting because it confirms in a controlled trial the author's previously mentioned 31-year experience treating diagnoses of cognitive decline, premature aging, and dementia. The possibilities and impact of treatment of these diagnoses of aging are inestimable. Considered in combination with all the other potentially treatable diagnoses based on the mechanism of oxygen and pressure epigenetics, the 132 conditions listed in the 1987 critique of HBOT, "A Therapy in Search of a Disease,"[50] may in fact be a limited list.

In conclusion, hyperbaric therapy is the use of increased pressure and hyperoxia to treat diseases through temporary gene expression and suppression. After 355 years, we finally understand hyperbaric therapy as the most long-standing, panoramic, and effective gene therapy known to man; yet the therapy is in its infancy of dose exploration and disease application.

References

1. Proclamation 6158-Decade of the Brain, 1990-1999, July 17, 1990. http://www.presidency.ucsb.edu/ws/index.php?pid=1869
2. Dementia and Alzheimer's Disease statistics. https://www.cdc.gov/chronicdisease/resources/publications/aag/pdf/2016/alzheimers-agg.pdf.
3. Satz P. Brain Reserve Capacity on Symptom Onset After Brain Injury: A Formulation and Review of Evidence for Threshold Theory. *Neuropsychology*.1993;7(3):273-295.
4. Harch PG. Testimony: "The Impact of Hyperbaric Medicine on Government Health Care, Disability and Education Expenditures." Hearings, before the Labor, Health and Human Services and Education Subcommittee of the Committee on Appropriations, United States House of Representatives, One Hundred Seventh Congress, Second Session, Ralph Regula, Ohio, Chairman. Part 7A, Testimony of Members of Congress and Other Interested Individuals and Organizations. US Government Printing Office, Washington, May 2, 2002. Pps. 589-619.
5. Harch PG, McCullough VM. *The Oxygen Revolution*: Third Edition. Hatherleigh Press, New York, NY, 2016. Pps. 216-218, xxii, and 18-26.
6. Trimble VH. *The Uncertain Miracle, Hyperbaric Oxygenation*. Doubleday and Company, Inc., Garden City, NY, 1974.
7. Jain KK. History of Hyperbaric Medicine, Chapter 1. In: *Textbook of Hyperbaric Medicine*, ed. K.K. Jain. Hogrefe and Huber Publishers, Toronto, Canada, 1996. Pps. 2-9.

8. https://www.accessdata.fda.gov/cdrh_docs/pdf5/k052713.pdf.
9. Hampson NB, chairman and editor. Hyperbaric oxygen therapy: 1999 committee report. Kensington, MD: Undersea and Hyperbaric Medical Society, 1999.
10. Jain KK. Worldwide Overview of Hyperbaric Medicine, Chapter 49. In: *Textbook of Hyperbaric Medicine*, 6th Edition, ed. Kewel K. Jain. Springer, Cham, Switzerland, 2017. Pps. 609-614.
11. Harch PG, Neubauer RA. Hyperbaric Oxygen Therapy in Global Cerebral Ischemia/Anoxia and Coma, Chapter 18. In: *Textbook of Hyperbaric Medicine*, 3rd Revised Edition, ed. K.K. Jain. Hogrefe and Huber Publishers, Gottingen, Germany, 1999. Pps. 319-349.
12. Kazantseva NV. Mechanisms of Curative Effect of Minimized Hyperbaric Treatment in Cerebral Ischemia, in: The Proceedings of the 2nd International Symposium on Hyperbaric Oxygenation for Cerebral Palsy and the Brain-Injured Child. JT Joiner (ed). Best Publishing Co: Flagstaff, 2002. Pps. 199-212.
13. Collet JP, et al, HBO-CP Research Group. Hyperbaric oxygen for children with cerebral palsy: a randomized multicentre trial. Lancet. 2001;357, 582-86.
14. Macdonald AG, Fraser PJ. The transduction of very small hydrostatic pressures. *Comp Biochem Physiol A Mol Integr Physiol*. 1999;122 (1), 13-36.
15. Harch PG. Hyperbaric Oxygen Therapy for Post-Concussion Syndrome: Contradictory Conclusions from a Study Mischaracterized as Sham-Controlled. *J. Neurotrauma*. 2018;30:1995-1999.
16. Rossignol DA, et al. Hyperbaric treatment for children with autism: a multicenter, randomized, double-blind, controlled trial. *BMC Pediatr*. 2009;9:21.
17. Wolf G, et al. The effect of hyperbaric oxygen on symptoms following mild traumatic brain injury. *J Neurotrauma*. 2012;29(17), 2606-12.
18. Harch PG, et al. A phase I study of low-pressure hyperbaric oxygen therapy for blast-induced post-concussion syndrome and post-traumatic stress disorder. *J Neurotrauma*. 2012;29, 168-185.
19. Harch PG. Hyperbaric oxygen in chronic traumatic brain injury: oxygen, pressure, and gene therapy. *Med Gas Res*. 2015;5:9. doi: 10.1186/s13618-015-0030-6.
20. Harch PG, Fogarty EF. Subacute normobaric oxygen and hyperbaric oxygen therapy in drowning, reversal of brain volume loss: a case report. *Med Gas Res*. 2017;7(2):144-149.
21. Siddiqui A, Davidson JD, Mustoe TA. Ischemic tissue oxygen capacitance after hyperbaric oxygen therapy: a new physiologic concept. *Plast. Reconstr. Surg*. 1997;99:148–155.
22. Gutsaeva DR, et al. Oxygen-induced mitochondrial biogenesis in the rat hippocampus. *Neuroscience*. 2006;137(2):493-504.
23. Ishii Y, et al. Effects of hyperbaric oxygen on procollagen messenger RNA levels and collagen synthesis in the healing of rat tendon laceration. *Tissue Eng*. 1999;5(3):279-86.
24. Freiberger J, et al. Superoxide dismutase responds to hyperoxia in rat hippocampus. *Undersea Hyperb Med*. 2004;31(2):227-32.
25. Kim CH, et al. Hyperbaric oxygenation pretreatment induces catalase and reduces infarct size in ischemic rat myocardium. *Pflugers Arch*. 2001;442(4):519-25.
26. Yin W, et al. Down regulation of COX-2 is involved in hyperbaric oxygen treatment in a rat transient focal cerebral ischemia model. *Brain Res*. 2002;926(1-2):165-71.
27. Lin S, et al. Hyperbaric oxygen selectively induces angiopoietin-2 in human umbilical vein endothelial cells. *Biochem Biophys Res Commun*. 2002:296(3):710-5.
28. Shyu WC, et al. Hyperbaric oxygen enhances the expression of prion protein and heat shock protein 70 in a mouse neuroblastoma cell line. *Cell Mol Neurobiol*. 2004;24(2):257-68.
29. Li Y, et al. Multiple effects of hyperbaric oxygen on the expression of HIF-1 alpha and apoptotic genes in a global ischemia-hypotension rat model. *Exp Neurol*. 2005;191(1):198-210.
30. Hirata T, et al. The temporal profile of genomic responses and protein synthesis in ischemic tolerance of the rat brain induced by repeated hyperbaric oxygen. *Brain Res*. 2007;1130(1):214-22.
31. Godman CA, et al. Hyperbaric oxygen induces a cytoprotective and angiogenic response in human microvascular endothelial cells. *Cell Stress and Chaperones.* December 2009.
32. Ezkurdia L, et al. Multiple evidence strands suggest that there may be as few as 19,000 human protein-coding genes. *Human Molecular Genetics*. 2014;23(22):5866-5878.
33. Oh S, et al. Comparison of the effects of 40% oxygen and two atmospheric absolute air pressure conditions on stress-induced premature senescence of normal human diploid fibroblasts. *Cell Stress and Chaperones*. 2008;13(4):447-458.
34. Chen Y, et al. Microarray Analysis of Gene Expression in Rat Cortical Neurons Exposed to Hyperbaric Air and Oxygen. *Neurochem Res*. 2009;34:1047-56.
35. Dupont C, Amant DR, Brenner CA. Epigenetics: Definition, Mechanisms, and Clinical Perspective. *Semin Reprod Med*. 2009;27(5):351-357.
36. Rossignol DA. Hyperbaric oxygen therapy might improve certain pathophysiological findings in autism. *Med Hypotheses*. 2007;68:1208-27.
37. Harch PG. HBO therapy in global cerebral ischemia/anoxia and coma, Chapter 20. In *Textbook of Hyperbaric Medicine* 6th ed., K.K. Jain, ed. Springer, Cham, Switzerland. 2017, pp. 269-319.
38. Niu CC, et al. Hyperbaric oxygen treatment suppresses MAPK signaling and mitochondrial apoptotic pathway in degenerated human intervertebral disc cells. *J Orthop Res.* 2013;31(2):204-209.
39. Suematsu M, Suganuma K, Kashiwagi S. Mechanistic probing of gaseous signal transduction in microcirculation. *Antioxid Redox Signal*. 2003;5(4):485-92.
40. Apodaca G. Modulation of membrane traffic by mechanical stimuli. *Am J Physiol Renal Physiol*. 2002;282:F179-190.
41. Murphy-Lavoie H, et al. Hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss. *Undersea Hyperb Med*. 2012;39(3):777-92.
42. Rockswold SB, et al. A prospective, randomized Phase II clinical trial to evaluate the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intracranial pressure, oxygen toxicity, and clinical outcome in severe traumatic brain injury. *J Neurosurg*. 2013;118(6):1317-28.
43. Shandling AH, et al. Hyperbaric oxygen and thrombolysis in myocardial infarction: the "hot MI" pilot study. *Am Heart J*. 1997;134:544-50.
44. Alex J, et al. Pretreatment with hyperbaric oxygen and its effect on neuropsychometric dysfunction and systemic inflammatory response after cardiopulmonary bypass: a prospective randomized doubleblind trial. *J Thor and Cardiovasc Surg*. 2005;130(6):1623-30.
45. Fischer BH, Marks M, Reich T. Hyperbaric oxygen treatment of multiple sclerosis. A randomized placebo-controlled double-blind study. *N Engl J Med*. 1983;308:181-6.
46. Camporesi EM ,et al. Hyperbaric oxygen therapy in femoral head necrosis. *J Arthroplasty*. 2010;25(6 Suppl):118-23.
47. Yildiz S, et al. A new treatment modality for fibromyalgia syndrome: hyperbaric oxygen therapy. *J Int Med Res*. 2004;32(3):263-7.
48. Kiralp MZ, et al. Effectiveness of hyperbaric oxygen therapy in the treatment of complex regional pain syndrome. *J Int Med Res*. 2004;32(3):258-62.
49. Wang SP, et al. Hyperbaric oxygen combined with donepezil in the treatment of vascular dementia. *Chinese Journal of Physical Med & Rehab*. 2009;31(7):478-80.
50. Gabb G, Robin ED. Hyperbaric oxygen, a therapy in search of diseases. *Chest.* 1987; 92(6):1074-82.

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Beginning with brain-injured divers and boxers in 1989, he applied his protocol to the first HBOT-treated cerebral palsy and autistic children in this country and multiple other cerebral disorders, including most recently a subacute drowned child (*Medical Gas Research*. March 2017). He has successfully treated US servicemen with TBI and PTSD, publishing the latest findings in *Medical Gas Research,* October 2017. His studies in brain-injured veterans have continued with a randomized trial funded by a Louisiana-generated congressional appropriation. The early case experience was confirmed in an animal model of chronic traumatic brain injury that was published in *Brain Research* in October 2007.

He has presented his research seven times to the US Congress and been nominated for the NIH Director's Pioneer Award. In April 2007, he published *The Oxygen Revolution* with co-author Virginia McCullough. This groundbreaking book, which has been released in its third updated edition in May 2016, explains HBOT as an epigenetic gene therapy and its projected revolutionary effects on medicine and neurology.

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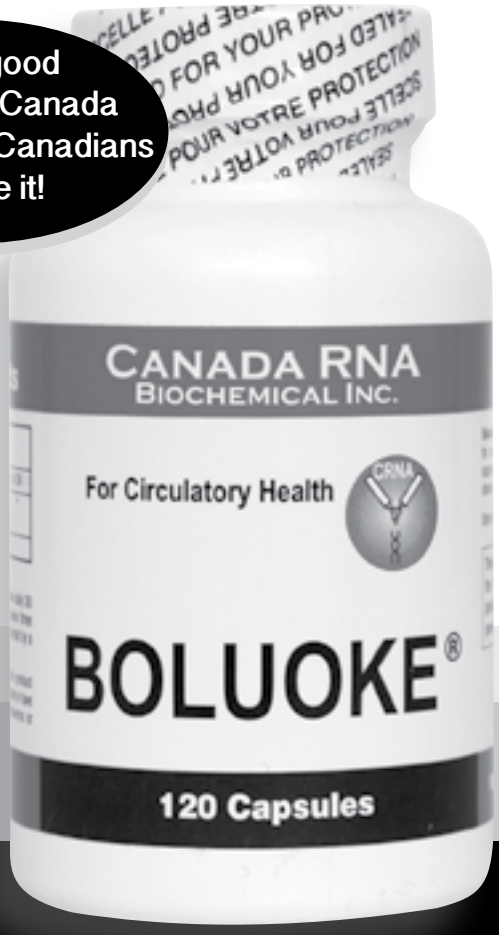

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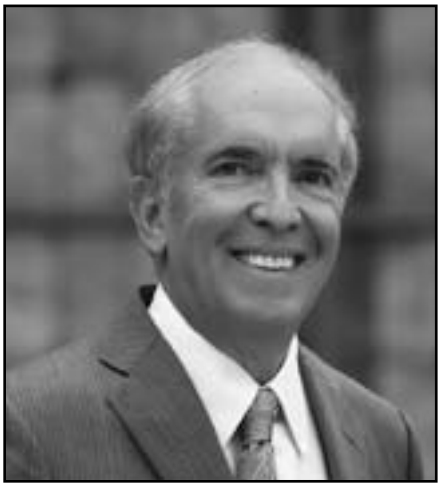

Current Controversies

by Ira L. Goodman, MD, FACS, ABIHM, FAARM
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Exponential Medicine 2017 Meeting Review and Commentary

I attended the 6th Annual Exponential Medicine meeting recently held at Hotel Del Coronado in San Diego, California, which was built in the 1800s and has hosted numerous celebrities and Presidents. As magnificent a setting as this was, the TED-style event had superb audio visuals, comfortable lounge chairs and couches, healthy food, beach-side "un-conferences," a silent disco, an innovation laboratory, and an all-star lineup of speakers. There were 731 participants with 476 companies represented, 24 industries, 51 companies in the innovation lab, 37 countries, and 85 speakers – all over four days. Other elements of this conference that I have never seen at any of the hundreds of conferences I have attended were about 10 talks by patients, who have survived truly unusual medical challenges, a Swami on-site to lead meditation classes on the beach, a requiem for a past speaker who passed away last year, musical interludes with truly talented performers, and a real-time artist documenting many speakers' presentations on large white boards prominently displayed during the four days. This all combines to create Daniel Kraft's vision of what a meeting should be like – a combination of humanistic, scientific, entertainment, and comfort elements all in sync. Well done, Dr. Kraft.

The patient talks included one by a woman who survived two separate double-lung transplants to go on to become an accomplished opera singer who gave a performance at the event. Another was a Crohn's disease patient who survived a total bowel transplant, immunosuppressant therapy, lymphoma, and who developed a company that digitally analyzes the contents of colostomy and urinary bladder bags for long-term users. There were several other patient speakers along the same lines. The scientific sessions included an introduction to exponentials with speakers on artificial intelligence, robotic surgery, advanced information technology currently being used in large organizations, genomics advances like Crispr to edit genes, the human longevity institute goal of sequencing 1 million full genomes by 2020, and virtual as well as augmented reality talks. There was a fascinating talk by Michael Gelb on how to think like Leonardo Da Vinci, who not only painted the *Mona Lisa* and *The Last Supper* but was a pioneer in aviation, biology, anatomy, math, architecture, music, engineering, literature, astronomy, and much more. A true polymath whose curiosity and passion demonstrates what human nature can become.

Speaking of polymaths, I was honored to interview Robert Hirari, who discovered the pluripotent stem cell, was the past CEO of Celgene, and is now working with Craig Venter (first to sequence the full human genome) and Peter Diamandis (founder of the X prize and co-founder with Ray Kurzweil of Singularity University) at Human Longevity Institute. Peter joined Robert and me during a high-powered exchange featuring challenging questions. Robert is also an accomplished jet plane pilot of over 60 different jets, an academic neurosurgeon, a serial entrepreneur in aerospace and biomedicine, a stem cell pioneer currently working on placental stem cell transplants that do not require typing, has authored over 150 chapters in textbooks, and discovered physiological activities of tumor necrosis factor alpha (TNF). Interviewing Peter Diamandis and Robert Hirari at the same time and talking about stem cells, the recent findings of the Health Nucleus associated with HLI, the future of genomics,

and the implications for medicine, society, and health is kind of like interviewing Michelangelo and Da Vinci talking about art. These are true polymaths like Leonardo who have taken deep dives into apparently disparate fields and managed to impact all of them. We talked briefly on what drives both of them, their beliefs and values, and what they see for the future. Robert will be making a groundbreaking scientific announcement soon, which I am hoping to cover.

In addition to all of that, there were notable talks on the following:

Will 100 become the new 60? Peter Diamandis, MD, Ira Goodman, MD, FACS, and Robert Hariri, MD, PhD

1. Artificial pancreas development by a father of a juvenile diabetic;
2. A talk by futurist psychologist Ken Dychtwald, who has written many books on demographics, gerontology, the age wave, and now is attempting to redefine money, success, family, work, and retirement. He is teaming with Peter Diamandis to fund an X prize to cure Alzheimer's;
3. Several talks on new imaging techniques in cancer diagnosis by industry and medical leaders;
4. A screening of a film called *Unrest,* which is about a PhD student at Harvard who developed chronic fatigue syndrome, was bedridden but managed to crowd fund and produce a feature film from her bed on the experience of the thousands of people who face this and similar autoimmune diseases. She was truly inspirational.

The crowning jewel of the event was a virtual appearance by the leading futurist in the world, Ray Kurzweil, who is associated with Google and Singularity University. His predictions have historically been 80% accurate; so, when he predicts the merging of technology and biology within the next 40 years, or the virtual immortality of humans with the ability to download your brain to the cloud, or the ability to know anything when your brain is connected to the web, it does not seem so far-fetched.

We live in a miraculous time with advances in communications, medicine, genomics, technology, computing power, artificial intelligence, and much more. The future will hardly be recognizable, which is not a comforting thought to most humans but a reality that must be dealt with since it's coming ready or not. If you want to be at the forefront of knowledge like this, keep in touch with these thought leaders and consider attending this meeting at some point. ◆

Literature Review & Commentary

by Alan R. Gaby, MD
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Omega-3 Fatty Acids for Dry Eyes

One hundred five patients (mean age, 57 years) with dry eye syndrome (keratoconjunctivitis sicca) were randomly assigned to receive, in double-blind fashion, 4 capsules per day of an omega-3 fatty acid preparation (providing a daily total of 1,680 mg of eicosapentaenoic acid and 560 mg of docosahexaenoic acid) or placebo (linoleic acid) for 12 weeks. Compared with placebo, the omega-3 fatty acids significantly increased tear break-up time (indicating slower evaporation of tears) and significantly decreased (improved) the mean Ocular Surface Disease Index score.

Comment: The findings from this study are consistent with those from numerous other studies in which oral administration of fish oil or the omega-3 fatty acids present in fish oil (eicosapentaenoic acid and docosahexaenoic acid) was moderately effective for relieving dry eye symptoms, including in patients with dry eyes associated with the use of contact lenses. In most of these studies, omega-3 fatty acids also increased tear secretion and decreased the rate of tear evaporation. In contrast, one study found that fish oil in combination with other nutrients was not more effective than placebo, although symptoms improved significantly in both groups. The dosage of omega-3 fatty acids used in the present study is equivalent to around 5-9 g per day of fish oil, but fish oil doses as low as 2 g per day were effective in some studies. Omega-3 fatty acids may work by an anti-inflammatory mechanism.

Epitropoulos AT, et al. Effect of oral re-esterified omega-3 nutritional supplementation on dry eyes. *Cornea*. 2016;35:1185-1191.

Topical Vitamin B12-Containing Ointment for Psoriasis

Twenty-four adults (mean age, 48.2 years) with mild-to-moderate plaque psoriasis were randomly assigned to apply, in single-blind fashion, a vitamin B12-containing ointment to affected areas on one side of the body and a control cream to affected areas on the other side twice a day for 12 weeks. The active treatment (Mavena B12 ointment) is a registered medication in the European Union; it contains 0.07% cyanocobalamin, 20% avocado oil, polyunsaturated fatty acids, and moisturizing factors. The control treatment was a glycerol and petrolatum-based hydrating cream. Mean disease severity (as determined by the Psoriasis Area Severity Index) decreased to a significantly greater extent with active treatment than with control treatment (86% vs. 12.3%; $p < 0.001$). The difference between active and control treatment became statistically significant within two weeks of the start of treatment.

Comment: In this study, topical application of a vitamin B12-containing ointment resulted in marked improvement in patients with mild-to-moderate plaque psoriasis. These findings confirm the results of a previous trial in which twice-daily application of a cream containing 0.07% vitamin B12 and an unspecified concentration of avocado oil for 12 weeks improved the mean Psoriasis Area Severity Index in patients with chronic plaque psoriasis.[1] It is not clear how much of the benefit (if any) in these studies was due to the avocado oil. While avocado oil has been reported anecdotally to improve psoriasis, it has not, to my knowledge, been investigated in a controlled trial.

Del Duca E, et al. Superiority of a vitamin B_{12}-containing emollient compared to a standard emollient in the maintenance treatment of mild-to-moderate plaque psoriasis. *Int J Immunopathol Pharmacol*. 2017;30:439-444.

Topical Vitamin B12-Containing Cream for Atopic Dermatitis

Twenty-two adults (ages not specified) with mild atopic dermatitis were randomly assigned to apply, in single-blind fashion, a vitamin B12-containing barrier cream to affected areas on one side of the body twice a day and a control cream to affected areas on the other side of the body three times per day for 12 weeks. The vitamin B12-containing cream (Mavena B12 barrier cream) contained 0.07% cyanocobalamin, a polysorbate carrier system to enhance penetration into the skin, and 1% urea. The control cream was a glycerol and petrolatum-based emollient cream. The mean percent improvement (as determined by the SCORing Atopic Dermatitis [SCORAD] index) was significantly greater at two weeks (53% vs. 12%; $p < 0.001$) and at 12 weeks (82% vs. 20%; $p < 0.01$) on the vitamin B12 side than on the control side.

Comment: This study found that topical application of a vitamin B12-containing barrier cream was an effective treatment for mild atopic dermatitis in adults. The findings are consistent with previous randomized controlled trials in which topical preparations containing 0.07% vitamin B12 improved atopic dermatitis in both adults[2] and children.[3] While the mechanism of action of vitamin B12 is not clear, it has been shown to prevent the production of certain inflammatory cytokines, an effect that might help prevent flare-ups of atopic dermatitis.

Nistico SP, et al. Superiority of a vitamin B12-barrier cream compared with standard glycerol-petrolatum-based emollient cream in the treatment of atopic dermatitis: A randomized, left-to-right comparative trial. *Dermatol Ther*. 2017 Jul 4 [Epub ahead of print].

Multi-Strain Probiotic for Atopic Dermatitis

Fifty children (aged 4-17 years; mean, 9.2 years) in Spain with moderate atopic dermatitis were randomly assigned to receive, in double-blind fashion, a daily capsule containing 10^9 total colony-forming units of *Bifidobacterium lactis* CECT 8145, *B. longum* CECT 7347, and *Lactobacillus casei* CECT 9104 or placebo for 12 weeks. The mean improvement in the SCORing Atopic Dermatitis (SCORAD) index was significantly greater in the probiotic group than in the placebo group (83% vs. 24%; $p < 0.001$). In addition, the use of topical steroids to treat flares was significantly lower by 29% in the probiotic group than in the placebo group (7.7% vs. 10.8% of patient-days; $p < 0.001$).

Comment: In this study, a multi-strain probiotic preparation was effective in the treatment of moderate atopic dermatitis in children. The study was funded by Biopolis, a company that develops and manufactures probiotics, and three of the study authors were employees of the company. The results should therefore be interpreted with caution. Numerous other randomized controlled trials have invested the effect of various probiotic agents in children with atopic dermatitis. About half of those studies found a beneficial effect, while the others did not. The conflicting results might be due in part to the presence of small amounts of cow's milk proteins in probiotic preparations that were grown on milk or casein (a milk protein). In a case report, an infant who was allergic to cow's milk had a moderately severe allergic reaction to a probiotic preparation that had been grown on casein.[4]

Further research is needed to identify patient characteristics that might predict a positive response to probiotics, and what probiotic strains are most effective. Milk-allergic children with atopic dermatitis should not use probiotics that were grown on culture media that contain milk proteins.

Navarro-Lopez V, et al. Effect of oral administration of a mixture of probiotic strains on SCORAD index and use of topical steroids in young patients with moderate atopic dermatitis: a randomized clinical trial. *JAMA Dermatol*. 2017 Nov 8 [Epub ahead of print].

High-Dose Intravenous Magnesium for Severe Asthma

Thirty-eight children (aged 6-16 years) in Paraguay presenting to an emergency department with severe non-infection-mediated asthma that had failed to improve after two hours of standard therapy were randomly assigned to receive intravenous magnesium sulfate at a bolus dose of 50 mg per

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kg of body weight given over one hour, or a more prolonged infusion with a higher total dose (50 mg per kg per hour for 4 hours; maximum dose, 8 g over 4 hours). Patients were monitored for cardiorespiratory complications. The proportion of patients who were discharged to home within 24 hours was significantly higher in the prolonged-infusion group than in the bolus group (47% vs. 10%; p = 0.032). The number-needed-to-treat to facilitate one discharge at or before 24 hours was 2.7. The mean length of hospital stay (34 vs. 48 hours; p = 0.013) and the mean cost per patient ($603 vs. $834; p < 0.02) was significantly lower in the prolonged-treatment group than in the bolus group. There were no adverse events serious enough to require intervention or discontinuation of treatment.

Comment: Magnesium is a potent bronchodilator. Intravenous magnesium has been reported in many, though not all, randomized controlled trials to be an effective treatment for acute exacerbations of asthma. Studies conducted in children typically used magnesium sulfate at a dosage of 40-50 mg per kg of body weight, administered over 20 minutes. The results of the present study suggest that a more prolonged infusion with a larger total dose, as compared with the usual treatment protocol, can accelerate discharge from the emergency department and reduce healthcare costs in children with treatment-resistant non-infection-mediated asthma. High-dose intravenous magnesium can cause potentially serious adverse effects such as hypotension and bradycardia, so it should be used with caution and patients should be monitored closely.

Irazuzta JE, et al. High-dose magnesium sulfate infusion for severe asthma in the emergency department: efficacy study. *Pediatr Crit Care Med*. 2016;17:e29-e33.

Vitamin D During Pregnancy Prevents Allergies in Children

Two hundred sixty pregnant women in New Zealand were randomly assigned to receive, in double-blind fashion, 1,000 or 2,000 IU per day of vitamin D or placebo from week 27 of gestation until delivery. The infants then received 400 or 800 IU per day of vitamin D or placebo, corresponding to low-dose vitamin D, high-dose vitamin D, or placebo, respectively, during the mother's pregnancy. Specific IgE was measured at 18 months of age. Compared with placebo, both doses of vitamin D significantly decreased the proportion of children sensitized to mites at 18 months of age. The proportion of children who had primary care visits for asthma was 11% with placebo, 0% with low-dose vitamin D, and 4% with high-dose vitamin D (p = 0.002).

Comment: In this study, vitamin D supplementation during pregnancy and infancy reduced the proportion of children sensitized to mites at 18 months of age and decreased the number of primary care visits due to asthma. The infant dose of 800 IU per day was not more effective than 400 IU per day for decreasing the number of visits for asthma. A previous randomized controlled trial found that vitamin D in doses of 800 or 1,200 IU per day, as compared with 400 IU per day, resulted in subtle impairments in motor development in breastfed infants.[5] The American Academy of Pediatrics recommends that all breastfed infants receive 400 IU per day of supplemental vitamin D. However, the available evidence does not support the routine use of larger vitamin D doses in the infant population.

Grant CC, et al. Vitamin D supplementation during pregnancy and infancy reduces aeroallergen sensitization: a randomized controlled trial. *Allergy*. 2016;71:1325-1334.

Beetroot Juice Enhances Athletic Performance

Thirty-two trained male soccer players (mean age, 23 years) were randomly assigned to receive, in double-blind fashion, 140 ml per day of nitrate-rich beetroot juice (providing 800 mg per day of nitrate) or nitrate-depleted beetroot juice (placebo) for six days. After a washout period of at least eight days, each person consumed the alternate drink for an additional six days. All subjects performed a high-intensity intermittent running test (the Yo-Yo IR1 test) on the last day of each supplementation period. In this test, which assesses both aerobic and anaerobic performance, subjects perform repeated 2 times 20 m sprints at progressively increasing speeds, with a 10-second recovery period between each sprint. The test ends the second time a subject fails to cross the finish line in the required time. The primary outcome measure was the total distance covered during the test. Compared with placebo, nitrate-rich beetroot juice increased the mean distance covered during the Yo-Yo IR1 test by 3.4% (p < 0.03).

In a second study, eight trained male runners completed two 1,500 m and two 10,000 m time trials on a treadmill. Three hours before each test, the subjects received 140 ml of nitrate-rich or nitrate-depleted (placebo) beetroot juice. Performance in the 1,500 m trial was significantly faster with nitrate-rich beetroot juice than with placebo (mean, 320 vs. 326 seconds; p < 0.05). In the 10,000 m trial, nitrate-rich beetroot juice resulted in a nonsignificantly faster performance (mean, 2,643 vs. 2,650 seconds).

Comment: These studies demonstrate that supplementation with nitrate-rich beetroot juice can improve performance in high-intensity intermittent exercise and middle-distance running events. The results are also consistent with improved performance in long-distance running events, although that improvement was not statistically significant. The effect of nitrate may be mediated by its conversion to nitric oxide, which functions as a vasodilator and a regulator of cellular activity.

While short-term administration of nitrate is probably safe for most people, its long-term safety has not been adequately studied. Nitric oxide is an unstable molecule that promotes the formation of reactive oxidants such as peroxynitrite. Peroxynitrite and other nitric oxide-derived oxidants are inflammatory mediators that may promote the development of atherosclerosis. The substance that has been shown most clearly to scavenge reactive nitrogen molecules is gamma-tocopherol, which is one of the naturally occurring forms of vitamin E.[6] In the process of quenching nitric oxide-derived

oxidants, gamma-tocopherol is converted to 5-nitro-gamma-tocopherol,[7] which appears to be an inactive metabolite.[8] If long-term nitrate administration has potential adverse effects, they might be preventable by supplementing with gamma-tocopherol in the form of mixed tocopherols.

Nyakayiru J, et al. Beetroot juice supplementation improves high-intensity intermittent type exercise performance in trained soccer players. *Nutrients*. 2017;9:E314.

Shannon OM, et al. Dietary nitrate supplementation enhances short but not longer duration running time-trial performance. *Eur J Appl Physiol*. 2017;117:775-785.

6. Christen S, et al. Gamma-tocopherol traps mutagenic electrophiles such as NOx and complements alpha-tocopherol: physiological implications. *Proc Natl Acad Sci*. 1997;94:3217-3222.
7. Hensley K, et al. Measurement of 3-nitrotyrosine and 5-nitro-gamma-tocopherol by high-performance liquid chromatography with electrochemical detection. *Free Radic Biol Med*. 2000;28:520-528.
8. Wu JH, Hodgson JM, Ward NC, et al. Nitration of gamma-tocopherol prevents its oxidative metabolism by HepG2 cells. *Free Radic Biol Med*. 2005;39:483-494.

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Probiotic for Functional Abdominal Pain in Children

Fifty-five children (aged 5-17 years) with functional abdominal pain or irritable bowel syndrome were randomly assigned to receive, in double-blind fashion, *Lactobacillus reuteri* DSM 17938 (10^8 colony-forming units per day) or placebo for 12 weeks, and were then followed for an additional four weeks. During the treatment and follow-up period, the median number of days with pain was significantly lower by 60% in the probiotic group than in the placebo group (26 vs. 65; $p < 0.03$).

Comment: These results indicate that administration of *Lactobacillus reuteri* DSM 17938 significantly decreased pain in children with functional abdominal pain or irritable bowel syndrome. This probiotic preparation is commercially available as *L. reuteri* Protectis, under the brand name Gerber Soothe Colic Drops. Its temperature should not exceed 77° F.; it should therefore be shipped cold during the summer.

Jadresin O, et al. Lactobacillus reuteri DSM 17938 in the treatment of functional abdominal pain in children: RCT study. *J Pediatr Gastroenterol Nutr*. 2017;64::925-929.

References

1. Stucker M, et al. Vitamin B12 cream containing avocado oil in the therapy of plaque psoriasis. *Dermatology*. 2001;203:141-147.
2. Stucker M, et al. Topical vitamin B12 - a new therapeutic approach in atopic dermatitis - evaluation of efficacy and tolerability in a randomized placebo-controlled multicentre clinical trial. *Br J Dermatol*. 2004;150:977-983.
3. Januchowski R. Evaluation of topical vitamin B12 for the treatment of childhood eczema. *J Altern Complement Med*. 2009;15:387-389.
4. Moneret-Vautrin DA, et al. Probiotics may be unsafe in infants allergic to cow's milk. *Allergy*. 2006;61:507-508.
5. Wicklow B, et al. Impact of vitamin D supplementation on gross motor development of healthy term infants: a randomized dose-response trial. *Phys Occup Ther Pediatr*. 2016;36:300-342.

Bastyr University San Diego Clinic: Student Case Reports

edited by Baljit Khamba, ND, MPH

Fourth-year interns at Bastyr University are actively developing their clinical skills through treating patients at the school's clinic. They engage their didactic skills in rigorous case taking, examinations, evaluation, and a naturopathic-focused treatment plan under the supervision of their attending doctor. The interns are able to gain experience in areas such as mental health, mind-body medicine, oncology, hydrotherapy, physical medicine, out-reach community care, IV treatment, biofeedback, and so on. Each one of these opportunities presents a prime opportunity for the students to enrich their knowledge about conditions and approaches to care. In efforts to salient their understanding, the students write case reports under the supervision of Dr. Baljit Khamba in their course "Advanced Case Studies." By completing these reports, future practitioners gain a valuable skill that they can then utilize once they graduate.

The first case report in this new column is by Gregory Nacarelli.

Iodine Administration Leading to Shortness of Breath

by Gregory Nacarelli

Abstract

This case report discusses a 35-year-old Caucasian male who consumed 15 mg of Lugol's iodine for 10-12 days. After ceasing iodine administration, he began to experience shortness of breath, chest palpitations, and night sweats. This resulted in two emergency room visits prior to visiting the Bastyr University California clinic for treatment regarding these symptoms. Blood analysis in the emergency room revealed depressed TSH. Analysis of patient in-office revealed he was still dealing with effects of this issue despite it being three weeks since his last iodine administration. Laboratory findings showed low glucose and alkaline phosphatase levels. The patient was still displaying shortness of breath in a follow-up visit six weeks later. Laboratory testing revealed low insulin and low c-peptide. The finding of depressed pancreatic function may be an incidental finding. Studies linking iodine administration and subsequent hypoinsulinemia are lacking. A possible link to kryptopyrroluria is discussed.

Introduction

Iodine is essential in the production of the thyroid hormones T3 and T4. Iodine is classified as a trace mineral, and the recommended daily allowance is set to 150 mcg daily for non-pregnant adults, 90 mcg per day for children ages 6-12, and 250 mcg per day during pregnancy and lactation.[1] Iodine-rich foods consist of seaweed, cranberries, fish, eggs, dairy, and sea salt. Iodine can also be administered in supplemental form. One popular form of supplemental iodine is known as Lugol's iodine. Lugol's iodine is two parts potassium iodine and one part elemental iodine. This form of iodine is typically used as a disinfectant but can be used to protect the thyroid gland from radiation.[2]

Iodized salt contains 77 micrograms of iodine per 1 gram of salt.[1] This is the major form of salt consumed in the United States. This constitutes the major source of iodine consumption in developed countries; iodine-deficient-based thyroid disorders are more commonly seen in third world countries without iodized salt.

The idea behind excess iodine being detrimental to health has been well documented. The Wolf-Chaikoff effect alludes to the phenomenon in which excess iodine consumption will decrease normal thyroid function, making said person hypothyroid.[3] This effect will typically last three-to-four weeks.[3] Through lab testing, one can measure this effect by seeing an initial drop in circulating T3 and T4 levels and an increase in TSH levels. It is also well documented that iodine administration can also be detrimental if someone already

has pre-existing hyper or hypothyroidism.[4] In regions of iodine deficiency, hyperthyroidism was seen in upwards of 20% of the population in which iodine was administered.[4] It is rare for iodine to cause hyperthyroidism in patient populations in which there was no underlying thyroid issues present previously.[5]

According to one study only 10% of iodine ingested via iodized salt is bioavailable.[2] Based upon this study and others like it, some members of the medical community suggest increasing iodine consumption beyond the RDA set by the FDA, as we are not absorbing enough iodine to meet our bodies' needs when following the RDA's requirements. Another reason for the suggestion for increasing iodine consumption is the increase in environmental toxins over the last several decades, mainly bromine, fluoride, and chloride derivatives, which will alter the metabolism of iodine in the body.[6]

Diagnosis of iodine-induced thyroid disease should include measurements of Free T3, Free T4, TSH, TSH receptor antibodies, radioactive iodine uptake assessment, and thyroid ultrasound. The presence of TSH receptor antibodies are indicative of Graves' disease. The radioactive iodine assessment should help to distinguish Graves' hyperthyroidism from iodine-induced hyperthyroidism. Iodine-induced hyperthyroidism can last from one month to 18 months and is treated by discontinuing iodine and, if indicated, administering a beta-adrenergic antagonist, such as atenolol.[4] Methimazole can also be utilized if symptoms are severe. Methimazole works by inhibiting thyroid peroxidase, which is responsible for facilitating the addition of iodine to thyroglobulin.[4]

Symptoms of iodine-induced hyperthyroidism may include resting tremor, enlarged thyroid, hair loss, arrhythmia, onycholysis, gyneocomastia, proptosis, hyperreflexia, heat intolerance, irritability, insomnia, weight loss, increased appetite, diarrhea, amenorrhea, decreased libido, and photophobia.[4] Wolf-Chaikoff hypothyroid symptoms may include lethargy, memory loss, hearing loss, weight gain, insomnia, joint/muscle aches, hair loss, constipation, cold intolerance, paraesthesias, thinning lateral eyebrows, periorbital edema, weak pulse, edema, and cold/dry skin.

This case report discusses a patient who is displaying signs and symptoms concordant with thyroid dysfunction after ingesting 15 mg of iodine per day for 10-12 days. The question to be had from this research report is if the patient is indeed experiencing thyroid dysfunction from the iodine supplementation or if there is some other underlying issue present. Laboratory findings suggestive of hypoinsulinemia are discussed as well as the correlation to the patient's current disposition.

Case Description

The patient described in this case is a 35-year-old Caucasian male. His first visit to the Bastyr University Clinic was in January 2016. He came to the clinic with reports of malaise and fatigue. His review of systems was positive for diarrhea, thinning eyebrows, cold intolerance, dry skin, numbness in hands, dizziness, and anxiety. Other health history includes a paleolithic-based diet in which he avoids grains, dairy, and nightshades. He does not consume caffeine and has one glass of wine per night. A working diagnosis of hypothyroidism was made, and labs were ordered.

Results of significance were as follows: High: ALT (49 IU/L), AST(32 IU/L), Bilirubin (1.5 mg/dL), A/G (2.9), and borderline low glucose (66 mg/dL). His thyroid levels were as follows: TSH: 1.27 uIU/mL (0.45-4.5); free T3: 2.5 ng/dL (2-4.4); free T4: 1.58ng/dL (0.82-1.77). His anti-TPO antibodies were a 7 IU/mL with a range of 0-34 IU/mL. His CBC and other CMP parameters were all within range. His anti-TG antibodies were negligible. The patient did not return for a follow-up for discussion of his lab results.

The patient then returned to the Bastyr University clinic on July 6, 2017, complaining of shortness of breath and chest palpitations. He said that four weeks prior he took 15 milligrams of Lugol's iodine per day for 10-12 days. He did this because he felt like he met the criteria for hypothyroidism and thought that iodine administration would help his symptoms. The bulk of the patient's information regarding what form of iodine to take and the dosage came from Dr. David Brownstein's website. After the 10-12 days of iodine administration, the next day he began to experience chest palpitations, anxiety, shortness of breath, and night sweats. These symptoms lasted for three days. At one point he noticed chest palpitations and took his blood pressure, which was "really low." When he began to experience dizziness, he went to the ER. At the ER, they found that he had high neutrophils (71.7%), low lymphocytes (21.6%), and a borderline depressed TSH (0.596 uIU/mL). After the ER visit his symptoms lessened but never fully went away. He would still notice the shortness of breath, night sweats, and chest palpitations at night, especially after falling asleep. Two weeks later he returned to the ER complaining of dizziness and shortness of breath. An x-ray was run on him, which was normal. To rule out cardiac myocyte injury, they measured the cardiac marker troponin I, which was not elevated. An EKG was run which displayed possible atrial enlargement. His TSH was measured at this second ER visit and was 0.493 uIU/mL. The patient's last ER visit was two days prior to the Bastyr University clinic visit.

Other medical history included gastrointestinal issues after a trip to Nepal 10 years before. The patient believed the onset of his hypothyroid-like symptoms started then. While the patient has complained about hypothyroid-like symptoms in the past, he states he never experienced any cardiac/respiratory issues prior to taking the iodine supplementation. The patient experienced prostatitis-like symptoms six months ago that resolved with the use of antibiotics. The patient is still consuming the same paleolithic, grain-free, dairy-free diet that he was consuming last visit. He occasionally takes magnesium supplements but is not currently taking any other supplements daily. His profession involves work around Chinese medicine. He tried Mai Men Dong botanical Chinese formula around the onset of his symptoms, but he said this made his symptoms worse. The patient has been getting between four to eight hours of sleep per night, depending on the severity of his chest palpitations. He rates his current stress level at a 4/10, though

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in previous weeks he rated it 7/10 due to the stress his health issues are causing.

His review of systems was positive for the following: insomnia, stress, lateral eyebrow thinning, syncope, chest palpitations, shortness of breath, cold sweats at night, muscle weakness, muscle cramps, concentration impairment, and depression. On physical examination, his height was 5 ft. 8.6 in., blood pressure was 96/70, pulse was 65 beats per minute, his temperature was 98.3 Fahrenheit, respirations per minute were 12, and oxygen saturation was 98%. His weight was 128.6 lb., which was a 20-pound drop from his weight in January 2016. The patient attributes his weight loss to decreased physical activity and weight lifting. Cardiac auscultation revealed regular heart rate and rhythm, no murmurs or gallops. Lungs were clear to auscultation, though the patient had to pause between breaths due to feeling shortness of breath. No clubbing or cyanosis was present in digits. Deep tendon reflexes were +2 and muscle strength was +5. It should be noted the patient was comfortably wearing three layers of clothing in an 80°F clinic room.

Given the history, positive review of symptoms (ROS), and physical exam (PE) findings, the patient was diagnosed with cold intolerance, weight loss, and shortness of breath. We suspect these symptoms are due to thyroid dysfunction, possibly due to excess iodine administration. We decided to run the following labs: CMP, TSH, FT4, FT3, TSI, anti-TG, and anti-TPO antibodies. We recommended the patient use a stool parasite testing kit from Doctor's Data to see if there were any lingering parasite issues since the trip to Nepal. We recommended that he follow-up in three weeks after his test results came in.

The following lab results came back abnormal: glucose was 55 mg/dL and alkaline phosphatase was 37 mg/dL (39-117). His thyroid levels were as follows: TSH: 0.6 uIU/mL (0.45-4.5); FT3: 3 ng/dL (2-4.4); FT4: 1.5 ng/dL (0.82-1.77). His anti-TPO antibodies and anti-TG antibodies were within range. We are still waiting on his TSI and parasitology results.

The patient followed-up for review of his lab results on August 17, 2017. His vitals were all within normal limits. His weight was 131.6 lbs., a three-pound increase from his last visit. The patient mentioned that his chest palpations have decreased significantly but his shortness of breath has gotten worse, while also experiencing occasional dizziness. On physical exam, lungs were clear to auscultation. The patient had to pause between breaths. The patient mentioned that if he doesn't eat every couple hours his shortness of breath and dizziness get worse. Testing for ketone production via urinalysis was negative.

Based upon his ROS, PE, and previous lab results, we decided to test the patient's fasting serum insulin, serum c-peptide, GAD-65, insulin antibodies, and glucose. These were ordered to get a better idea of his pancreatic function. His fasting insulin was low at 1.7 uIU/mL (range: 2.6-24.9 uIU/mL); his c-peptide was low at 1 ng/mL (range: 1.1-4.4 ng/mL); and his glucose was borderline low at 65 mg/dL. His GAD-65 and insulin antibody levels were normal at <5 U/mL. We called the patient to let him know his lab results were suggestive of hypoinsulinemia and referred him to an endocrinologist.

Discussion

From the information gathered from the history, ROS, PE, we suspect the iodine administration is implicated with the hypoinsulinemia. We are also considering further testing for kryptopyrroluria. Kryptopyrroluria involves the overproduction of hydroxyhempyrolin, a protein in the heme biosynthetic pathway.[7] Stress is one of the main triggers for this, but the cause can be genetic.[7] Loss of function of the enzyme aminolevulinate synthase is linked with excessive production of pyrroles and, also, x-linked sideroblastic anemia.[7] Some of the symptoms of pyrrole disorder include hypoglycemia, low alkaline phosphastase, fatigue, dizziness, and memory impairment. The patient has all these symptoms. The test for pyrrole disorder involves testing for kryptopyrroles via a urine test. Testing for this involves an at-home urine test; information for the patient to purchase this testing kit has been provided. The link between increased hydroxyhempyrolin production and thyroid dysfunction requires further investigation.

Gregory Nacarelli is a fourth-year naturopathic medical student at Bastyr University California. Before attending Bastyr University, he was a research scientist at Merck & Co. He possesses a master's degree in molecular biology from Lehigh University and a bachelor's degree in biology from Cabrini University. His interests include genetics, nutrition, and botanical medicine.

Baljit Khamba, ND, MPH, is a clinic supervisor at Bastyr University Clinic and a core faculty member at Bastyr University, California. She treats a variety of conditions but has special interest in nutritional approaches to mental health, particularly anxiety, stress, depression, ADHD, memory, and cognition.

Dr. Khamba completed her honor's Bachelor of Science at York University, Toronto, Canada, specializing in psychology, as well as her Master in Public Health from Lakehead University. Her interest in mental health guided her graduate thesis on nutritional influences of mood disorders. She received her naturopathic doctoral degree from the Canadian College of Naturopathic Medicine (CCNM).

Upon graduating, Dr. Khamba worked in integrative psychiatric clinics and was actively involved with research projects at the University of Alberta reporting on adverse effects from natural health products used alongside psychiatric medication.

Dr. Khamba is a licensed naturopathic doctor in California and accepts patients at Bastyr University Clinic alongside student interns.

Sufficient thyroid production requires the following compounds: B6, selenium, zinc, vitamin C, B2, magnesium, iodine, among other compounds.[9,11] If the patient does indeed have kryptopyrroluria, it would be sequestering his body of B6 and zinc.[8] This would make him nutrient deficient in the co-factors necessary for thyroid hormone production. Future plans involve checking his body for current levels of vitamins and minerals. Depending on the patient's vitamin and mineral levels, we will recommend supplementation and/or IV vitamin and mineral therapy to make sure the patient is getting adequate nutrition.

Environmental toxicity is also a concern for exacerbating or causing thyroid dysfunction.[10] In order to assess the patient's toxin load, a future plan will involve running an environmental toxicity panel. If there is a toxin burden, we will suggest a detoxification protocol which consists of sauna, detoxification nutritional support and, if necessary, heavy metal chelation. More research is needed to elucidate the effect of heavy metal chelation on circulating iodine levels. There exists a link between excess iron burden and kryptopyrroluria.[13] This is due to iron's ability to displace zinc from its binding sites.[13]

We are limited because iodine testing in humans is unreliable at this time. The current literature mentions that Wolf-Chaikoff-induced hypothyroidism lasts roughly 3-4 weeks.[3] and iodine-induced hyperthyroidism can last between 1-18 months.[4] The standard for patients in iodine excess is to treat the symptomology. The patient's severity of symptoms will be assessed next visit. Beta-adrenergic antagonists, such as atenolol, will be considered if he is still experiencing the heart palpitations. A link between excess iodine consumption and low insulin status remains to be elucidated. The finding of hypoinsulinemia seems to be an incidental finding.

Conclusion

While an argument can be made regarding whether or not the RDA for iodine is sufficient for the average, healthy, adult human being, supplemental iodine administration should be used with caution as it can exacerbate pre-existing health conditions. Iodine dosing should be recommended under the guidance of a physician trained to rule out previously existing thyroid-related pathologies.

Testing for the etiology of thyroid pathologies is a complex process that involves ruling out food allergies, toxic exposures, nutritional deficiencies, as well as other pre-existing medical conditions, such as autoimmune diseases. This case report discusses a patient who is displaying symptoms of having thyroid dysfunction after iodine administration. Thorough investigation revealed he was affected by hypoinsulinemia. Treatment of a patient in this situation requires an endocrinologist as well as nutritional counseling for optimal thyroid functioning.

References

1. Food and Nutrition Board, Institute of Medicine. *Dietary reference intakes for vitamin A, vitamin K, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanandium, and zinc*. Washington, D.C.: National Academy Press; 2001:258-289.
2. Keeling DH, Williams ES. Changes in the normal range of thyroidal radioiodine uptake, *J Clin Pathol*. 1972 Oct; 25(10): 863–866.
3. Chaikoff WJ. Plasma inorganic iodide as a homeostatic regulator of thyroid function. *J Biol Chem.* 1948; 174:555.
4. Roti E, Uberti ED. Iodine excess and hyperthyroidism. *Thyroid*. 2001; 11:493.
5. Skare S, Frey HM. Iodine induced thyrotoxicosis in apparently normal thyroid glands. *Acta Endocrinol* (Copenh) 1980; 94:332.
6. Pavelka S. Metabolism of bromide and its interference with the metabolism of iodine. *Physiol Res.* 2004;53 Suppl 1:S81-90.
7. Hawkins D, Pauling L. *Orthomolecular Psychiatry: Treatment of Schizophrenia*. San Francisco: WH Freeman and Company; 1973:146-178.
8. Pfeiffer CC. *Nutrition and Mental Illness: An Orthomolecular Approach to Balancing Body Chemistry*. Rochester, VT: Healing Arts Press;1987.
9. Kawicka A, et al. Metabolic disorders and nutritional status in autoimmune thyroid diseases., *Ostepy Hig Med Dosw* (Online). 2015 Jan 2;69:80-90.
10. Eisenbrand G, Gelbke HP. Assessing the potential impact on the thyroid axis of environmentally relevant food constituents/contaminants in humans. *Arch Toxicol*. 2016 Aug;90(8):1841-57.
11. Kieliszek M, Błażejak S. Current Knowledge on the Importance of Selenium in Food for Living Organisms: A Review. *Molecules*. 2016 May 10;21(5).
12. Diamanti A, et al. Autoimmune diseases and celiac disease which came first: genotype or gluten? *Expert Rev Clin Immunol*. 2016;12(1):67-77.
13. Bergdahl IA, et al. Lead binding to delta-aminolevulinic acid dehydratase (ALAD) in human erythrocytes. *Pharmacol Toxicol.* 1997;81(4):153.
14. Christianson A, Murray M. *Textbook of Natural Medicine*, 4th edition, Chapter 177, 1473-1480.

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Globulin Component Macrophage Activating Factor (GcMAF) Immunotherapy

by James Odell, ND, OMD, LAc

At the turn of the 20th century, the emerging field of medical oncology chose a cytotoxic approach to cancer therapy over an immune-centered approach. In the intervening years, nearly 120 years of data have established that (a) even the best cytotoxic regimens only infrequently cure late-stage malignancy and (b) strategies that supplement and augment existing antitumor immune responses offer the greatest opportunities to potentiate durable cancer remission.

The immune system consists of a multitude of cells and cell lines that communicate with one another through specific messenger substances. Immunotherapy uses cells, messenger substances, and molecules to trigger a reaction in the immune system. It employs known antibodies, complement proteins, and cytokines – as well as metabolites of the vitamin D axis. The vitamin D3-binding protein (Gc protein)-derived macrophage activating factor (GcMAF) activates tumoricidal macrophages against a variety of cancers indiscriminately. This article outlines current immunotherapy practices using GcMAF.

Macrophage activating factor (MAF) is a lymphokine or other receptor-based signal that primes macrophages towards cytotoxicity to tumors, cytokine secretion, or clearance of pathogens. MAF is formed by dissociation of two sugar compounds from the vitamin D3-binding protein. This enzymatic transformation is significantly stimulated by T and B lymphocytes and results, among other things, in a striking increase in activity levels of the macrophages.

MAF specifically serves to activate macrophages triggering an immunomodulatory effect, by linking to the vitamin D receptor (VDR). However, to do so, the saturation of the protein with two further components is necessary: vitamin D and oleic acid. Hence, vitamin D and oleic acid must be present to activate the relevant macrophages and cause a targeted immunomodulation. The VDR functionally works as a transcription factor within the cell nucleus and modulates the expression of more than 900 known genes. VDR blockades play an important role in the pathogenesis of many chronic diseases.

Macrophages are specialized cells involved in the detection, phagocytosis and destruction of cancerous cells, bacteria and other harmful organisms. Macrophages act as a first line or primary defense against intruders; they migrate to and circulate within almost every tissue, patrolling for pathogens and eliminating dead cells. They also direct other types of white blood cells, especially lymphocytes. Macrophages readily infiltrate diseased and damaged tissues, including tumors. As such, macrophage-based cancer therapies have long been investigated.

Macrophages are released from the bone marrow as immature monocytes. After circulating in the blood, they are recruited by chemokines into the tissue and undergo differentiation into macrophages. They can exhibit different phenotypes and functions, depending on the physiologic or pathologic situation to which they are recruited. Moreover, macrophages can exhibit different responses depending on the type of stimuli they receive from the surrounding microenvironment, varying from pro-inflammatory to anti-inflammatory. There are several activated forms of macrophages. Based on their activation state, there are two main phenotypes designated M1 and M2. The differences displayed by macrophages in terms of receptor expression, cytokine production, and function, define these two populations.

M1 (classically activated) macrophages can produce large amounts of proinflammatory cytokines and are involved in the killing of pathogens and tumor cells. In most tumors, the infiltrated macrophages are of the M2-phenotype, which provides an immunosuppressive microenvironment for tumor growth. Furthermore, these tumor-associated macrophages secrete many cytokines, chemokines, and proteases that promote tumor angiogenesis, growth, metastasis, and immunosuppression.

More than 25 years ago, the immunologist Dr. Nobuto Yamamoto isolated GcMAF as a specific immunotherapy. Since then, studies have demonstrated that GcMAF enhances the ability of the immune system to fight

pathogens and cancer cells, by enhancing M1-macrophages as well as reducing the enzyme α-N-acetylgalactosaminidase (nagalase).[1-12] Accordingly, its administration has potential benefits in patients with a variety of conditions, ranging from cancer to HIV and other chronic viruses.[13-15]

Dr. Yamamoto has authored or co-authored over 50 papers on immunology. In 2014, however, three of his articles were retracted,[16-18] giving rise to considerable negative media and controversy around GcMAF immunotherapy. Since then, numerous others have picked up the torch and continued this line of research, further demonstrating that GcMAF has wide application for use in many diseases by activating macrophages and stimulating the immune system.

Dr. Yamamoto patented the process of preparing GcMAF by treating glycosylated human group-specific component, also known as human vitamin D-binding protein, with glycosidases in 1990 and 2015.[19, 20] The manufacturing process of GcMAF is very technical and an impurity can be introduced at any step. Hence, there is certainly risk of product contamination. Reputable manufacturers test the final product for purity and efficacy.

Function, Biological and Pharmacological Properties of Gc-Globulin and GcMAF

Macrophages play a principal role in the fight against cancer cells, but only following a complex activation mechanism. In the context of cancer, classically activated macrophages (M1-macrophages) play an important role in the recognition and destruction of cancer cells, and their presence usually indicates good prognosis. After recognition, malignant cells can be destroyed through several mechanisms, which include contact-dependent phagocytosis and cytotoxicity.

Vitamin D-binding protein (known as Gc) can be converted to the potent macrophage activating factor (GcMAF) by stepwise modification of Gc with beta-galactosidase of B cells and sialidase of T cells. Gc protein is synthesized in the liver and carries vitamin D and its metabolites through the circulation and mediates the response of tissue. Gc protein, in addition to the storage and transport of vitamin D, has an important physiological function as a scavenger of extracellular G-actin to increase neutrophil chemotaxis as well as macrophage activation. Gc protein, when modified, can affect the activation and fortification of immune cells exhibiting anticancer activity. Macrophages activated by GcMAF offer different properties that are effective against a variety of cancers in human and animal models.[21-23]

GcMAF Indications and Associated Treatment Methods

Injectable GcMAF and oral forms of colostrum-derived MAF are not used as stand-alone therapies. Instead, in the world of bioregulatory medicine, this form of immunotherapy is used in concert with a comprehensive, multi-therapeutic modality approach. This involves incorporating individualized dietary approaches, nutritional supplementation, organ and extracellular matrix detoxification, improvement of acid-base balance, as well as all-important psycho-emotional supportive therapies. In relationship to cancer patients, it is important to know which patients and which types of cancers are the best candidates for GcMAF therapy. Prostate, breast, colon, liver, stomach, lung (including mesothelioma), kidney, bladder, uterus, ovarian, head/neck and brain cancers, fibrosarcomas and melanomas are the types of cancer tested thus far.[24] Although many types of cancer have been the focus for GcMAF therapy, it has not been used as a clinical treatment for lung and brain cancer.

Route of Administration

GcMAF therapy has been developed as an injectable and, in Germany, is usually administered by intravenous infusion (drip) or by IV "push." Some doctors also administer GcMAF as an intratumoral injection together with oxidative therapy. Another option is to use a nebulizer to deliver the protein to activate macrophages in the bronchus-associated lymphoid tissue of the lungs.

Oral forms of GcMAF are ineffective because the protein, when orally consumed, is destroyed by stomach hydrochloric acid and pancreatic protease enzymes. However, there are now some oral colostrum forms that are viable in increasing bodily GcMAF. In fact, reports of these products are very promising. One German company has developed a colostrum-derived MAF (Cd-MAF) protein.[25] This proprietary product also contains vitamin D3 (cholecalciferol), Sango coral powder, oleic acid, and probiotic microorganisms.

A 2015 study showed that colostrum MAF greatly enhanced phagocytic activity in the peritoneal macrophages and intestinal macrophages of mice, *in vitro* and *in vivo,* respectively.[26] Colostrum-derived MAF has multiple positive attributes, including being a safe food, easy to obtain and use, and being a non-inducer of inflammatory cytokines. Colostrum-derived MAF is becoming more commonly used as an effective macrophage activator in various immunotherapy programs.

Doctors using oral colostrum-derived MAF in Europe often combine this therapy with intravenous vitamin C for maximum immune effects. Vitamin C contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system. Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis and phagocytosis. It is also needed for apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis and potential tissue damage. The role of vitamin C in lymphocytes is less clear, but it has been shown to enhance differentiation and proliferation of B- and T-cells, likely due to its gene-regulating effects.

Frequency and Dosage

As with any immunotherapy**,** it is important to determine the dosage of GcMAF, the frequency of administration, and the length of time required for response to therapy before decisions about its administration can be made. In his early published human studies, Dr. Yamamoto always used the same dose: 100 nanograms (ng) per week in a single injection. (Equivalent to 100 billionths of a gram, this is an extremely small amount.) Dr. Yamamoto determined

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that the half-life of the activation effect in an activated macrophage is approximately six days. Therefore, he chose a once per week interval between GcMAF doses. Following this protocol, Saisei Mirai clinics in Japan inject their GcMAF product intramuscularly at 1500 ng/0.5 ml, two to three times per week. Together with this immunotherapy, they also incorporate an integrative approach to treating cancer and other illnesses. They further recommend that more frequent dosing (daily or every second day) may be safely used with more advanced stage of disease, or initially in the treatment course. In certain cases, as in many German clinics, Saisei Mirai doctors administer their GcMAF by intravenous injection, 0.5-1.0 ml two to three times per week in 20 ml or more saline.

Moreover, the frequency of administration depends upon the individual responsiveness associated with any vitamin D receptor (VDR) polymorphism. The association between polymorphisms of gene coding for VDR should always be considered. Additionally, blood levels of 25-hydroxyvitamin D should be periodically monitored. Insufficient vitamin D is linked to virtually every age-related disorder including cancer, vascular disease, and chronic inflammation. Generally, many doctors consider the ideal ranges for 25-hydroxyvitamin D are between 50-80 ng/mL. For some individuals, to maintain that ideal level, it may be necessary to take vitamin D3 doses of up to 5,000 IU to 10,000 IU daily.

Duration and Maintenance of Treatment

The duration of GcMAF therapy depends on the individual's condition. Usually, with most cancer patients or those with chronic viral infections, four to six months is necessary to fully activate the immunity. Maintenance is often continued with oral colostrum MAF, together with vitamin D3, oleic acid supplementation, and intravenous vitamin C.

Monitoring GcMAF Treatment

GcMAF administration must always be monitored by a physician trained in its use. Aside from the usual cancer tests (monitoring the effectiveness of treatments), there are two additional tests that are often used. The first is the monocyte count of a white blood cell differential. As previously discussed, monocytes produced in the bone marrow enter the blood, then migrate to organs and tissues where they mature into macrophages. Low monocyte count, low phagocytic activity of monocytes, low lymphocyte count, low NK cell activity, and depressed TNF-α are often observed following standard external beam radiation therapy or cytotoxic chemotherapy for cancer. This has consequences for anticancer immune competence in the weeks and months following completion of cytotoxic chemotherapy and radiotherapy and is one reason why immunotherapy is so important. GcMAF therapy increases the number of monocytes as it activates macrophages. A patient's monocyte count will generally rise in the early stages of GcMAF treatment and indicates a response to GcMAF. Normal monocyte levels are between 2% and 10% of the total differential. Upward of 6% or more is considered an optimum response to GcMAF treatment.

Cancers and viruses both make the enzyme α-N-acetylgalactosaminidase (nagalase) and increased serum levels of nagalase have been reported in many cancer patients. It has been suggested that this enzyme is responsible for the inactivation, or specifically deglycosylation of GcMAF.[27-29] Even though the intracellular (lysosomal) form of nagalase is vital for proper hepatic cell function, the extracellular form (secreted by cancer cells) seems only to benefit the progression of cancer.[30]

Specialized laboratories can now measure the level of nagalase in the blood. An elevated nagalase test result reveals that either cancer or a virus (or both) could be present. It has been established that nagalase activity is directly proportional to viable tumor burden, whereas decreased nagalase activity is associated with improved clinical conditions. Hence, some doctors using GcMAF employ nagalase testing to determine the efficacy of the therapy.

According to some articles and research centers, the recommended reference range of nagalase in the serum of healthy people is between 0.32 and 0.95 nM/min/mg of substrate, although in some articles the normal range is slightly lower (up to 0.65 nM/min/mg).[31] Be advised that reference ranges differ slightly depending on the laboratory.

Additional research is required to ascertain a universal and reliable normal threshold. Because the measurement of this enzyme can diagnose the presence of cancerous lesions below levels detectable by other diagnostic means, nagalase testing may eventually become a standard biomarker for early cancer detection.

GcMAF Side Effects

No harmful side effects from GcMAF treatment have been reported, even when it was successfully administered to autistic children.[32] The primary reason being that its molecular structure is bioidentical (identical to the GcMAF made by the body). So long as the GcMAF is pure, there is no reason to expect any side effects.

A pure GcMAF protein contains only molecules of a single protein (no other molecules of any kind). Impurities cause compromised effectiveness, adverse reactions, and symptoms of toxicity. Beware because there are "bootleg" or phony versions of GcMAF being manufactured that are impure, contaminated, and consequently potentially toxic. These products are often sold over the internet, and their packaging may look identical to the real product. It is best to purchase GcMAF directly from the clinics in Japan[33] or Europe. These clinics usually require the patient to undergo GcMAF treatment at the clinic, and then dismiss the patient

with enough injectable product or oral colostrum MAF product to follow up at home.

Current Global Status of GcMAF Therapy and Oral Colostrum-Derived MAF

Accumulated evidence suggests that GcMAF is a potent factor that activates tumoricidal macrophages, resulting in tumor regression. Thousands of cancer patients over the last two decades have been treated with injectable GcMAF in the United Kingdom, Europe and Asia. But many of its practitioners have faced adversity from government authorities. In short, GcMAF therapy is no stranger to controversy nor even to conspiracy theory. Some time ago a UK factory where GcMAF was being manufactured was closed under claims that the product "might be contaminated." Importation of injectable GcMAF into the UK and the US has been halted. To date, oral Cd-MAF (colostrum-derived) can still be purchased and imported into the US for personal use.

It is estimated that more than 300 doctors in 80 countries are now using both injectable GcMAF and oral CdMAF. The laboratory and clinical study of cancer immunotherapy is rapidly advancing; but unfortunately, current research of GcMAF is limited to Japan and selective parts of Europe. Several large pharmaceutical companies and their partner regulatory agencies have done much to discredit - and make unavailable - the product. The internet is full of quackery websites discrediting GcMAF and the doctors who advocate its use. It is tragic that this harmless body protein, studied for over 25 years as a promising immunotherapy agent, is not given more consideration for further research in the US.

Despite the doubts raised as a result of three retracted clinical studies, the efficacy and safety of this product has been endorsed in numerous other studies. Because GcMAF is produced by the human body, it is non-toxic (provided the manufacturing process is pure). At present, it appears non-scientific reasons are preventing FDA approval. With so many lives at risk and no real cures at hand, the FDA would be wise to allow GcMAF therapy to proceed with the requirement of real-time adverse event reporting to ensure patient safety.

References

1. Dr. Nobuto Yamamoto was born in Japan on April 25, 1925. Dr. Yamamoto, who holds a PhD in biochemistry from Gifu University in Japan, has been a US-based researcher since 1959, when he was invited to be a visiting associate researcher at the Fox Chase Cancer Center in Philadelphia. He was later hired as a biophysics and biochemistry researcher at the National Institute of Health in Maryland before becoming associated, in multiple capacities, with Temple University in Philadelphia until 1980. In 1980, Dr. Yamamoto was appointed Professor of Microbiology and Immunology at Hahnemann University School of Medicine, where he continued his research in viral evolution. His immunological studies focused on the mechanism of macrophage activation and GcMAF. When Dr. Yamamoto retired from Hahnemann University in 1990, he returned to Temple University Medical School as a Research Professor of Biochemistry and studied the tumoricidal capacity of macrophages activated by GcMAF and cancer therapy with GcMAF. In 1994, Dr. Yamamoto founded the Socrates Institute for Therapeutic Immunology, from which he continues to study the therapeutic efficacy of GcMAF for a variety of cancers and HIV.
2. Yamamoto N, Kumashiro R. Conversion of vitamin D3 binding protein (group specific component) to a macrophage activating factor by the stepwise action of ß-galactosidase of B cells and sialidase of T cells. *J Immunol*. 1993;151: 2794–2802.
3. Yamamoto N, et al. Vitamin D3 binding protein required for in vitro activation of macrophages after alkylglycerol treatment of mouse peritoneal cells. *Immunology*. 1991;74:420–424.
4. Yamamoto N, Homma S Vitamin D3 binding protein (group specific component) is a precursor for the macrophage-activating signal. *Proc Natl Acad Sci USA*. 1991;88:8539–8543.
5. Corbeled M, Narayana VR, Yamamoto N. The value of serum alpha-N-acetylgalactosaminidase measurement for the assessment of tumour response to radio- and photodynamic therapy. *Br J Cancer*. 1998 Mar; 77(6):1009-14.
6. Naraparaju VR, Yamamoto N. Roles of b-galactosidase of B lymphocytes and sialidase of T lymphocytes in inflammation primed activation of macrophages. *Immunol Lett*. 1994;43:143–148.
7. Yamamoto N, Homma S. Vitamin D3 binding protein (group-specific component, Gc) is a precursor for the macrophage activating signal factor from lysophosphatidylcholine-treated lymphocytes. *Proc. Natl. Acad. Sci. USA*. 1991;88:8539-8543.
8. Yamamoto N, Ueda M, Benson CE. Treatment of HIV-infected patients with Gc protein-derived macrophage activating factor (GcMAF) eradicates HIV-infection. Proc 13th Int Cong Immunol. Italy: Medimond, Bologna. 2007; 35–38.
9. Yamamoto N, Kumashiro R.. Conversion of vitamin D3 binding protein (Group specific component) to a macrophage activating factor by the stepwise action of b-galactosidase of B cells and sialidase of T cells. *J Immunol*. 1993;151:2794–2802.
10. Yamamoto N, Homma S, Millman I. Identification of the serum factor required for in vitro activation of macrophages: Role of vitamin D3 binding protein (Group specific component, Gc) in lysophospholipid activation of mouse peritoneal macrophages. *J Immunol*. 1991;147:273–280.
11. Yamamoto N, et al. Macrophages Activated By GCMAF Develop Enormous Variation of Receptors That Recognize and Eradicate Adenocarcinomas. Clinical Immunology, Volume 119, Supplement 1, 2006, Page S96. FOCIS 2006 Abstract Supplement - 6th Annual Meeting.
12. Yamamoto N, et al. Macrophages Activated By GCMAF Develop Enormous Variation of Receptors That Recognize and Eradicate Adenocarcinomas. *Clinical Immunology.* 2006.
13. Thyer L, et al. GC protein-derived macrophage-activating factor decreases α-N-acetylgalactosaminidase levels in advanced cancer patients. *Oncoimmunology*. 2013;2(8): e25769.
14. Yamamoto N, Suyama H, Yamamoto N. Immunotherapy for prostate cancer with Gc protein-derived macrophage-activating factor, GcMAF. *Transl Oncol*. 2008;1: 65-72.
15. Gregory KJ, et al. Vitamin D Binding Protein-Macrophage Activating Factor Directly Inhibits Proliferation, Migration, and uPAR Expression of Prostate Cancer Cells. *PLoS ONE*. 2010;5(10): e13428.
16. Yamamoto N, Suyama H, Yamamoto N, Ushijima N: Immunotherapy of metastatic breast cancer patients with vitamin D-binding protein-derived macrophage activating factor (GcMAF). *Int J Cancer*. 2008;122: 461-467. – **Retraction**: Immunotherapy of metastatic breast cancer patients with vitamin D-binding protein-derived macrophage activating factor (GcMAF). [Int J Cancer. 2014]
17. Yamamoto N, Ushijima N, Koga Y: Immunotherapy of HIV infected patients with Gc protein-derived macrophage activating factor (GcMAF). *J Med Virol.* 2009;81:16-21. **Retraction**. Immunotherapy of HIV-infected patients with Gc protein-derived macrophage activating factor. [J Med Virol. 2014]
18. Yamamoto N, Suyama H, Nakazato H, Yamamoto N and Koga Y: Immunotherapy of metastatic colorectal cancer with vitamin D-binding protein-derived macrophage activating factor, GcMAF. *Cancer Immunol Immunother*. 2008;57: 1007-1016. – **Retraction**: Immunotherapy of metastatic colorectal cancer with vitamin D-binding protein-derived macrophage-activating factor, GcMAF. [Cancer Immunol Immunother. 2014]
19. http://patents.com/us-5177002.html - In vitro enzymatic conversion of glycosylated human vitamin D binding protein to a potent macrophage activating factor: Abstract: A novel, potent macrophage activating factor is prepared in vitro by treating glycosylated human group-specific component, also known as human vitamin D-binding protein, with glycosidases. Group-specific component, which is isolated from retired blood by known procedures, is thus readily converted to a highly potent macrophage activating factor.
20. http://www.freepatentsonline.com/20150361151.pdf
21. Mohamad SB, Nagasawa H, Uto Y, Hori H. Preparation of Gc protein-derived macrophage activating factor (GcMAF) and its structural characterization and biological activities. *Anticancer Res*. 2002;22:4297–300.
22. Pacini S, et al. Effects of vitamin D-binding protein-derived macrophage-activating factor on human breast cancer cells. *Anticancer Res*. 2012;32:45–52.
23. Homma S, Yamamoto N. Activation process of macrophages after in vitro treatment of mouse lymphocytes with dodecylglycerol. *Clin Exp Immunol*. 1990;79:307–13.
24. Thyer L, Ward E, Smith R, et al. GC protein-derived macrophage-activating factor decreases alpha--acetylgalactosaminidase levels in advanced cancer patients. *Oncoimmunology*. 2013;2:e25769.
25. MITOcare GmbH & Co.KG; Firmensitz: Lindenschmitstr. 44; 81371 München; https://www.gesundheitsfundament.de/shop/mitocare-big-harmony-activator-540-kps/. Accessed January 28, 2018.
26. Uto Y, et al. Degalactosylated/Desialylated Bovine Colostrum Induces Macrophage Phagocytic Activity Independently of Inflammatory Cytokine Production. *Anticancer Res.* 2015;35(8), 4487-4492.
27. Yamamoto N, et al. Deglycosylation of serum vitamin D3-binding protein by alpha-N-acetylgalactosaminidase detected in the plasma of patients with systemic lupus erythematosus. *Clin Immunol Immunopathol*. 1997;82:290-8.
28. Reddi AL, et al. Serum alpha-N-acetylgalactosaminidase is associated with diagnosis/prognosis of patients with squamous cell carcinoma of the uterine cervix. *Cancer Lett*. 2000;158:61-4.
29. Korbelik M, Naraparaju VR, Yamamoto N. The value of serum alpha-N-acetylgalactosaminidase measurement for the assessment of tumour response to radio- and photodynamic therapy. *Br J Cancer*. 1998;77:1009-14.
30. Mohamad SB, et al. Tumor cell alpha-N-acetylgalactosaminidase activity and its involvement in GcMAF-related macrophage activation. *Comp Biochem Physiol A Mol Integr Physiol*. 2002;132:1-8.
31. Saburi, Ehsan, et al. Is α-N-acetylgalactosaminidase the key to curing cancer? A mini-review and hypothesis. *Journal of BU ON.*: official journal of the Balkan Union of Oncology. 2017;22.6: 1372.
32. Bradstreet J, Vogelaar E, Thyer L. Initial observations of elevated Alpha-N-acetylgalactosaminidase activity associated with autism and observed reductions from GC protein-macrophage activating factor injections. *Autism Insights*. 2012;4:31–8.
33. Saisei Mirai is a medical organization in Osaka, Japan, whose purpose is to treat patients and develop and produce therapies, in particular immunotherapies such as GcMAF and colostrum MAF.

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Enhancing the Skin Microbiome to Address Inflammatory Dermatologic Conditions

by Trevor Cates, ND

Imbalances in the skin microbiome play a key role in skin disorders; and while most microbiome research to date has been focused on the gastrointestinal tract, more research is being revealed about the cutaneous microbiome and its important role in maintaining skin health. Both internal and external factors are at play in the skin microbiome and dysbiosis. More research is unfolding about these connections, which can point to a new way of looking at dermatologic conditions and how we can transform the cutaneous microbiota to address inflammatory conditions such as acne, atopic dermatitis, rosacea, and premature aging.

It is estimated that human skin is inhabited by approximately one million bacteria/cm,[1] and, the microbiota varies around different areas of the body as well as amongst different individuals. Lifestyle, environment, hygiene, diet, age, and sex all greatly impact the makeup of the skin microbiome.[2] It's interesting to consider the various lifestyle factors and hygiene practices that have changed over the last few decades and how they have contributed to the high rates of acne, atopic dermatitis and other inflammatory skin disorders. The germ-phobia trend in Western cultures has altered our microbiota in various areas of the human body, and the skin is not immune to this impact.

The skin microbiome is also impacted by where individuals live and with whom they live. People who live in rural areas have greater diversity than those living in urban environments,[3] and people in the same household can impact each other's skin microbiomes.[4] This puts even greater emphasis on the idea that when treating an individual, it may be particularly important to look at the home environment and the health and practices of their co-habitants, including pets in the home.

Research shows that commensal skin microbiota (*Staphyloccocus epidermidis*) influence skin immunity and limit pathogen invasion by inducing specialized T cells to move to the epidermis.[5] This indicates the importance of maintaining a balanced skin microbiome to protect the skin from disease.

And the internal connection with the gut is key as well. Due to research on the gut-brain-skin axis, we're discovering more about the connection between stress, anxiety, and depression with changes in the gut microbiota and leaky gut, which creates can trigger inflammatory dermatologic issues, such as acne.[6,7] Knowing this helps us draw the connection between addressing gut dysbiosis and permeability and how it, in turn, has the potential to improve the skin microbiota. For years, naturopathic physicians have drawn the connection between digestive health and the skin, so this is not a new concept. However, it is nice to see the research supporting the correlation.

Superficially, an important factor in supporting the skin microbiota involves the pH of the skin. The external pH of human skin has a natural pH level of about 4.5 pH.[8] This mildly acidic environment helps keep the skin's microbiota in balance. On the other hand, a more alkaline pH (around 8 to 9) can disrupt the microbiota.

Considering water has a pH of 7, it is too alkaline for optimizing skin pH. After rinsing with water, a more optimal cutaneous pH can be supported by using skincare products in the 4.5-5.0 pH range. Many common skincare products, including soaps, cleansers, masks, moisturizers, and over-the-counter topical medications have a pH of 5.5 and higher, which can make the skin more prone to infections and premature aging.[9]

A common approach by natural or holistic-minded individuals to topical skincare is that less is more. People will sometimes minimize their skincare routine to reduce exposure to toxic skincare ingredients, so they resort to simplifying their skincare to water, bars of soap, and natural oils such as coconut oil. Unfortunately, this approach does not actually promote an optimal skin microbiome. It does help reduce exposure to known endocrine disruptors such as parabens and di-ethyl phthalate (found in fragrance), but it does not support the mild acidity of the skin, which, in turn, supports the skin microbiome.

In healthy individuals without chronic skin concerns, their skin's acidic mantle will likely rebalance and restore the skin after the use of more neutral or alkaline product applications on the

skin. But, if we're looking at individuals with dermatologic skin disorders whose skin microbiome is already disrupted, it is unlikely their skin will be able to rebalance as easily. Instead, supporting the individual's skin with skincare and topical treatments in the ideal pH range may support their recover from inflammatory skin conditions more rapidly.

When looking for skincare products and topical treatments with the 4.5-5.0 pH range, there are a few things to consider. Skincare companies generally do not list the pH of their products on the label, but they should have that information when you contact the manufacturer. When looking at labels, you can identify certain ingredients that indicate a lower pH, such as hyaluronic acid, alpha hydroxy acids, amino fruit acids and retinoic acids. At the same time, skincare products with too low of a pH can also disrupt the skin's natural barrier and irritate the skin, so the formulations need to include other ingredients to ensure the ideal pH range. In addition to ingredients with a low pH, there are others that naturally support the acid mantle, such as argan kernel oil.

In addition to the pH of products, other aspects of topical products can significantly impact the skin microbiota. Antibacterial agents such as tricolan and topical antibiotics, for example, can disrupt the microbiota balance. Deodorant and anti-perspirant has been shown to increase Actinobacteria, therefore modifying the microbiota and leading to an overgrowth of odor-producing bacteria.[10]

The natural inclination is to consider topical probiotics to support the skin microbiome, and the research shows some positive movement in this direction. Probiotics applied topically appear to adhere to human keratin and prevent biofilm formation.[11] Research shows that topical products containing prebiotics and/or probiotics may help skin by modulating the immune system and may provide therapeutic benefits for atopic diseases.[12]

Certain topical probiotic formulations have the potential to prevent skin dysbiosis, stimulate the activity and growth of beneficial microbiota, and improve skin barrier function.[12] This is particularly important for dermatologic conditions with dry, sensitive, and reactive skin. It is also something to consider after individuals are exposed to invasive cosmetic procedures or overzealous hygienic routines, as well as after using medications such as antibiotics and corticosteroids.

At the same time, with 1 million bacteria on the skin and variability in microbiota in moist, sebaceous and dry areas as well as between individuals, more research is needed to determine the exact strains of probiotics that will be the most therapeutic for various dermatologic conditions. We can't assume that commensal bacteria residing on skin of healthy individuals is going to be therapeutic in individuals with impaired skin immune function and disease. Until there is more information on testing for and treatment using specific strains of microorganisms, we can focus on the tools we currently have to support balanced microbiota.

This means, supporting the gut microbiome with a fiber-rich diet and including foods containing active cultures such as fermented vegetables. Laboratory testing to identify gut dysbiosis issues can help direct the appropriate treatment such as with oral probiotics. In addition, using a skincare regime with a pH range of 4.5-5.0 can topically support the skin barrier function and acid mantle. Compounded topical treatments to address skin dysbiosis may also help treat certain skin conditions. With time, research and experience, more supportive treatments will be unveiled that will balance the skin microbiota to treat inflammatory dermatologic conditions.

References

1. Grice EA et al. Topographical and temporal diversity of the human skin microbiome. *Science* 2009; 324: 1, 190-1, 192.
2. Rodrigues H. The cutaneous ecosystem: the roles of the skin microbiome in health and its association with inflammatory skin conditions in humans and animals. *Vet Dermatol*. 2017;28(1):60-e15.
3. Hanski I, et al. Environmental biodiversity, human microbiota, and allergy are interrelated. *Proc Natl Acad Sci USA.* 2012; 109(21),8334-339.
4. Song SJ, et al. Cohabiting family members share microbiota with one another and with their dogs. *Elife* 2013; 2: e00458.
5. Naik S, et al. Commensal–dendritic-cell interaction specifies a unique protective skin immune signature. *Nature*. 2015;520(7545):104-108.
6. Arck, P, et al. Is there a 'gut–brain–skin axis'?. *Experimental Dermatology*. 2010;19: 401–405.
7. Bowe W, Pate NB, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis: from anecdote to translational medicine. *Benef Microbes*. 2014;5(2):185–199.
8. Lambers H, et al. Natural skin surface pH is on average below 5, which is beneficial for its resident flora. *Int J Cosmet Sci*. 2006;28(5):359-70.
9. Jung YC, Kim EJ, et al. Effect of skin pH for wrinkle formation on Asian: Korean, Vietnamese and Singaporean. *J Eur Acad Dermatol Venereol*. 2013;27(3):e328-32.
10. Callewaert C, et al. Deodorants and antiperspirants affect the axillary bacterial community. *Arch Dermatol Res.* 2014;306(8):701-10.
11. Lopes EG, et al. Topical application of probiotics in skin: adhesion, antimicrobial and antibiofilm in vitro assays. *J Appl Microbiol*. 2017;122(2):450–461.
12. Al-Ghazzewi FH, Tester RF. Impact of prebiotics and probiotics on skin health. *Benef Microbes*. 2014;5(2):99–107.

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On the cover

Management of the Allergic Patient: The Role of Different Diagnostic Tests

by Diego Saporta, MD, and David Hurst, MD, PhD

Introduction

Management of the allergic patient is based on diagnosing which allergens trigger the symptoms and then mixing a vaccine that will be administered for several years. This treatment is known as immunotherapy.

Every allergist has encountered patients whose clinical presentation is that of allergy, but the testing is negative. Yet those same patients respond to nasal steroids and antihistamines. This quandary suggests that either the diagnosis or the test is wrong and has led to much discussion among clinicians.[1]

Most in-vivo allergy testing for in the USA and Europe relies on the skin prick test (SPT)[2] despite its sensitivity of 50-90%.[3] Prick testing is recognized to be extremely specific, which makes it ideal in selecting patients for scientific studies. This is accomplished by sacrificing sensitivity. The negative predictive value of a negative SPT for cat allergen is 72%.[4] The positive predictive value for *Dermatophagoides pteronyssinus* ranges from 29% to 43%.[5]

There are two schools of thought in reference to the management of the allergic patient. The most popular is that based on the work of Noon[6] in the 1900s and adopted as described in the guidelines of both the American Academy of Allergy Asthma & Immunology (AAAAI) and the European Academy of Allergy and Immunology (EAACI). The less popularized method is that derived from the work of Hansel and Rinkel[7,8] in the 1940s and adopted by a group of allergy practitioners that use these concepts according to the guidelines of the American Academy of Otolaryngic Allergy (AAOA),[9] Pan American Allergy Society (PAAS) [10] and American Academy of Environmental Medicine(AAEM).[11]

Despite huge advances in molecular biology, recognition and typification of allergens, and the ability to produce allergenic molecules that are safer to inject,[12] no major changes in skin testing techniques have occurred since this type of treatment was described in the 1930s -1940s.[13]

There are differences between these two schools in reference to the management of the allergic patient. These differences have existed for many decades. Most of the disagreement revolves around the definition of what constitutes an allergic reaction and what test is used for the diagnosis of significant allergens.

Understanding these differences becomes important when deciding which method to use when testing and treating a patient, as the management of these patients can potentially be different as will be explained in this paper.

The allergic patient has a dysfunctional immunological system, with a predominance of the Th2 response to allergens such as dust or animal dander. With Specific Immunotherapy (SIT), the Th2-dominant immune response involving IgE, IL-5, eosinophil, and mast cell production is modified towards a Th1 response,[14] leading to a decline in allergen-specific IgE, an increase in allergen-specific IgG and production of anti-inflammatory cytokines IL10 and IL12 [15,16]

SIT vaccines contain the allergens actually responsible for the symptoms that the patient develops. Vaccines can be given through injections ("allergy shots") or sublingual drops. Small amounts of the appropriate allergens are administered at small intervals with increasing doses over a long period of time. This leads to gradual desensitization to those offending allergens. Obviously, if the responsible allergens cannot be identified or are only partially identified, the results of the treatment will not be as successful.

Clinically important is the difference between the concept of the few "predominant" or "relevant allergens" versus the concept of the "total allergic load".

Relevant Allergens vs Total Allergic Load

The AAAAI and EAACI follow the concept of the "relevant allergen(s)" [17-19] The objective of the test is to diagnose only those allergens that are considered the most important for a geographical area or for a particular patient. According to this concept, using only this minimal number of allergens is sufficient to treat the patient, with the idea that these few allergens are responsible for the majority of the symptoms the patient has developed and therefore a vaccine containing only these allergen(s) will be sufficient to produce symptom-control.[17,20]

Practitioners from AAOA, PAAS and AAEM use the concept of the "total load."[21,22] The idea is that the patient is confronted with a multitude of aggressions (not only allergenic) that eventually lead to development of the symptoms. Decreasing the reactivity to as many of these environmental offenders as possible, the better the symptoms can be eliminated. Limiting the discussion only to the field of allergies, the "total load" concept dictates that the more allergens that can be desensitized, the better the long-term results of the treatment. Thus, the idea of treating any allergen that is positive by an allergy test becomes important.

Comparing the different tests used for the diagnosis of allergic conditions shows that there are significant differences in their potential for demonstrating reactive allergens.

Different Types of Tests

Allergy tests can be done "in-vitro" or "in-vivo." In-vitro tests are run on a sample of the patient's blood. Usually known as "RAST tests," they evaluate the presence of antibodies against different allergens. Technically, RAST refers to the original test that relied on radioactive technology which is no longer used. Current in-vitro tests use ELISA or Immuno-cap technology. Since the modern definition of allergy states that it is an IgE-mediated phenomenon, only in-vitro tests that measure IgE antibodies against the tested allergens are usually used. It is not infrequent for the usual battery of "RAST tests" to yield a negative result that contradicts a convincing patient history. This circumstance can be explained if the four types of hypersensitivity reactions described by Gell and Coombs are considered.[23] Classic IgE-mediated allergy is a Type 1 Gell and Coombs reaction, but the other three classes are triggered by other mechanisms that are not detected by an artificial mechanical test. This shortcoming is addressed by skin testing.

In-Vivo Tests

The most commonly used in-vivo tests are the SPT and the intradermal (ID) test. In the SPT, the allergen is deposited on the surface of the skin. Even though the prick device is pressed against the skin, the integrity of the skin is not violated, therefore the allergen will not penetrate the dermis. In the ID test, the allergen is directly introduced into the dermis by injection.

The allergy guidelines attribute to the SPT a high level of usefulness.[24] It is considered highly specific. Patients treated by most general allergists are usually managed based on the information obtained from SPT's, commonly performed with a multi-prick device so several allergens are tested at the same time. It would appear from the information in the guidelines[24] and other literature that the SPT is the "gold standard" considered as the "core diagnostic test for type I immediate allergy."[25]

SPT vs ID Test

A skin test being reactive (positive) is dependent on the mast cell degranulating and producing IgE, histamine, and other bio-active chemicals when challenged with an allergen to which the patient's mast cells have been sensitized.

Because the mast cells populate the dermis usually close to the blood vessels,[26] it is only logical to assume that the diagnostic power of a test that deposits the allergen literally in the vicinity of the mast cells (ID test) will have better diagnostic power than a test that deposits the allergen in the surface of the skin (SPT), where mast cells are likely to be absent.

According to the AAAAI allergy guidelines,[24] a negative SPT should be followed by an ID test, at an allergen concentration of no less than 1:1000 weight/volume (wt/vol) of the allergenic extract. (Weight/Volume is a rough unit of concentration commonly used with allergenic extracts. At the present time, many allergens have been standardized so the number of allergy units per milliliter can be defined).

A negative SPT therefore does not exclude the possibility of the patient still being reactive to an injected allergen. A negative SPT can potentially be a false negative result and the tested allergen could still react to a more concentrated intradermal injection of 1:1000 wt/vol of the same allergen. Some studies support the ID test as being more sensitive than the SPT to diagnose reactivity to inhalant allergens [27-31] even studies by the main allergy community.[24 (statement 14),32]

If an SPT produces a large wheal, it is logical to assume that the patient is very reactive; but the opposite may not necessarily be true. If the patient is not very reactive and the SPT is negative, even the dilution of 1:1000 wt/vol may not be enough to demonstrate reactivity.

Another skin test, the Intradermal Dilutional Test or IDT (previously known as Skin End Point Titration or SET) uses multiple dilutions of each allergen.[33-35] The IDT is endorsed by the AAOA, PAAS and AAEM. Briefly, for each allergen to be tested, six successive serial five-fold dilutions of the allergen extracts are prepared. For allergen extracts that are available as 1:20 wt/vol, the six dilutions contain an allergenic concentration of: 1:100 for dilution #1; 1:500 for dilution #2; 1:2500 for dilution #3; 1:12,500 for dilution #4; 1:62,500 for dilution #5 and 1:312,000 for dilution #6.

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The sixth dilution is the weakest and contains an allergenic concentration of 1:312,000 wt/vol, which is much weaker than the 1:1000 wt/vol dilution advocated by the allergy guidelines. The first two dilutions of 1:100 wt/vol and 1:500 wt/vol contain allergen much stronger than the 1:1000 wt/vol dilution advocated by the allergy guidelines as the concentration for an ID to be injected after a negative SPT.[24]

Using multiple intradermal dilutions during skin testing (IDT) offers two advantages over the ID with one single dilution: safety and increased sensitivity: safety and sensitivity.

IDT enables the practitioner to diagnose patients that are very sensitive and therefore will react to small doses of allergen. Starting the skin injections with a weak concentration of the allergen (#6 dilution) adds a tremendous amount of safety to the test. Challenging a patient initially with the sixth dilution and gradually increasing the strength of the injected allergen is much safer than an injection of a concentration of 1:1000 wt/vol dilution of the same allergen after a negative SPT. This is why it is not surprising that the IDT proved to be very safe in a prospective study.[28]

IDT enables the practitioner to diagnose patients with low level of reactivity. These patients are not very sensitive. They require a much larger dose of allergen to elicit a skin reaction than offered by the prick test. Often, even an ID injection of 1:1000 wt/vol may be too weak to trigger a skin response, therefore eliciting a false negative result. Yet, the patient may react to an allergen dilution of 1:500 wt/vol (2nd dilution) or 1:100 wt/vol (1st dilution). (NOTE: Not all allergy practitioners use dilution #1 in their ID tests).

It has been argued that ID tests using these high concentrations of allergens identify patients with such low levels of clinical sensitivity, that these may be false positives. This is why test results obtained with the stronger concentrations of allergen are disregarded by many in the allergy community.[24 (summary statement 30),36]

From a clinical point of view, it is observed that patients who are "low reactors" (identified only by reactions to the stronger concentrations of dilutions #3, #2 or #1) may have significant allergic disease such as nasal allergies, asthma, chronic sinusitis, chronic otitis media or skin rashes. These patients will not be diagnosed using only a prick test, and, as explained above, often will be missed by a single dilution ID of 1:1000 wt/vol. This is of clinical significance as treating low reactor patients with immunotherapy leads to clinical improvement. This is obvious and commonly observed by practitioners that use these concepts, but there are few references in the literature to support this.[29]

Practical Application from Testing an Allergy Patient with an IDT

The information provided by the IDT enables mixing a vaccine whose composition will be in accordance to the level of reactivity for each allergen in each individual patient. For example, a patient's treatment serum might include dust mite allergen at a concentration corresponding to dilution #5 and mold allergen at a concentration of dilution #2. This allows starting immunotherapy treatment with safety but at the same time with efficacy. Patients treated with this technique develop clinical improvement soon after onset of treatment. Because the initial level of reactivity was determined for each allergen, dose advancement usually proceeds without major problems leading to a successful treatment of the different allergic conditions mentioned above.

Surveys of AAAAI allergists have found cases of mortality during testing or immunotherapy administration.[37,38] Patients with asthma are at higher risk for severe reactions during testing and immunotherapy based on that technique.[39-41] Fatalities from immunotherapy, although rare, are more common in asthmatics.[38,42]

A survey of the AAOA members who were using IDT reported no cases of mortality during testing or immunotherapy administration.[43] Other studies corroborate the safety profile of the IDT and immunotherapy administration based on results from over 4.2 million injections.[44]

A relatively common occurrence in an allergy practice is to see patients who, following SPT, were told they had allergic rhinitis and/or asthma and yet were only offered medical intervention. There is no need to do an allergy test in order to prescribe medications. A good history will help the practitioner to plan implementation of environmental control measures in addition to prescribing appropriate medications. The same observation is valid for the patient that less frequently had a combination of a SPT and a single dilution ID test or a blood test with only a few positive results: diagnosis is done and medication is prescribed. Perhaps this may reflect the experience of some allergists that after their patients had been treated for the few allergens discovered by SPT their symptoms responded poorly.

Dr. Saporta completed his training in 1990 at Columbia Presbyterian Hospital in New York City. He is board certified in otolaryngology and has been a fellow of the American Academy of Otolaryngic Allergy (AAOA) since 2001. His private practice in Elizabeth, New Jersey, is heavily oriented to the management of allergic conditions. Interested in the use of oral vaccines since early in his practice, Dr. Saporta presented a protocol for sublingual immunotherapy at the 64th annual meeting of the AAOA that since then has been successfully used for the management of allergic rhinitis with or without asthma.

When IDT is utilized and additional "minor" allergens are detected and treated, improvement is then accomplished. Sometimes patients "need" the result of the test to convince them that they really have allergy. Ideally, testing should be reserved for those patients that may benefit from immunotherapy.

A classic example of this problem is the diagnosis "non-allergic rhinitis." In this case the SPT and the blood test are negative. The patient is offered avoidance of triggers and usual medications.[45] These cases are diagnosed as Local Allergic Rhinitis[46] or "Non-Allergic Rhinitis with Eosinophilia Syndrome (NARES)"[47]since both the SPT and the blood test are negative.

Advising patients to avoid triggers and administering medication may well keep the symptoms under control but will not treat the underlying inflammation that can end with airway remodeling, chronic otitis[48] and chronic sinusitis which may even require surgery after years of disease. When the clinical diagnosis of allergy by a trained physician does not match the test, the patient is usually deprived of the only treatment that can correct the underlying inflammation. Treating with immunotherapy carries risks, but immunotherapy is the only treatment modality that can change the reactivity level of the affected patient, leading to clinically significant improvement[14] or even cure of the underlying inflammation. It has been demonstrated that immunotherapy prevents the development of asthma.[49]

The essential key to making an accurate and thorough diagnosis of which allergens affect a patient is using a testing method that provides maximum sensitivity with a minimum of false positives while using safe testing techniques. This can only be accomplished with the IDT. The use of serial dilutions in the IDT allows for maximal safety during testing, and enables the practitioner to mix a vaccine that will be highly effective with the least chances of eliciting a reaction during treatment. The authors, like other practitioners from the societies mentioned above, (AAOA, PAAS and AAEM), use IDT and plan immunotherapy according to the results of this test. Patients are tested for dust, animal dander, pollens and molds. With this approach, the authors have treated allergy patients very successfully for many years.

References

1. Oppenheimer J, Marshall G. What does a positive intradermal skin test result really mean? *Ann Allergy Asthma Immunol*. Apr 2009;102(4):267-26810.1016/S1081-1206(10)60329-8.
2. Heinzerling L, et al. The skin prick test – European standards. *Clinical and Translational Allergy*. 2013;3(1):3.3565910,10.1186/2045-7022-3-3.
3. Bernstein IL, Storms WW. Practice parameters for allergy diagnostic testing. Joint Task Force on Practice Parameters for the Diagnosis and Treatment of Asthma. *Ann Allergy Asthma Immunol*. Dec 1995;75(6 Pt 2):543-625.
4. Wood RA, et al. A comparison of skin prick tests, intradermal skin tests, and RASTs in the diagnosis of cat allergy. *Journal of Allergy and Clinical Immunology*. 1999;103:773-779.
5. King MJ, Tamulis T, Lockey RF. Prick puncture skin tests and serum specific IgE as predictors of nasal challenge response to dermatophagoides pteronyssinus in older adults. *Ann Allergy Asthma Immunol*. 2008 Jul;101(1):12-7.
6. Noon L. Prophylactic inoculation against hay fever. *The Lancet*. June 1911; 177(4580):1572–1573, 10 June 1911.
7. Hansel FK. Diagnosis of allergy of the nose and paranasal sinuses with particular attention to the atypical types. *Arch Otolaryngol*. 1941;34(6):1152-1162.
8. Rinkel, HJ. Inhalation allergy. I. The whealing response of the skin to serial dilution testing. *Ann Allergy*. 1949;7:625.
9. aaoaf.org. Offers courses on inhalant and food allergies for ENT practitioners.
10. paas.org. Offers courses on inhalant and food allergies to any interested practitioner.
11. aaemonline.org. Offers courses on inhalant and food allergies to any interested practitioner.
12. Stokes JR, Casale TB. Novel Approaches of Immunotherapy. *Current Treatment Options in Allergy*. 2014;1(1): 58.
13. Rinkel HJ. The Management of Clinical Allergy. Part I. General Considerations. *Arch Otolaryngol*. 1962;76(6):490-509.
14. Malling HJ, Weeke B. Immunotherapy. Position Paper of the European Academy of Allergology and Clinical Immunology. *Allergy*. 1993; 48(Suppl 14):9-35.
15. Chung F. Anti-inflammatory cytokines in asthma and allergy: interleukin-10, interleukin-12, interferon-gamma. *Mediators Inflamm*. 2001 Apr; 10(2): 51–59.
16. Bellinghausen I, Knop J, Saloga J. The Role of Interleukin 10 in the Regulation of Allergic Immune Responses. *Int Arch Allergy Immunol*. 2001;126:97–101.
17. Young A, Wu Y. Immunotherapy – Vaccines for allergic diseases. *J Thorac Dis*. 2012 Apr 1; 4(2): 198–202.
18. Bousquet J, Lockey R, Malling HJ. Allergen immunotherapy: Therapeutic vaccines for allergic diseases A WHO position paper. *JACI*. 102 (4):558–562.
19. Daigle BJ, Rekkerth DJ. Practical recommendations for mixing allergy immunotherapy extracts. *Allergy Rhinol* (Providence). 2015 Spring; 6(1): e1–e7.
20. www.aaaai.org/conditions-and-treatments/treatments/allergy-shots-(immunotherapy). Accessed October 20, 2017.
21. Rea WJ. *Chemical Sensitivity Volume 1 – Principles and Mechanisms*. CRC Press, Taylor & Francis Publisher, 1992. ISBN-13: 9780873719643.
22. Kroker GF. Diagnostic Synthesis: Part VI – The Total Load: Two Pearls. http://angryallergist.squarespace.com/the-angry-allergist-journal/2007/7/23/diagnostic-synthesis-part-vi-the-total-load-two-pearls.html
23. Gell PGH, Coombs RRA, eds. *Clinical Aspects of Immunology*. Oxford, England: Blackwell; 1963.
24. Bernstein L, et al. Allergy Diagnostic Testing: An Updated Practice Parameter. *Ann Allergy Asthma Immunol*. 2008; 100 (3): S 3.
25. Heinzerling L, Mari A, Bergmann KC et al. The skin prick test – European standards. *Clin Transl Allergy*. 2013; 3: 3.
26. Janssens AS, et al. Mast cell distribution in normal adult skin. *J Clin Pathol*. 2005 Mar; 58(3): 285–289.
27. McKay SP, et al. Intradermal positivity after negative prick testing for inhalants. *Otolaryngol Head Neck Surg*. Aug 2006;135(2):232-235.
28. Gordon BR, et al. Safety of intradermal skin tests for inhalants and foods: a prospective study. *Int Forum Allergy & Rhinology*. Mar 2013;3(3):171-176.
29. Boyles, JH. A comparison of techniques for evaluating IgE-mediated allergies. *ENT Journal*. 2011;(90)4:164-169.
30. Hurst D. The clinical relevancy of intradermal test results in patients with allergic otitis media with effusion, rhinitis and/or asthma. Presented at AAOA Annual Meeting on September 28, 2013 in Vancouver, BC. IDT found more positive allergens than SPT. SPT detected 16% of allergens found by IDT. Patients reported significant improvement when treated for antigens detectable only by IDT.
31. Weiss J, Saporta D. Comparison of Inhalant Allergy Test Results by In Vivo and In Vitro Methods. Presented at the Pan American Allergy Society Annual Meeting on March 18, 2017 in Houston, Texas. The SPT was able to diagnose only 29% of the tests diagnosed by ID test. The SPT had a specificity of 93% but a sensitivity of 40%. ID test also performed better than the in-vitro tests.
32. *WAO White Book on Allergy.* www.worldallergy.org/UserFiles/file/WhiteBook2-2013-v8.pdf. page 111.
33. Fornadley JA. Skin Testing in the Diagnosis of Inhalant Allergy. In *Allergy and Immunology, an Otolaryngic Approach*. JH Krouse, SJ Chadwick, BR Gordon, and MJ Derebery, Eds., Ch 8:114-123, Lippincott Williams & Wilkins, Philadelphia, PA, USA, 2002.
34. King HC, Mabry RL, Mabry CS. *Allergy in ENT Practice*. New York: Thieme, 1998.
35. Mabry RL. Skin End Point Titration, AAOA Monograph Series. Thieme Medical Publishers, New York, NY, USA, 1994.
36. Calabria CW, Hagan L. The role of intradermal skin testing in inhalant allergy. *Ann Allergy Asthma Immunol*. Oct 2008;101(4):337-347; quiz 347, 418.
37. Reid MJ, et al. Survey of fatalities from skin testing and immunotherapy 1985–1989. *J Allergy Clin Immunol*. 1993;91:6–15.
38. Bernstein DI, et al. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990–2001. *J Allergy Clin Immunol*. 2004;113:1129–1136.
39. Davis WE, et al. Anaphylaxis in Immunotherapy. *Otolaryngol Head Neck Surg*. 1992 Jul;107(1):78-83.
40. Borchers AT, Keen CL, Gershwin ME. Fatalities following allergen immunotherapy. *Clin Rev Allergy Immunol*. 2004 ,27(2):147-58.
41. Gordon BR. Prevention and management of office allergy emergencies. *Oto Cli NA*. 1992 Feb;25(1):119-34.
42. Lockey RF, et al. Fatalities from immunotherapy and skin testing. *JACI*. 1987;79(4):660-77.
43. Cook PR, et al. Systemic Reactions to Immunotherapy: The AAOA Morbidity and Mortality Survey. *Otolaryngol Head Neck Surg*. 1994;110:487-493.
44. Hurst DS, et al. Safety of home-based and office allergy immunotherapy: A multicenter prospective study. *Otolaryngol Head Neck Surg*. 1999 Nov;121(5):553-61.
45. www.mayoclinic.org/diseases-conditions/nonallergic-rhinitis/diagnosis-treatment/drc-20351235.
46. Rondon C, et al. Local allergic rhinitis: allergen tolerance and immunologic changes after preseasonal immunotherapy with grass pollen. *Journal of Allergy and Clinical Immunology*. Apr 2011;127(4):1069-1071.
47. Ellis AK, Keith PK. Nonallergic rhinitis with eosinophilia syndrome. *Curr Allergy Asthma Rep*. 2006 May;6(3):215-20.
48. Hurst D. *Freedom from Chronic Ear Infections*. Back Channel Press, 2011. ISBN1934582379, 9781934582374
49. Jacobsen L, et al. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. *Allergy*. Aug 2007;62(8):943-948.

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Vaccination's Dilemma: Unsafe at Any Dose

by Richard Gale, and Gary Null

Progressive Radio Network

The CDC and advocates for mandatory vaccination consistently repeat a dangerous mantra that finds no warranted basis in medical science. This monolithic industry, now a massive network of private and government institutions, state senates, and supported by a compliant media, want us to believe that science has finally settled the debate over vaccine safety and efficacy. All the data is in, so we are told, and no further research and discussion is necessary because vaccines have been officially ruled to pose no neurological and immunological risk to infants, children, pregnant mothers, adults and the elderly. This official policy is founded upon flawed premises and a primitive understanding about the complexities of the human body and its multifaceted immunological system.

This argument's fallacy is actually quite simple. Valid science is never settled. The myth of "settled science," which is especially endemic to the biological and medical sciences that rely on private financial interests, is sheer propaganda. Valid science, on the other hand, constantly seeks new discoveries to acquire further knowledge and greater understanding. The pursuit to fully comprehend the complexity of our biological, immunological and physiological systems, therefore, is in perpetual infinite regress. Today's justifications for medical intervention, whether by drugs or vaccines, eventually become tomorrow's barbarities as science further penetrates the hidden functions and operations of the human organism. Hence, valid medical research should elicit new questions and not settle upon incomplete facts that are then proselytized as universal truths.

A medical science that refuses to ask new questions and settles upon disputed beliefs to sustain an industry's financial portfolio is Scientism, a quasi-faith-based creed now institutionalized to promulgate repressive laws. These laws then advance Scientism's authority. Unfortunately, today this accurately represents the sad state of vaccine research and vaccination policy. Modern vaccine science and conventional medicine, in general, have morphed into a new fascism, a rigid doctrine that has sacrificed the foundations of scientific integrity on the altar of institutional greed, privilege, and profit.

During the past decade, we have witnessed outbreaks of infectious disease among the fully vaccinated. We observe new viral strains appearing that escape current immunization. There are rising rates in autism and neurological disorders and increases in autoimmune conditions never before observed in large percentages of children. And there is a growing body of research pointing to vaccination's adverse effects upon our immune systems. All of these trends, and many more, give sufficient reason to undertake a serious review of official claims over vaccine safety and efficacy. The evidence for the alarming rates in childhood illnesses parallel to the ever-increasing number of childhood vaccinations and the government's ridiculous one-size-fits-all policy behind mass, indiscriminate vaccination should convince us that vaccine safety is far from a settled matter.

The official CDC position on vaccines is that they are "unavoidably unsafe." As New York University's professor of law Mary Holland has repeatedly stated, the CDC can't have it both ways. Vaccines cannot be simultaneously safe and unsafe. Yet, by mincing terms, spinning propaganda, and misinterpreting and manipulating scientific research to whitewash vaccine's life-threatening risks, this is what the government pressures parents to believe.[1]

If we can accept the claim that vaccines are "unavoidably unsafe," then the question is how unsafe are they? And now we possess an enormous body of yet to be challenged research, clinical trials, case examples of severe vaccine injury, and court compensations paid out to families with vaccine-injured children to conclude that vaccine development has a very long way to go before a medically proven safe vaccine will ever be created. Unfortunately, it is our opinion that this research is being ignored or at best marginalized by the most rabid CDC supporters and proponents of mass vaccination.

If the most compelling and thorough medical research indicates that there is no such thing as a safe vaccine, then what are we to make about those in the growing community opposing vaccination who demand safer vaccines while claiming to be pro-vaccine?

First, we must acknowledge that all vaccines are "unavoidably unsafe"; this was a 2011 Supreme Court ruling in the Bruesewitz versus Wyeth case.[2] Therefore, all vaccines on the market are categorically unsafe. Perhaps in some distant future a vaccine, which remains only in the imagination of science fiction, will be developed to effectively and safely immunize against an infectious disease. So far, such a vaccine does not exist. Therefore, conscientious efforts to adhere to the precautionary principle and

vigilant and consistent evaluation and reevaluation of the risks and benefits of vaccination is both essential and a human right that governments should encourage, protect, and uphold.

The majority of vaccine ingredients have been shown repeatedly to have toxic consequences contributing to serious neurological and autoimmune conditions. These effects can be immediate, such as in the case of a child who undergoes seizures and is left with permanent neurological damage shortly after vaccination. Effects through repeated vaccination can also be accumulative and display symptoms many years later. In fact, there is very little scientific data, and nothing conclusive, about repeated vaccinations' long-term and accumulative immunosuppressive risks. The vaccine industry continues to rely upon outdated research, industry-funded studies, conflicts of interest with federal agencies and even scientifically irrelevant data to make its case that vaccine additives and ingredients pose no medical risks. What the industry's arsenal of research sorely lacks is biological and gold standard placebo-controlled clinical trials to support this position. In short, accepted vaccine research is little more than junk science. And junk science can make for the best propaganda to convince a population into the deception of vaccine safety. Joseph Goebbels understood this all too well when he stated, "A lie told often enough, people will believe it, and you will even come to believe it yourself."

For those who demand the removal of vaccines' toxic ingredients yet remain pro-vaccine in principle, another and perhaps darker equation of vaccine risks is being ignored or seriously misunderstood. It is not simply the aluminum compounds, ethyl mercury or thimerosal, Polysorbate 80, formaldehyde and other vaccine additives that are associated with vaccines' portfolios of risks and adverse reactions, including those listed in every vaccine manufacturing and product insert and found in the National Institutes of Health PubMed database of peer-reviewed medical literature. These compounds' neurotoxic risks are well known, and physicians, pediatricians, and scientists are increasingly being forced to acknowledge them and question the vaccine paradigm.

For example, any and every vaccine that contains aluminum, in any amount, is categorically unsafe regardless of a person's age. This principle should be accepted as a biological and medical fact without question, yet pro-vaccinators deny it outright. In 2015, autoimmune disease researcher Dr. Yehuda Shoenfeld at Tel Aviv University published the definitive textbook on vaccines' adverse effects that are now contributing to a wide variety of autoimmune diseases, including fibromyalgia, acute disseminated encephalomyelitis, narcolepsy, connective tissue disease, rheumatoid arthritis, chronic fatigue syndrome, lupus, type 1 diabetes, and a host of others. The majority of the 37 scientific papers in Shoenfeld's *Vaccines and Autoimmunity* identify the adjuvant aluminum as a crucial culprit contributing to the epidemic rise in autoimmune disorders both in the US and abroad.[3]

In mid-2014, concerns over aluminum adjuvants in vaccines, and the HPV vaccine in particular, reached the French Parliament for review. Unlike scientific committee reviews conducted in the US Congress, French politicians publicly weighed in carefully on the data behind the increase in HPV vaccine-injuries in order to rule on the benefits and risks of promoting the Gardasil and other vaccines containing aluminum.[4] France has now established a precedent for the way other governments' health officials and legislative bodies should address the growing questions toward vaccine safety.

Pro-vaccine political correctness is fundamentally based upon the faulty assumption that only known neurologically toxic ingredients, such as aluminum and mercury, need to be removed or replaced with safer compounds. There is no sound argument against the removal of these ingredients that will make vaccines safer. Federal agencies tell us that these toxic metals are in insufficient amounts to pose a toxicological risk and are readily expelled naturally by a child's body. Although no amount of aluminum and mercury in any quantity has been proven absolutely safe, when an infant receives three, four, or more vaccinations during a single doctor's visit, the amount of toxins introduced into its body mounts well above the EPA's and FDA's level of safety.

Fifteen years ago, the CDC's argument may have been sufficient to increase confidence in today's dominant vaccine paradigm. But science advances. Knowledge of the human genome, the emergence of the new science of epigenetics, and a deeper understanding of the body's immunological activity is opening our horizons to a larger panorama of bio-molecular possibilities and the viral and bacterial activities that are forcing a growing number of scientists to conclude that we really don't know as much about vaccination's impact and risks upon the human organism as we previously thought.

If it can be ascertained that there are serious health risks from the viral and bacterial components that go into a vaccine and the genetic debris and contamination due to vaccine manufacturing's primitive technology, then the removal of toxic chemicals is insufficient for safer vaccines. However, one wishes to interpret it, vaccines introduce pathogens into the body. These pathogens interact with our body's cells and DNA in known and unknown ways. Our medical understanding about host-pathogen interactions and viral epigenetics are adolescent. For example, in 2010, researchers from the National Brain Research Center in India reported that our scientific understanding of viral "mechanisms of epigenetic control of gene expression continues to baffle scholars." What we know so far, the scientists conclude, "is still complete."[5] Evidence suggests that undesirable viral and genetic activity introduced through vaccines is contributing to the every-increasing infectious disease outbreaks among heavily vaccinated populations, such as the April 2016 mumps outbreak at Harvard University infecting over 40 students and the many pertussis outbreaks during the past several years. That is, infected persons are mostly fully vaccinated. Consequently, we are witnessing what European scientists warned in 2012, that viral epigenetic mechanisms are steadily evading our immune systems.[6] Therefore, vaccines are increasingly becoming ineffective as new viral strains emerge and the length of immunity provided by vaccines is lessening.

The Human Genome Project ended less than two decades ago. Genomics' new subdivision of epigenetics has only gained attention during the past ten to fifteen years. Already epigenetics is turning our earlier beliefs about DNA and genes upon its head. Barbara Lo Fisher summarizes epigenetics as "stimuli-triggered changes in gene expression that are inheritable

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and occur independent of changes to the underlying DNA sequence."[6] In other areas of epigenetic and toxicological research, other than vaccine science, there is greater acceptance of environmental factors' affects upon our body's DNA. It is now accepted that chemicals commonly found in everyday products, such as the endocrine disruptive phthalates and bisphenol-A, are altering gene expression and creating havoc with normal hormonal activity. Food companies are increasingly becoming convinced that pesticides used in huge amounts on genetically modified crops are interfering with our bodies' genes and are removing GMO ingredients from their products. High fructose corn syrup, processed sugar, and junk food are also becoming more widely accepted as genetic risks contributing to the dramatic increases in obesity, allergies and weakened immune systems.

Science still has very limited knowledge about how bacterial and viral genes interact with our own DNA, gene regulation, and individual genetic dispositions after being injected into the body. This remains a dark area of medical science that scientists are only recently beginning to dive deeper into. Therefore, current vaccine science, says Dr. Toni Bark, is "Frankenscience."[7] Doctors, physicians, CDC heads, and health officials really have very little clear idea about what we are actually injecting into our children nor its long term consequences on our natural immune systems.

Back in 1971, University of Geneva scientists published a remarkable discovery in the journal *World Medicine*. According to their study, foreign biological materials that enter directly into the blood stream can potentially become part of us and even combine with our own DNA. This activity known as "jumping genes," and first postulated in the 1930s by Nobel laureate Barbara McClintock, still largely remains a mystery.[8] These were some of the early precursory hypotheses and studies that would later become epigenetics.

Nevertheless, during the last dozen years biomedical and environmental research, which is unfailingly ignored and denied by the vaccine industry, is gradually mapping new terrains in our genetic understanding. Renowned British epigenetic researcher Dr. Mae-Wan Ho from the Institute of Science in Society has observed that "vaccines themselves can be dangerous, especially live, attenuated viral vaccines or the new recombinant nucleic acid vaccines; they have the potential to generate virulent viruses by recombination and the recombinant nucleic acids could cause autoimmune disease."[9] One day it will be conclusively shown that viral and bacterial vaccine components, as well as vaccines' toxic chemicals, are fundamentally altering the human genome, weakening natural immunity that gives rise to autoimmune diseases, and directly contributing to both short- and long-term onset of debilitating life-threatening illnesses affecting millions of people throughout the world.

As we have noted, environmental medicine is diligently pursuing epigenetic investigations to better understand how exogenous chemicals and toxins affect the body's immune system and genetic disposition. Simultaneously, epigenetics remains an anathema within the vaccine industry. This is because epigenetics is the vaccine industry's greatest threat and may well be the harbinger of vaccination's collapse in the future. For that reason, we increasingly observe the pro-vaccine community aggressively associating vaccine-injury illnesses with parental gene inheritance. Seeming vaccine injuries, the CDC informs us, are all due to inherited genes and are not stimulated by vaccine interference. More recently we are being told that genes associated with autism have always been present in the human genome.[10] Yet, no one references the other body of research, such as a University of Montreal analysis, that has discovered the majority of these so-called autism genes are de novo.[11] De novo genes are genetic mutations that appear for the first time in a parent's germ cell or during the development of the fertilized egg itself. The most likely causal candidates accounting for de novo mutations are epigenetic. Consequently, a woman who is vaccinated during pregnancy will have her unborn child at a higher risk of de novo mutations due to the toxic stew of chemicals, additives, and viruses she was injected with. In order to skirt the evidence supporting this scientifically plausible hypothesis, the CDC and its minions in the vaccine industry must continue to rely upon an older, determinist, and regressive view of genetics that denies epigenetic activity. Fortunately, this outdated genetic paradigm is rapidly being deconstructed and proven unsound by other scientific disciplines.

Other examples are Ehlers-Danlos Syndrome or EDS (a connective tissue disorder) and Osteogenesis Imperfecta (a disorder characterized by brittle bones). Both conditions are known inherited genetic disorders and associated with a series of identifiable gene mutations. And both illnesses are increasing at an alarming rate among young children and adolescents.

In 2014, Dr. Lloyd Phillips conducted independent research to determine why so many young adolescent and teenage girls were rapidly coming down with more serious expressions of EDS. His findings concluded that these otherwise healthy girls carried an EDS genetic marker which remained dormant until shortly after receiving the HPV vaccine or Gardasil.[12]

A similar discovery was made by Dr. Robert Kendall Endres in 2009, who noted in 1962 there were approximately 10,000 cases of brittle bone syndrome worldwide. By 1978 there were 836,000 cases and over 4 million in 2000. This increase parallels the rapid increase in the number of vaccinations recommended in the CDC's vaccine schedule and the WHO's global vaccination initiatives. Although both disorders are associated with certain inherited gene mutations, the plausibility of vaccination as the triggering culprit responsible for their expression and activation cannot be ruled out.[13]

Any one of the many vaccines on the market today can cause enormous genetic and epigenetic disruption in any human being. Epidemiologists are puzzled about why some people respond according to plan for any given vaccine and why others don't. For example, only 10% of people receiving the MMR vaccine generate high levels of measles antibodies following vaccination while another 10% don't respond at all. Dr. Gregory Polland at Mayo's Vaccine Research Group realizes this is undoubtedly due to genetic mutations and an individuals' genetic code.[14] The one-size-fits-all vaccination policy now advocated by the CDC and its leading spokespersons such as Paul Offit therefore has no rational and sound basis in science.

Since 1996, the CDC's vaccine divisions and the World Health Organization (WHO) have known they have a very serious health problem with genetic contamination in every vaccine that relies upon animal cell culturing. This is a very dark side of the vaccine industry's manufacturing methodology. The fact that genetic contamination, much of which remains unknown and unidentified, is being injected into infants as young as 24 hours after birth receives absolutely no attention and is ignored by those who espouse political correctness on their pro-vaccine posturing.

In the past we have reported on the primitive methodology that vaccine makers still utilize to culture the viruses that go into vaccines.[15] In 1999, the FDA convened a non-public regulatory meeting to review the health hazards of undesirable viral DNA fragments and protein contamination in all vaccines relying on animal cell culturing. Concerns were particularly focused upon vaccines using fertilized chicken eggs: the influenza, MMR, and yellow fever vaccines. Among the most worrisome contaminants were prions (tiny proteins responsible for incurable diseases in both humans and animals), viral oncogenes capable of causing cancer, viral variants that might cause AIDS, and multiple known and unknown viruses present in the viruses' culture medium. The executive scientists present acknowledged that recombination activity between viral codes and cells in the tissue culture is common and therefore the same can certainly occur in a child's body after vaccination.[15] Again, Barbara Lo Fisher warns that "because viruses are constantly mutating and recombining with each other and scientists do not understand how viruses and genes interact, it is clear that what is not known about the effects on human health of widespread use of live virus vaccines is far greater than what is known."[6]

Current vaccine technology makes it impossible to filter out all genetic contamination and DNA debris from vaccine preparations. Therefore, the FDA has set weight limits on the amount of foreign genetic contamination permitted. Since vaccine manufacturers have been unable to meet these restrictions, the CDC has reduced the requirements to apply only to cancerous cell lines. Other DNA contamination allowances were increased one hundred-fold. According to the FDA's industry guidelines on vaccine production, the removal of foreign DNA and protein contamination from vaccines employing human and animal cell lines is a "non-binding recommendation."[15] A recent example of a vaccine temporarily removed from the market by the FDA is Glaxo's rotavirus vaccine Rotarix. In 2010, an independent California laboratory identified a foreign pig virus, porcine circovirus 1 or PCV1, present in Rotarix. The CDC immediately reported that this contaminant posed no risks, although babies as young 2 months old were being vaccinated with this swine virus contaminant. The laboratory also found avian leukosis virus in the MMR vaccine and monkey retrovirus fragments in Paul Offit's RotaTeq vaccine.[16]

There are approximately 100 million allowable segments of DNA contamination permitted in any single vaccine dose. Much of this unwanted genetic and foreign protein rubbish has never been fully identified and sequenced. And vaccine makers are not required to identify what all of this genetic debris consists of. If a child follows the CDC's recommended vaccination schedule from moments after birth until she or he reaches six years of age, 49 doses of 14 vaccines will have been administered. Isn't it therefore time to pause and review the huge amount of DNA contamination, known and unknown viral genetic fragments children are receiving directly into their bloodstreams, and ask whether or not this may be contributing to the enormous rise in childhood autoimmune conditions, including common adult diseases now frequently appearing in children?

Dr. Howard Urnovitz is an immunologist trained at the University of Michigan and a leading advocate for informing scientists about vaccine-associated genetic mutations. He is perhaps best known for his research into genetic alterations among veterans suffering from Gulf War Syndrome. Although GWS has been associated with a wide range of toxic exposures, including chemical weapons, organophosphates, depleted uranium, an experimental anthrax vaccine, pesticides and other causes, Urnovitz's discovery was singular. He identified genetic sequences in a particular chromosome well known as a "hot spot" for polymorphisms among many veterans. What was unusual was that the sequences were non-human and similar to the enteroviral segments from the oral polio vaccine administered to the veterans.[17] Although this research cannot conclude that veteran's GWS symptoms are directly related to the vaccine's polio virus, it confirms the deep concern over viral genes introduced via vaccination jumping and recombining with our body's DNA.

In light of the above discussions about gene jumping, recombination of pathogenic viral sequences merging with our bodies own DNA, undesirable mutations, and expression and activation of hereditary genetic predispositions leading to serious autoimmune complications and diseases, consider the following: Merck's Rotateq vaccine for the protection of infants from rotavirus is a genetically engineered vaccine that includes five combined human and cow strains of rotavirus, first developed by Paul Offit at the Children's Hospital of Pennsylvania. This viral concoction combines bovine rotavirus strains that causes diarrhea in cows with viral

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strains causing diarrhea in humans. This recombinant, engineered viral strain is then cultured on African Green Monkey kidney tissue. The seed stock that is later used to manufacture future lots of the vaccine also includes fetal bovine (cow) serum and porcine trypsin (an enzyme derived from a pig's pancreas).[16] Are we the only ones who share grave trepidations that an infant will receive a series of three rotavirus injections by the age of six months? And are we to believe that it is normal and safe for an infant to be unnaturally exposed to an artificial and abnormal pathogen in this manner?

The genetically engineered rotavirus vaccines, similar to many of the newer vaccines positioned to come on the market in the very near future, contain an attenuated live virus. These vaccines are already raising serious questions about their influential impact upon the vitality of the immune system, our bodies' gut microbiome, and even environmental ecologies. In 2012, Norwegian scientists at the University of Tromsø concluded that "genetically engineered or modified viruses (GMVs) are being increasingly used as live vaccine vectors and their applications may have environmental implications…. In all cases there may be circumstances that enable GMVs to jump species barriers directly or following recombination with naturally occurring viruses."[18]

Finally, the CDC aggressively follows a one-size-fits-all policy in its efforts to keep the entire American population vaccinated. Today there are over two hundred new vaccines in the pipeline and eventually coming to market. As new spikes in diseases occur consistently with each new vaccine approved and entered in the CDC's recommended vaccination schedule, so also will other disease conditions increase as well as new disorders never observed before. Americans today are less healthy than previous generations. More and more people have compromised immune systems and are rapidly becoming immunodeficient. Surprisingly no federal agency or official institution tries to track the total number of Americans with serious compromised immune systems other than recipients of organ transplants, and people with cancer or positive HIV diagnoses. The American Autoimmune Related Diseases Associations estimates that 50 million people have any one of 100 and perhaps over 140 different life-threatening autoimmune diseases. Federal health officials downplay the severity of this epidemic by only counting 24 autoimmune diseases.[19]

In addition, poverty is on the rise and conservative estimates record 22% of all children living below the poverty level. Forty-eight million Americans live in insecure food households and are clinically malnourished. This, too, is contributing to the increase in weakened immune systems and diseases. Other health disorders such as chronic lack of sleep, stress, and anxiety are now associated with weakened immunity and immunosuppressive disorders.All told, anywhere between 30-50 percent of Americans have weakened immune systems that make them far more susceptible to adverse complications due to vaccines. And live attenuated virus vaccines, which include measles, mumps, rubella, influenza, rotavirus, chickenpox, smallpox, and the live polio vaccine in foreign countries have been shown repeatedly to weaken natural immunity and make the recipient more predisposed to other viral infections.

It is essential that we accept that the science and technology to support vaccine safety remains in its infancy. For those vaccine developers who are looking at vaccination's epigenetic effects on the human genome, our bodies' microbiome, and the immune system, new and unexpected concerns over safety are coming to light. Moreover, no one is a greater expert on a child's reaction to a vaccine than a parent. But most parents don't have the scientific background to advocate for vaccine-induced injuries. Nor do the physicians, pediatricians, nurses, and pharmacists who oversee vaccination have the time and specialized medical training to fully understand each and every vaccine's immunological and genetic complexities. Consequently, the official doctrine of vaccine safety is completely based upon blind belief and faith. Medical interventions imposed and mandated on the public should be based solely on scientific proof of safety, and the pro-vaccine industry and federal authorities have never convincingly made their case based on gold standard scientific principles. Until the vaccine industry does so, no child's or adult's life should ever be put at unnecessary risk.

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Gary Null, PhD, is the host of the nation's longest running public radio program on nutrition and natural health and a multi-award-winning documentary film director, including *Autism: Made in the USA, War on Health: The FDA's Cult of Tyranny* and *Silent Epidemic: The Untold Story of Vaccination.*

References

1. Habakus L, Holland M. *Vaccine Epidemic*. Skyhorse Press, New York 2012
2. Bruesewitz et al vs Wyeth LLC. http://www.supremecourt.gov/opinions/10pdf/09-152.pdf
3. Shoenfeld Y, Agmon-Levin N. *Vaccines and Autoimmunity*. San Francisco: Wiley, 2015
4. Erickson N. France: Aluminum Adjuvants and HPV Vaccines Up for Debate. Sanevax.org. May 19, 2014.
5. Adhya D, Basu A. Epigenetic modulation of host: new insights into immune evasion by viruses. *J Biosci.* December 2010;35(4):647-663.
6. Fisher, BL. Emerging Risks of Live Virus and Virus Vectored Vaccines. National Vaccination Information Center. 2014.
7. Null, G. *Silent Epidemic: The Untold Story of Vaccines* (documentary film). 2013.
8. Buttram HE. The Ultimate Gamble: Do Childhood Vaccines Result in Genetic Hybridization from Alien Human and Animal DNA Contents? March 13, 2012.
9. Ho M-W, Cummins J. The vaccines are far more deadly than the swine flu. Institute of Science in Society. July 27, 2009.
10. Autistic genes are in all of us, new research reveals (press release). March 21, 2016. www.sciencedaily.com.
11. Autism and Schizophrenia: Scientists measure gene mutation rate. September 3, 2010.
12. http://www.gardasilsyndrome.com
13. Shilhavy B. Are Vaccines Altering Our Genes Causing Brittle Bones in Infants? http://vaccineimpact.com. 2015
14. Mayo Clinic. Decoding vaccination: Researchers reveal genetic underpinnings of response to measles vaccine (press release). September 23, 2011. https://www.sciencedaily.com
15. Gale R, Null G. Vaccines Dark Inferno: What is Not on Insert Labels. September 28, 2009. http://blog.garynull.com/wp-content/uploads/2014/03/VaccinesDarkInferno2.pdf
16. Fisher BL. Vaccine Contamination: Pig Virus DNA Found in Rotarix. April 7, 2010.
17. Buttram H. Vaccines and Genetic Mutation. October 11, 2002. www.whale.to/a/yurko.html
18. Myhr AI, Traavik T. Genetically Engineered Virus-Vectored Vaccines – Environmental Risk Assessment and Management Challenges. http://cdn.intechopen.com/pdfs/25756.pdf
19. Schall T. How many Americans are immunocompromised. *Bioethics Bulletin*. February 11, 2015

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L-Methionine to Cure Age-Related Macular Degeneration (AMD)?

by Alfred V. Zamm, MD

Age-related macular degeneration (AMD) is an ophthalmic condition of unknown cause and unknown cure that involves damage to the macula of the retina; it typically occurs in the elderly and results in blurred or no vision of the central visual field. The following is an autobiographic single clinical-case observation, an anecdote. It is presented in the hope that (1) these findings will not be lost and (2) other clinicians will either verify or disprove whether L-methionine is useful in treating AMD. It is fortuitous that this essential amino acid, L-methionine, is innocuous, well tolerated, inexpensive, and available without a prescription. The administration of this amino acid had a subjective, salubrious effect on the symptoms of age-related macular degeneration.

After I underwent a routine ophthalmological examination followed by specialized testing, the examiner told me that I had AMD. In addition to failing the objective machine and computer tests, I also flunked a subjective test, the Amsler Grid Test. The Amsler Grid Test uses a grid composed of horizontal and vertical thin black lines intersecting at right angles and printed on a white background; the intersecting pattern forms a field of uniformly identical squares – in the center of the field there is a black dot. The examinee looks at the central black dot and the lines, which are straight, appear wavy to a viewer who has AMD. I saw wavy lines! My dialogue with the doctor then proceeded as follows:

AZ: Why do I have AMD?

Doctor: No one knows.

AZ: What do I do about it?

Doctor: You take a mixture of nutritional supplements every day. The mixture is based on a study by The National Eye Institute of The National Institutes of Health (NIH), The Age Related Eye Disease Study 2 (AREDS 2). The mixture contains zinc, vitamin C, copper, vitamin E, lutein, and zeaxanthin.[1,2]

AZ: If I take the AREDS 2 mixture, will it cure me?

Doctor: No.[1]

AZ: Will it at least reverse some of the damage?

Doctor: No.[1]

AZ: Then why should I take it?

Doctor: There is some evidence that it slows down the progression of the degenerative process.[2,3] Some clinicians suspect that it may mitigate the development of AMD.

My "takeaway" from this encounter was the following:

1. I have a condition of unknown cause and unknown cure that leads to some degree of decreased sight or maybe blindness.
2. I plan to find out everything I can about AMD.
3. I don't expect anyone to be able to help me.

Dr. Alfred Zamm is a board-certified dermatologist who practiced in Kingston, New York, until he retired to devote his time to research. In his medical practice, Dr. Zamm focused on conducting etiological investigations into his patients' myriad diseases as opposed to prescribing symptom-masking allopathic medications. He received his medical degree from the Chicago Medical School. Postgraduate studies included the Department of Internal Medicine at New York University Medical School, Bellevue Hospital of New York, University Hospital of New York, New York Skin and Cancer Clinic, and New York University Postgraduate Medical School. He is a Fellow of the American Academy of Dermatology, a Fellow of the American College of Allergy, Asthma and Immunology, and a Fellow of the American Academy of Environmental Medicine. He has published numerous medical articles, some of which have been referenced and excerpted in a variety of medical textbooks, and wrote the book *Why Your House May Endanger Your Health*. He was an invited lecturer at the Food and Drug Administration in Washington, DC.

4. If there is a solution to AMD, it's not going to be in an obvious or "logical" place because someone would have found it by now. The answer is going to be hiding in an unexpected place, an "illogical" place.
5. I would have to try one substance after another in a monotonous "trial-and-error" process and have a lot of patience and endurance.
6. Another problem: Even if I found something that worked, how would I know that it was working? (I solved that problem by planning to use the Amsler Grid chart; if the apparent wavy lines started to appear straight, then I would know I was working in the right direction.)

Serendipitously, I chose to start my quest by trying L-methionine. Previously, I found that L-methionine was helpful in treating hepatitis C (not curing), and it appeared to be a preventative and perhaps a cure for *Clostridium difficile* infection.[4] As a result of this familiarity with L-methionine, I suspected that there was a lot more to L-methionine than was apparent to me or was in the literature; at this point, it seemed as good a starting choice as any.

The Experiment

I started by taking one-fourth of a 500 mg capsule of L-methionine on the first day. The next day I took one-fourth capsule b.i.d.; every day I increased the dose until I was taking one 500 mg. capsule b.i.d. For the next two weeks, I stayed at the 500 mg b.i.d. dose; and by the end of this two-week period, the wavy lines that I previously saw in the Amsler chart now appeared straight. My vision had improved in general, and I felt an improved sense of well being. Now, at the three-month marker, all of the benefits that I initially experienced are still present. I will be returning for a follow-up ophthalmological examination at the six-month marker and hopefully there will be some objective measurement of improvement concordant with this subjective benefit that I am now experiencing.

After L-methionine was found to be helpful with my AMD, I went into a "reverse engineering research mode" and found a reference that in monozygotic twins who both had AMD, the twin with the higher dietary (not supplemental) L-methionine intake had a lower stage of AMD.[5]

The author verifies that he has no conflicts of interest.

References

1. Evans J, Lawrenson J. Antioxidant and mineral supplements for preventing age-related macular degeneration. *Cochrane Database of Systemic Reviews*. 2012. PMID 22696317.
2. Hobbs R, Bernstein P. Nutrient supplementation for age-related macular degeneration, cataract, and dry eye. *Journal of Ophthalmic and Vision Research*. 2013;9(4): 487-93.
3. Evans J, Lawrenson J. Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration. *The Cochrane Database of Systemic Reviews*. 2012. PMID 23152201.
4. Zamm A, Bhitiyakul S. L-methionine, *Clostridium difficile*, Hepatitis C, Chronic Superficial Thrombophlebitis: What's the Connection? *Townsend Letter*. June 2013; 61-62.
5. Seddon J, et al. Smoking, dietary betaine, methionine, and vitamin D in monozygotic twins with discordant macular degeneration: epigenetic implications. *Ophthalmology*. 2011 July;118(7):1386-94.

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Common Ocular Conditions in Clinical Practice: Macular Degeneration, Glaucoma, Cataracts and Beyond

by Chris D. Meletis, ND, and Kimberly Wilkes

The eyes are often called the "window into one's soul," and with good reason. The eyes are the only part of the body where a doctor – using an ophthalmoscope and looking through the pupil – can non-invasively observe blood vessels and nerves. This is an amazing way to glean health status or trends, because the eyes are also windows into overall health. Damage that occurs in the eyes can indicate damage happening in the brain. Likewise, age-related macular degeneration can signal concurrent imbalances in thyroid hormones in some people.

This article will review many of the most common eye disorders, their risk factors, and the connection between ocular health and the health of other areas of the body. We will also discuss the research behind both well-known and lesser utilized but highly effective dietary supplements as well as lifestyle and dietary support for vision.

Age-Related Macular Degeneration

In individuals older than 50 years, age-related macular degeneration (AMD) is the most common reason for the occurrence of irreversible vision loss, particularly in developed countries.[1] As the average age of the population rises, the number of individuals with AMD is expected to triple in the next three to four decades from 20 to 25 million to 60 to 75 million people globally.[2]

Macular degeneration occurs when the macula, the part of the eye involved in central vision and seeing fine details, is damaged. Most macular degeneration is age related. There are two types of age-related macular degeneration: nonexudative (dry) AMD and neovascular (wet) AMD. Dry AMD is the early stage of AMD. Eighty-five to 90% of all cases are the dry form.[3]

The presence of fatty deposits called drusen in the macula are a hallmark of dry AMD, which is associated with little to no vision loss, but increases the risk of developing advanced AMD. Wet AMD is the advanced form of the disease and accounts for only 10 to 15% of cases but is responsible for 90% of AMD-related blindness.

AMD progresses to the wet form when blood vessels begin to grow in an abnormal manner at the back of the eye (what's known as angiogenesis). Blood or fluid from these vessels escapes into the macula. Scars develop that harm central vision and may lead to permanent blind spots.

Beyond aging itself, a number of risk factors exist for AMD, including cigarette smoking, genetics,[1] and exposure to light, especially short wavelength light, including ultraviolet and blue light.[4-6] Exposure to blue light is associated with abnormal synthesis of factors that trigger angiogenesis and cause the development or progression of AMD. The blue light spectrum in natural sunlight is believed to be the most important cause of ocular damage.

Due to the possibility that blue light exposure may play a role in the development of AMD, blue light-filtering intraocular lenses (IOLs) are being used as an alternative to traditional IOLs that only filter UV sunlight.[7]

Beyond sun exposure, modern humans encounter many other sources of blue light including fluorescent and LED lighting, flat-screen televisions, display screens of computers, electronic notebooks, smartphones, and other digital devices. Although these devices emit considerably less blue light than the sun, people spend a lot of time in front of these gadgets, often with their eyes close to the screens.

Another risk factor for AMD is high levels of homocysteine, an amino acid associated with an increased risk of cardiovascular disease.[8,9] Studies have demonstrated a direct correlation between high homocysteine blood levels and an increased risk of AMD.[8,9] In one study, homocysteine concentrations were 27.9% higher in individuals with wet AMD compared with the dry AMD group, and 21.9% higher compared with controls.[10] Supplementation with folate, vitamins B_6 and B_{12}, and betaine are known to lower homocysteine concentrations, indicating homocysteine may be a modifiable risk factor for AMD.[11,12] Furthermore, a randomized trial of women at increased risk of cardiovascular disease found that daily supplementation with folic acid, pyridoxine (vitamin B_6), and vitamin B_{12} lowered the risk of AMD.[13]

Epigenetics are also involved in AMD. Epigenetics refer to modification of gene expression rather than changes in the genetic code itself. Epigenetics serve as a switch that turn genes on and off. Many environmental factors such as diet or exposure to toxins trigger these epigenetic changes in gene expression. One way in which gene expression is altered is through micro-RNAs (miRNAs). miRNAs are thought to be involved in the development of the retina and abnormal miRNA expression correlates with the development of AMD.[14] Resveratrol inhibits neovascularization in the retina during rodent experiments and its beneficial ocular effects in animals and humans may be due to its ability to impact the expression of miRNAs.[15] A study in rats indicated that resveratrol may be able to protect the retina against ischemia in part through a mechanism that involves its effects on miRNAs.[16]

Another factor related to an increased risk of AMD is eating a high-glycemic diet. Mice that consumed a high-glycemic diet developed many features of AMD, including retinal pigmented epithelial cell hypopigmentation and atrophy, lipofuscin accumulation, and photoreceptor degeneration.[17] These abnormalities were not observed in mice that consumed a lower-glycemic diet. Interestingly, switching from the high-glycemic to the low-glycemic diet late in life halted or reversed these AMD features. Low-glycemic diets limited the accumulation of advanced glycation end products (AGEs), proteins or lipids that become glycated due to their exposure to sugars. Low-glycemic diets also were associated with reduced accumulation of long-chain polyunsaturated lipids and their peroxidation end-products and an increased amount of carnitine in the retina. The mechanism by which the diet affected the retina was thought to involve the microbiota. In mice consuming a low-glycemic diet, the microbiota produced a number of metabolites, especially serotonin, which inhibited the development of AMD features.[17] Microbiota in the Clostridiales order were associated with AMD and the high-glycemic diet, whereas the low-glycemic diet correlated with a prevalence of Bacteroidales organisms, which were protective against AMD features. In a human study of 1,952 participants 49 years or older followed for 10 years, consumption of food with a higher mean dietary glycemic index correlated with an increased risk of early AMD.[18] Conversely, individuals who ate low-glycemic breads and cereals such as oatmeal had a lower risk of incident early AMD.

Another connection exists between AMD and thyroid hormones. Human retinal pigment epithelial cells express thyroid hormone receptors, an effect which may lead to thyroid hormones triggering damaging effects including depletion of hyaluronic acid.[19] In a study of 5,573 people 55 years old or older, even among subjects whose free thyroxine (FT4) levels were normal, individuals who had the highest FT4 levels had a 1.34-fold greater risk of developing AMD, compared to those whose FT4 concentrations hovered in the middle range.[20] Furthermore, higher FT4 concentrations were associated with an increased risk of retinal pigment alterations. This led the researchers to conclude that thyroid hormone is involved in more than just promoting the progression of AMD and may actually be involved in its development.

In addition to addressing all of the aforementioned risk factors for AMD, supplementation with the carotenoids lutein and zeaxanthin provide effective support. In some studies, lutein has improved macular pigment optical density and visual sensitivities in patients with early AMD.[21] A combination of nutrients used in the Age-Related Eye Disease Study 2 (vitamin C, vitamin E, zinc, copper, and lutein) along with 10 mg meso-zeaxanthin given to patients with non-advanced AMD led to significant increases in macular pigment and improvements in measures of visual function.[22] Lutein and zeaxanthin have been shown to reduce the progression from early AMD to the late form of the disease.[21] Dietary intake of lutein and zeaxanthin may result in a 26% reduced risk for late AMD.[23]

Cataracts

A cataract causes the normally clear lens of the eye to become cloudy or opaque. In the United States, over half of those aged 65 and over have cataracts.[24] There are three types of age-related cataracts: nuclear cataracts that affect the center of the eye lens, cortical cataracts that impact the edges of the lens, and posterior subcapsular cataracts, which affect the rear of the lens.

Risk factors vary depending on the type of cataract. Aging, higher hemoglobin A(1c) – a marker of blood sugar control over time – and history of diabetes mellitus are independent risk factors for cortical-only lens opacities.[24] Aging, smoking cigarettes, and myopia (nearsightedness) independently increase the risk of nuclear-only cataracts.[24] Higher systolic blood pressure and history of diabetes are both independent risk factors for posterior subcapsular cataracts.[24] Aging, myopia, diabetes, higher systolic blood pressure, female gender, and large drusen independently raise the risk for mixed cataracts.[24]

Diabetes is an important risk factor for all types of age-related cataracts. High blood sugar is thought to increase the risk of cataracts through direct glycation of lens proteins.[24] Furthermore, sugar alcohols synthesized through the aldose reductase pathway are directly toxic to the lens of the eye.[24] Individuals with diabetes mellitus may also have high levels of calcium, impacting the lens crystallins and leading to opacification of the lens.[25] Better diabetes control may therefore inhibit the formation of cataracts.

Myopia is another common risk factor. The role that myopia may play in nuclear cataracts may involve a longer vitreous cavity in this group of subjects resulting in reduced delivery of nutrients to the posterior lens and consequently impaired oxidative defense mechanisms leading to free radical damage.[25,26]

N-acetylcarnosine lubricant eye drops may play a role in improving visual function in people with cataracts. In older subjects with cataracts treated with 1% N-acetylcarnosine lubricant eye

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drops, visual acuity and glare sensitivity markedly improved compared with controls, who did not experience any improvement in visual function.[27] There is indication that the mechanism of action of N-acetylcarnosine may involve reducing the rate of telomere shortening in lens cells exposed to oxidative stress in the absence of sufficient antioxidant protection.[27] Telomeres are protective caps at the end of chromosomes. As telomeres are worn down with aging and other factors, this leaves the chromosomes vulnerable to damage.

As with macular degeneration, dietary intake of lutein and zeaxanthin correlated with a lower risk of nuclear or posterior subcapsular cataracts in a dose-response manner.[28]

Glaucoma

Glaucoma is a neurodegenerative disorder that damages the optic nerve and leads to impaired vision and blindness. Globally, 64.3 million people suffer from the disease and that number is expected to rise to 111.8 million in 2040.[29] Open-angle glaucoma is characterized by increased intraocular pressure. Glaucoma-related degeneration occurs due to direct damage to the retinal ganglion cells caused by high intraocular pressure, ischemia, and aging. Recent evidence also suggests that glaucoma may be a disease that originates in the central nervous system (CNS) and moves downstream to the optic nerve and retinal ganglion cells.[30] It is known that injury to the visual cortex and/or optic nerve, which then leads to damage to the retina, may be involved in the development of glaucoma.[30,31] All of these factors inhibit oxygen supply and impair retinal function.[30,31]

High blood pressure is a risk factor for glaucoma, as are genetics, aging, and ethnicity (African Americans and Mexican Americans are at greater risk).[32] Recently, researchers have proposed that glaucoma may be diabetes type 4 (the brain diabetes theory).[33,34]

According to this theory, glaucoma is a result of brain insulin resistance or central insulin signaling impairment, triggering the development of transsynaptic neurodegeneration. This theory indicates that therapeutic options for primary open angle glaucoma/normal pressure glaucoma should potentially target the brain as well as the eye.[35]

Oral and topical forskolin in the form of eye drops, alone or with other dietary supplements, has been shown to improve glaucoma symptoms.[36] *Coleus forskohlii* is an aromatic herb found in India from the Himalayas to the southern part of the country. Forskolin is derived from the roots of this plant. In one study, patients with primary open angle glaucoma who were taking intraocular pressure-lowering drugs also consumed an oral supplement containing forskolin, homotaurine, carnosine, folic acid, vitamins B_1, B_2, and B_6, and magnesium for a year.[37] Patients in the forskolin supplement group experienced a further decrease in intraocular pressure and an improvement in Pattern Electroretinogram (PERG) amplitude – an electrical retinal response caused by stimuli in the visual field. Light sensitivity in the fovea, a small depression in the retina of the eye where visual acuity is the greatest, also improved. The improvements in PERG and foveal sensitivity suggested that the supplement produced a short-term neuroactive benefit.

In another study, an oral combination of forskolin and rutin reduced the rise in intraocular pressure that occurs after laser iridotomy, a procedure used in the treatment and prevention of closed angle glaucoma.[38] Italian researchers also investigated the oral combination of forskolin and rutin in 52 patients with primary open angle glaucoma who were taking anti-glaucoma drugs and 45 controls.[39] All patients in the forskolin-rutin intervention group, independent of the combination of medications they were treated with, experienced an additional 10% decline in intraocular pressure, beginning one week after supplementation began and continued for the 30-day study. The improvement was more pronounced in patients with higher intraocular pressure (≥21 mmHg) compared with subjects with low (<21) intraocular pressure. Intraocular pressure in the control group remained stable throughout the study.

The Connection Between Eye Diseases and Cognitive Function

Alzheimer's disease and mild cognitive impairment are associated with a number of ocular problems.[40] The manifestations of Alzheimer's impact not only the brain, but also the retina, which is an extension of the brain. The retinas of Alzheimer's patients exhibit a number of abnormalities such as retinal ganglion cell degeneration, reduction of blood flow, and vascular alterations.[41]

There are many commonalities between the brain and the retina. Like the brain, the retina contains neurons, astroglia, microglia, and a blood barrier.[41] Axons of the optic nerve directly join the retina and the brain.[42] Amyloid β-protein (Aβ) deposits are known to accumulate in the brains of patients with Alzheimer's and are a hallmark of the disease. Evidence indicates that retinal ganglion cells (RGCs) synthesize amyloid precursor protein[42] and in Alzheimer's patients, Aβ deposits accumulate in the retina.[40]

The connection between cognitive and ocular health is further supported by the fact that higher levels of carotenoids such as lutein – known to reduce the risk of AMD and cataracts – also lower the risk of dementia and Alzheimer's.[43,44] Furthermore, lutein supplementation in older women enhanced cognitive function.[44]

Other Non-Ocular Diseases Connected to Eye Health

In addition to Alzheimer's, other conditions are related to poor eye health. Because the retina and optic nerve are components of the central nervous system, their impairment may be indicative of not only eye diseases like glaucoma but also neurodegenerative disorders such as Parkinson's.[30] Furthermore, open-

angle glaucoma is associated with an increased risk of stroke in people who also have hypertension and/or diabetes.[45] Additionally, depression and anxiety are common in older individuals with poor vision. One study found that the incidence of depression and anxiety in older people with ocular conditions is double that of older individuals in general.[46] Even dry eye disease is associated with a high prevalence of depression.[47] Therefore, in elderly patients with vision impairment, it is prudent to monitor for depression and anxiety in addition to directly treating ocular health.

Mitochondrial Involvement

Proper functioning of the mitochondria – the powerhouses of the cell responsible for manufacturing the energy molecule ATP – is crucial for eye health. This is not surprising given that within the brain, the visual system has some of the highest need for energy.[48]

Mitochondrial dysfunction plays a key role in many eye diseases. For example, mitochondria are thought to have a causal role in the development of glaucoma.[49] Mitochondrial function is associated with oxidative metabolism and reactive oxygen species (ROS) production.[49] Excessive ROS synthesis leads to the death of retinal ganglion cells and ultimately the loss of vision.[49]

In AMD, mitochondria in human retinal pigment epithelium cells are damaged, fragmented, and disrupted.[50] As the age of the subjects from whom the retinal cells were derived increased, there was a significant decline in the number and area of mitochondria, as well as other mitochondrial abnormalities.[50] Although these alterations were found in the mitochondria of retinal cells from both AMD and control subjects, these abnormalities were more pronounced in AMD compared with normal aging.[50] Other researchers have observed that AMD severity correlates with a greater amount of mitochondrial DNA lesions and fragmentations in retinal pigment epithelium cells.[51]

Excessive reactive oxygen species (free radical) generation caused by mitochondrial dysfunction is also known to be involved in cataracts. Lipid peroxidation in the eye, the means by which lipids in the body undergo oxidation after exposure to reactive oxygen species, is one of the mechanisms involved in the development of cataracts.[52] As one of the primary sources of reactive oxygen species, mitochondria therefore likely play a role in the lipid peroxidation of the eye lens.

Mitochondrial dysfunction occurs in diabetic retinopathy as well. In rats, dysfunction in mitochondrial energy production in the retina occurs as early as two months before development of diabetic hyperglycemia and retinopathy.[53] Additionally, metabolic abnormalities caused by high glucose lead to retinal cell loss associated with diabetic retinopathy.[54]

Due to the important role of the mitochondria in eye health and the ocular damage that occurs after excessive reactive oxygen species production, supporting mitochondria with effective antioxidant nutrients is advised. A number of studies have demonstrated that antioxidants such as vitamins C and E, coenzyme Q10 (CoQ10), omega-3 fatty acids and other substances such as green tea and gingko biloba may support normal intraocular pressure and protect retinal neurons against oxidative stress in primary open-angle glaucoma.[55]

Coenzyme Q10 also has been found to protect the mitochondria in AMD.[56] It is a particularly important nutrient for eye health in the elderly since CoQ10 concentrations in the retina decline by approximately 40% during aging.[57]

Melatonin, by virtue of its ability to act as an antioxidant and mitochondrial protector as well as other mechanisms, can support the health of individuals with a number of eye diseases including cataracts, glaucoma, AMD, and diabetic retinopathy.[58.59]

Modern Threats to Vision Health

The large amount of time individuals spend in front of their computer results in a new type of eye strain unique to modern man. Computer use results in eye fatigue, which can impair visual function. After the benefits of bilberry were publicized in a 2015 study, Dr. Meletis began recommending this botanical to his patients who spend a lot of time staring at a computer screen. In the study, a prospective, randomized, double-blind, placebo-controlled trial, 88 office workers aged 20 to 40 years who were frequent computer users were randomized to receive either 480 mg/day of bilberry or a placebo for eight weeks.[60] Eye dryness and various symptoms of eye fatigue were determined using a questionnaire. The researchers observed improved measures of eye fatigue in the group receiving bilberry extract compared with controls. Compared with controls, Bilberry extract reduced subjective symptoms of eye fatigue, including ocular fatigue sensation caused by computer viewing, ocular pain, eye heaviness, uncomfortable sensation, and the sense that there was a foreign body in the eye.

Dry Eyes and Floaters

Dry eyes and floaters are two other common ocular problems. Dry eyes occur more often in people over 67 years, although the prevalence of this condition becomes less common after the age of 80.[61] Dry eye leads to oxidative stress since tears soothe the eyes with molecules that protect against oxidative damage to the cornea.[62] Consequently, supplementation with antioxidants may protect the ocular surface against oxidative damage. In one study, a combination of essential polyunsaturated omega-3 fatty acids combined with vitamins A, C, and E, tyrosine, cysteine, glutathione, zinc, copper, and manganese given to patients with dry eyes, lowered markers of inflammation and dry eye symptoms.[63]

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In his clinical practice, Dr. Meletis has used oral hyaluronic acid (HA) in patients with dry eye and observed good results. HA protects the ocular surface epithelium due to its moisturizing effect.[65] A number of studies in humans and animals have shown that eye drops containing HA reduce symptoms and signs of dry eye.[64,65-67] In one study, eye drops containing crosslinked HA and CoQ10 given to 40 patients with mild to moderate dry eye disorder improved symptoms of dry eye more effectively than HA alone.[68]

HA can be effective for floaters as well. Floaters – those wiggly lines or dots that appear to float in front of your eyes – occur due to alterations in the vitreous body, the gel that fills much of the hollow sphere of the eye. Most of the vitreous gel is water, but 1% is comprised of solid elements including HA and collagen. HA plays an important role in regulating the gel consistency of vitreous through HA's affinity for water molecules. However, with aging, HA levels decline.[69]

This age-related breakdown in HA molecules causes them to release their water supply and form liquefied gaps in the vitreous gel. At the same time, collagen filaments clump together to form larger fibrils, which leads to further destruction of the vitreous gel. The collagen fibrils are suspended in the liquid vitreous pockets, appearing to float. The breakdown of the vitreous gel can lead to posterior vitreous detachment, where the vitreous completely separates from the retina. Most cases of posterior vitreous detachment occur in people over the age of 70. While there are no studies that we are aware of demonstrating a beneficial effect of HA supplementation on floaters, Dr. Meletis has used HA in patients experiencing this condition and believes the important role that HA plays in maintaining the integrity of the vitreous gel warrants its use in people with floaters.

Another Beneficial Nutrient for Ocular Health

Curcumin is emerging as a nutrient with potential benefits for eye health. A number of rodent studies have indicated it has a variety of beneficial effects on ocular health including inhibiting the development and progression of retinitis pigmentosa,[70] a group of inherited neurodegenerative diseases characterized by the reduction of photoreceptor cells, ultimately leading to blindness. Rodent studies also demonstrate a beneficial effect of curcumin in the management of diabetic retinopathy.[71,72] In humans, a lecithinized curcumin delivery system assisted with the management of diabetic microangiopathy and retinopathy.[73]

Conclusion

Many threats to eye health exist, especially as we grow older. However, a number of dietary supplements including lutein, forskolin, melatonin, hyaluronic acid, bilberry, CoQ10, and N-acetylcarnosine eye drops can protect vision. Furthermore, lifestyle changes such as eating a low-glycemic diet can also strengthen the eyes.

References

1. Lim LS, et al. Age-related macular degeneration. *Lancet*. 2012 May 5;379(9827):1728-38.
2. Chopdar A, Chakravarthy U, Verma D. Age-related macular degeneration. *BMJ*. 2003 Mar 1;326(7387):485-8.
3. American Academy of Ophthalmology. Age-Related Macular Degeneration. https://www.aao.org/bcscsnippetdetail.aspx?id=9711f063-ed7b-452b-8708-c4dad0d893e8 Accessed January 2, 2018.
4. Cruickshanks KJ, Klein R, Klein BE. Sunlight and age-related macular degeneration. The Beaver Dam Eye Study. *Arch Ophthalmol*. 1993 Apr;111(4):514-8.
5. Mainster MA. Light and macular degeneration: a biophysical and clinical perspective. *Eye (Lond)*. 1987;1(Pt 2):304-10.
6. Vila N, et al. Blue-light filtering alters angiogenic signaling in human retinal pigmented epithelial cells culture model. *BMC Ophthalmol*. 2017 Nov 2;17(1):198.
7. Sparrow JR, Miller AS, Zhou J. Blue light-absorbing intraocular lens and retinal pigment epithelium protection in vitro. *J Cataract Refract Surg*. 2004 Apr;30(4):873-8.
8. Rochtchina E, et al. Elevated serum homocysteine, low serum vitamin B12, folate, and age-related macular degeneration: the Blue Mountains Eye Study. *Am J Ophthalmol*. 2007 Feb;143(2):344-6.
9. Nowak M, et al. Homocysteine, vitamin B12, and folic acid in age-related macular degeneration. *Eur J Ophthalmol*. 2005 Nov-Dec;15(6):764-7.
10. Axer-Siegel R, et al. Association of neovascular age-related macular degeneration and hyperhomocysteinemia. *Am J Ophthalmol*. 2004 Jan;137(1):84-9.
11. Homocysteine Lowering Trialists' Collaboration. Dose-dependent effects of folic acid on blood concentrations of homocysteine: a meta-analysis of the randomized trials. *Am J Clin Nutr*. 2005 Oct;82(4):806-12.
12. Mazza A, et al. Nutraceutical approaches to homocysteine lowering in hypertensive subjects at low cardiovascular risk: a multicenter, randomized clinical trial. *J Biol Regul Homeost Agents*. 2016 Jul-Sep;30(3):921-7.
13. Christen WG, et al. Folic acid, pyridoxine, and cyanocobalamin combination treatment and age-related macular degeneration in women: the Women's Antioxidant and Folic Acid Cardiovascular Study. *Arch Intern Med*. 2009 Feb 23;169(4):335-41.
14. Ren C, et al. Circulating miRNAs as Potential Biomarkers of Age-Related Macular Degeneration. *Cell Physiol Biochem*. 2017;41(4):1413-23.
15. Richer S, et al. Observation of human retinal remodeling in octogenarians with a resveratrol based nutritional supplement. *Nutrients*. 2013 Jun 4;5(6):1989-2005.
16. Liu XQ, et al. Resveratrol mitigates rat retinal ischemic injury: the roles of matrix metalloproteinase-9, inducible nitric oxide, and heme oxygenase-1. *J Ocul Pharmacol Ther*. 2013 Feb;29(1):33-40.
17. Rowan S, et al. Involvement of a gut-retina axis in protection against dietary glycemia-induced age-related macular degeneration. *Proc Natl Acad Sci U S A*. 2017 May 30;114(22):E4472-81.
18. Kaushik S, et al. Dietary glycemic index and the risk of age-related macular degeneration. *Am J Clin Nutr*. 2008 Oct;88(4):1104-10.
19. Duncan KG, et al. The human fetal retinal pigment epithelium: A target tissue for thyroid hormones. *Ophthalmic Res*. 1999;31(6):399-406.
20. Chaker L, et al. Thyroid function and age-related macular degeneration: a prospective population-based cohort study – the Rotterdam Study. *BMC Med.* 2015 Apr 23;13:94.
21. Huang YM, et al. Effect of supplemental lutein and zeaxanthin on serum, macular pigmentation, and visual performance in patients with early age-related macular degeneration. *Biomed Res Int*. 2015;2015:564738.
22. Akuffo KO, et al. The Impact of Supplemental Antioxidants on Visual Function in Nonadvanced Age-Related Macular Degeneration: A Head-to-Head Randomized Clinical Trial. *Invest Ophthalmol Vis Sci*. 2017 Oct 1;58(12):5347-60.
23. Ma L, et al. Lutein and zeaxanthin intake and the risk of age-related macular degeneration: a systematic review and meta-analysis. *Br J Nutr*. 2012 Feb;107(3):350-9.
24. Richter GM, et al. Risk factors for cortical, nuclear, posterior subcapsular, and mixed lens opacities: the Los Angeles Latino Eye Study. *Ophthalmology*. 2012 Mar;119(3):547-54.
25. Micelli-Ferrari T, et al. Role of lipid peroxidation in the pathogenesis of myopic and senile cataract. *Br J Ophthalmol*. 1996 Sep;80(9):840-3.
26. Simonelli F, et al. Lipid peroxidation and human cataractogenesis in diabetes and severe myopia. *Exp Eye Res*. 1989 Aug;49(2):181-7.
27. Babizhayev MA, Yegorov YE. Telomere Attrition in Human Lens Epithelial Cells Associated with Oxidative Stress Provide a New Therapeutic Target for the Treatment, Dissolving and Prevention of Cataract with N-Acetylcarnosine Lubricant Eye Drops. Kinetic, Pharmacological and Activity-Dependent Separation of Therapeutic Targeting: Transcorneal Penetration and Delivery of L-Carnosine in the Aqueous Humor and Hormone-Like Hypothalamic Antiaging Effects of the Instilled Ophthalmic Drug Through a Safe Eye Medication Technique. *Recent Pat Drug Deliv Formul.* 2016;10(2):82-129.
28. Ma L, et al. A dose-response meta-analysis of dietary lutein and zeaxanthin intake in relation to risk of age-related cataract. *Graefes Arch Clin Exp Ophthalmol*. 2014 Jan;252(1):63-70.
29. Tham YC, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a

systematic review and meta-analysis. *Ophthalmology*. 2014 Nov;121(11):2081-90.
30. Calkins DJ, Horner PJ. The Cell and Molecular Biology of Glaucoma: Axonopathy and the Brain. *Invest Ophthalmol Vis Sci*. 2012 May 4;53(5):2482-4.
31. Crish SD, Calkins DJ. Central visual pathways in glaucoma: evidence for distal mechanisms of neuronal self-repair. *J Neuroophthalmol*. 2015 Sep;35 Suppl 1:S29-37.
32. National Eye Institute. Facts About Glaucoma. https://nei.nih.gov/health/glaucoma/glaucoma_facts Accessed January 2, 2018.
33. Faiq MA, et al. Glaucoma--diabetes of the brain: a radical hypothesis about its nature and pathogenesis. *Med Hypotheses*. 2014 May;82(5):535-46.
34. Faiq MA, Dada T. Diabetes Type 4: A Paradigm Shift in the Understanding of Glaucoma, the Brain Specific Diabetes and the Candidature of Insulin as a Therapeutic Agent. *Curr Mol Med*. 2017;17(1):46-59.
35. Dada T. Is Glaucoma a Neurodegeneration caused by Central Insulin Resistance: Diabetes Type 4? *J Curr Glaucoma Pract*. 2017 Sep-Dec;11(3):77-9.
36. Majeed M, et al. Efficacy and safety of 1% forskolin eye drops in open angle glaucoma - An open label study. *Saudi J Ophthalmol*. 2015 Jul-Sep;29(3):197-200.
37. Mutolo MG, et al. Oral Administration of Forskolin, Homotaurine, Carnosine, and Folic Acid in Patients with Primary Open Angle Glaucoma: Changes in Intraocular Pressure, Pattern Electroretinogram Amplitude, and Foveal Sensitivity. *J Ocul Pharmacol Ther*. 2016 Apr;32(3):178-83.
38. Nebbioso M, et al. Forskolin and rutin prevent intraocular pressure spikes after Nd:YAG laser iridotomy. *Panminerva Med*. 2012 Dec;54(1 Suppl 4):77-82.
39. Vetrugno M, et al. Oral administration of forskolin and rutin contributes to intraocular pressure control in primary open angle glaucoma patients under maximum tolerated medical therapy. *J Ocul Pharmacol Ther*. 2012 Oct;28(5):536-41.
40. Hart NJ, et al. Ocular indicators of Alzheimer's: exploring disease in the retina. *Acta Neuropathol*. 2016 Dec;132(6):767-87.
41. Koronyo Y, et al. Retinal amyloid pathology and proof-of-concept imaging trial in Alzheimer's disease. *JCI Insight*. 2017 Aug 17; 2(16): e93621.
42. Morin PJ, et al. Amyloid precursor protein is synthesized by retinal ganglion cells, rapidly transported to the optic nerve plasma membrane and nerve terminals, and metabolized. *J Neurochem*. 1993 Aug;61(2):464-73.
43. Feart C, et al. Plasma Carotenoids Are Inversely Associated With Dementia Risk in an Elderly French Cohort. *J Gerontol A Biol Sci Med Sci*. 2016 May;71(5):683-8.
44. Xu X, Lin X. [Advances in the researches of lutein and alzheimer's disease]. [Article in Chinese, Abstract in English.] *Zhonghua Yu Fang Yi Xue Za Zhi*. 2015 May;49(5):456-60.
45. Lee WJ, et al. Relationship Between Open-angle Glaucoma and Stroke: A 2010 to 2012 Korea National Health and Nutrition Examination Survey. *J Glaucoma*. 2018 Jan;27(1):22-7.
46. Heesterbeek TJ, et al. The incidence and predictors of depressive and anxiety symptoms in older adults with vision impairment: a longitudinal prospective cohort study. *Ophthalmic Physiol Opt*. 2017 Jul;37(4):385-98.
47. Zheng Y, et al. The Prevalence of Depression and Depressive Symptoms among Eye Disease Patients: A Systematic Review and Meta-analysis. *Sci Rep*. 2017 Apr 12;7:46453.
48. Wong-Riley M. Energy metabolism of the visual system. *Eye Brain*. 2010;2: 99-116.
49. Cheung LTY, et al. Targeted Delivery of Mitochondrial Calcium Channel Regulators: The Future of Glaucoma Treatment? *Front Neurosci*. 2017;11:648.
50. Feher J, et al. Mitochondrial alterations of retinal pigment epithelium in age-related macular degeneration. *Neurobiol Aging*. 2006 Jul;27(7):983-93.
51. Karunadharma PP, et al. Mitochondrial DNA damage as a potential mechanism for age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2010 Nov;51(11):5470-9.
52. Babizhayev MA. Mitochondria induce oxidative stress, generation of reactive oxygen species and redox state unbalance of the eye lens leading to human cataract formation: disruption of redox lens organization by phospholipid hydroperoxides as a common basis for cataract disease. *Cell Biochem Funct*. 2011 Apr;29(3):183-206.
53. Han WH, et al. Modifications in Retinal Mitochondrial Respiration Precede Type 2 Diabetes and Protracted Microvascular Retinopathy. *Invest Ophthalmol Vis Sci*. 2017 Aug 1;58(10):3826-39.
54. Tien T, et al. High Glucose Induces Mitochondrial Dysfunction in Retinal Müller Cells: Implications for Diabetic Retinopathy. *Invest Ophthalmol Vis Sci*. 2017 Jun 1;58(7):2915-21.
55. Pinazo-Durán MD, et al. Strategies to reduce oxidative stress in glaucoma patients. *Curr Neuropharmacol*. 2017 Jul 5. [Epub ahead of print.]
56. Zhang X, et al. Therapeutic potential of co-enzyme Q10 in retinal diseases. *Curr Med Chem*. 2017 Aug 1. [Epub ahead of print.]
57. Qu J, Kaufman Y, Washington I. Coenzyme Q10 in the human retina. *Invest Ophthalmol Vis Sci*. 2009 Apr;50(4):1814-8.
58. Crooke A, et al. The role and therapeutic potential of melatonin in age-related ocular diseases. *J Pineal Res*. 2017 Sep;63(2).
59. Dehdashtian E, et al. Diabetic retinopathy pathogenesis and the ameliorating effects of melatonin; involvement of autophagy, inflammation and oxidative stress. *Life Sci*. 2017 Dec 1. [Epub ahead of print.]
60. Ozawa Y, et al. Bilberry extract supplementation for preventing eye fatigue in video display terminal workers. *J Nutr Health Aging*. 2015 May;19(5):548-54.
61. Ottobelli L, et al. Age-related changes of the ocular surface: a hospital setting-based retrospective study. *J Ophthalmol*. 2014;2014:532378.
62. Higuchi A, et al. Selenoprotein P controls oxidative stress in cornea. *PLoS One*. 2010 Mar 29;5(3):e9911.
63. Pinazo-Durán MD, et al. Effects of a nutraceutical formulation based on the combination of antioxidants and ω-3 essential fatty acids in the expression of inflammation and immune response mediators in tears from patients with dry eye disorders. *Clin Interv Aging*. 2013;8:139-48.
64. Choi JH, et al. Efficacy of the mineral oil and hyaluronic acid mixture eye drops in murine dry eye. *Korean J Ophthalmol*. 2015 Apr;29(2):131-7.
65. Groß D, Childs M, Piaton JM. Comparison of 0.2% and 0.18% hyaluronate eye drops in patients with moderate to severe dry eye with keratitis or keratoconjunctivitis. Clin Ophthalmol. 2017 Apr 6;11:631-8.
66. Sand BB, Marner K, Norn MS. Sodium hyaluronate in the treatment of kera *Acta Ophthalmol (Copenh)* toconjunctivitis sicca. A double masked clinical trial. 1989 Apr;67(2):181-3.
67. Simmons PA, et al. Efficacy and safety of two new formulations of artificial tears in subjects with dry eye disease: a 3-month, multicenter, active-controlled, randomized trial. *Clin Ophthalmol*. 2015 Apr 15;9:665-75.
68. Postorino EI, et al. Efficacy of eyedrops containing cross-linked hyaluronic acid and coenzyme Q10 in treating patients with mild to moderate dry eye. *Eur J Ophthalmol*. 2017 Aug 2. [Epub ahead of print.]
69. Kishi S. [Vitreous and macular diseases]. [Article in Japanese, Abstract in English.] *Nippon Ganka Gakkai Zasshi*. 2003 Dec;107(12):813-34;discussion 835.
70. Emoto Y, et al. Curcumin suppresses N-methyl-N-nitrosourea-induced photoreceptor apoptosis in Sprague-Dawley rats. *In Vivo*. 2013 Sep-Oct;27(5):583-90.
71. Li J, et al. Curcumin Attenuates Retinal Vascular Leakage by Inhibiting Calcium/Calmodulin-Dependent Protein Kinase II Activity in Streptozotocin-Induced Diabetes. *Cell Physiol Biochem*. 2016;39(3):1196-208.
72. Li J, et al. Curcumin Inhibits Neuronal Loss in the Retina and Elevates Ca^{2+}/Calmodulin-Dependent Protein Kinase II Activity in Diabetic Rats. *J Ocul Pharmacol Ther*. 2015 Nov;31(9):555-62.
73. Steigerwalt R, et al. Meriva®, a lecithinized curcumin delivery system, in diabetic microangiopathy and retinopathy. *Panminerva Med*. 2012 Dec;54(1 Suppl 4):11-6.

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Hope, Gratitude, and Love

by Dr. Douglas Lobay, BSc, ND

It was a beautiful Friday afternoon in early October. It was one of those spectacular autumn days. The cloudless sky was a deep Caribbean blue. There was a gentle breeze that made the leaves rattle. The colors of apricot orange, lemon yellow, and watermelon red suffused the trees that adorned the street. The sun poured down like golden honey. The air was warm and healing.

It was a busy day at the naturopathic office seeing patients, running intravenous therapies and making phone calls. In the afternoon I proceeded to make plans to make a house call to a patient who was at our local hospital. I would also visit a bedridden patient at her home afterwards. I would also serendipitously run into a cancer patient at the hospital. It would turn out to be one of those magical days where the doctor would have an eye-opening experience. I would learn about the value of hope, gratitude, and love.

Ziggy was blind in one eye from a traumatic episode and legally blind in the other eye from cataracts. He was a strict vegan. He was 68 years old. He had been an auto body repairman most of his life until he couldn't see. He was tall and lanky and was single and never married. He lived alone on an orchard until it became too difficult for him, and he moved to a subsidized apartment in the city. He was strong willed and uncompromising in his ideals. One of his most amazing features was the color of his hair. His hair color and texture were that of a 25-year-old male. He and I both agreed that it was probably the result of his strict dietary regime. I would give Ziggy some advice on nutritional things he could do and take for his cataracts. He refused to have surgery and would butt heads with the ophthalmologists he would visit. He tried everything natural for his eyes with modest results.

One day I received a phone call from a social worker at the hospital. Ziggy had been hit by a car while he was crossing a street. He had been hospitalized for about two months. He was bed ridden and was improving slowly with time and physiotherapy. He was diagnosed with osteoporosis which was probably the result of his restrictive diet. The social worker and dietician at the hospital were at odds with Ziggy about his diet and supplements. They asked me to intervene and make a hospital visit to assess his condition. I obliged.

I greeted Ziggy at his hospital bed. He was surprised to see me. We exchanged some pleasantries. I asked him how he was doing. He said great, except for his left leg which was weak. He had some trouble standing and walking. I asked him about his eyes. He said great. He said his eyes were improving and he had no doubt they would get better. He had plans after getting out of the hospital and back to his apartment. We talked about his diet. He had a bag of peas by his bed, and he was eating a lot of organic fruit. He would not eat the hospital food brought to him. He was also eating some organic honey. Ziggy was completely lucid and coherent. He was his usual stubborn self. I suggested that increase his vegetarian protein and calcium foods to help his bones to heal. We agreed that tahini, nuts, and seeds would be incorporated into his diet. I learned from Ziggy the value of hope

and the expectations that things would improve and get better. Hope was a catalyst of healing for Ziggy.

As I was leaving the hospital across a parking lot, I heard someone call my name. I turned and glanced over as the sun pierced my eyes. It was a patient of mine named Roger. He was sitting in a wheelchair as his son was pushing him. I could see he was hooked to an IV and had a catheter. Roger was 70-year-old retired pilot. He had travelled the world and flew all sorts of planes, from float planes in the Yukon, to fighter jets in the Atlantic, to commercial 747s in the Pacific. He was married and had four wonderful children who were all doctors, chiropractors and osteopaths. He had strong family bonds and was fiercely proud of his family.

Roger had been diagnosed with stage 4 esophageal cancer with metastases to his lymph nodes and lungs. He had initially done some chemotherapy with equivocal results. He was following a strict vegetarian diet and was taking various nutritional supplements. He came to my office for intravenous vitamin C therapy. I obliged him, and we began high-dose vitamin C two to three times per week.

Roger was extremely positive and grateful for the life that had been given to him and the family that supported him. We had some in-depth conversations about flying, family, and the meaning of life. I learnt how a CF-16 fighter jet would land on an aircraft carrier. As it landed on the carrier, it would try to catch one of six cables laid across the runway. He told me how large 747s were guided by GPS to land accurately in the runways of airports. He explained how jet engines worked.

With only some moderate improvement in his condition, Roger's cancer progressed. He refused any further chemotherapy or radiation. He sought out many other forms of alternative therapy with no success. All his children who lived in United States and Europe took turns visiting him. His wife was extremely supportive and loving. He had no regrets. I learned from Roger the value of gratitude and thankfulness. No matter what his circumstances, he was always able to show appreciation and kindness.

As I left the hospital, I made my way to Val's house. She lived by herself and was to a large degree bedridden. She had been a patient for a number of years. She was a Christian who belonged to no particular church and was now recently divorced. She had one son who was a prominent lawyer in town. She had no contact with him. He wanted no contact with her. She had a brother whom she seldom talked with and few close friends. Val seemed to be alone and helpless.

Val suffered from a myriad of symptoms. She had multiple food allergies, digestive trouble, muscle atrophy, and neurological weakness. She had a family doctor who basically performed the same lab tests that came back within normal limits and prescribed her sleeping pills, anti-anxiety and anti-depressant drugs and thyroid medicine. She went to a neurologist at the hospital who performed a thorough work up and exam and basically said that there was nothing physically wrong with her. I later reviewed a copy of the CT scan of her head and picked up that there was some cerebellar atrophy. I further concluded that this contributed to her ataxia. She was happy and content that I gave this diagnosis.

Val had a restrictive diet that contributed to her overall weakness and state of health. She took many vitamins and supplements. I tried to give her some guidance on diet and nutrition. She had become progressively weaker and was to a large degree bedridden. She had minimal support and refused to move to any facility that might help her. I focused less on nutritional supplements and more on just listening to her and supporting her. She talked about her life. She had a poor childhood, a series of bad relationships, and seemingly bad luck. She talked how she raised her son the best she could. And now he wanted nothing to do with her. She was deeply hurt and remorseful. I learned from Val the power of love and how the absence of love could negatively affect a person. Affection, caring, and intimacy are extremely important in health and healing.

I left Val's house and returned to my office. The sun was warm and nourishing and was gently caressing the back of my neck as it began dipping in the horizon. I was deep in thought as I was driving down the highway. It was one of those watershed moments when I realized the value of my patients. Sometimes they teach you more than you can give them. I learned the value of hope, gratitude, and love and their strong impact on health and healing.

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Help for Our Stressed-Out Teens

review by Katherine Duff

Holistic Health for Adolescents by Nada Milosavljevic, MD, JD
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Readers inclined to skip past the Preface in books will miss an intriguing story of one person's evolution into complementary medicine in the book *Holistic Health for Adolescents*. Author Nada Milosavljevic, MD, JD, shares a journey from her work as an attorney in a law firm that specializes in intellectual property for pharmaceutical and biotechnology companies to her work as a physician treating adolescents with mental health issues.

The in-depth study of drugs required as an attorney showed her that many of the drugs came from nature. Where a drug company may have isolated a single compound from a plant for a drug, she was familiar with the use of whole plants as remedies from her childhood visits to family living in the former Yugoslavia. Milosavljevic left the law practice to attend medical school where she did her residency in psychiatry and neurophysiology of mental health. She then specialized in pediatric and forensic psychiatry. This was the path that led her to become a forensic psychiatrist working with the courts to provide evaluations, many times for children removed from their homes. Here she saw the limitations of standard drug therapies for adolescents with mental health issues and learned about alternative treatments.

Milosavljevic notes that standard treatments for adolescents are built on research with adults, but there are differences between teens and adults. A major difference is the fact that their brains are still developing. Teens are encountering new social, academic, and competitive experiences often without adequate coping mechanisms. They are experiencing such rapid changes that emotional and behavioral problems are common. Saying that they will grow out of it is not the answer because for some, these issues will become worse and possibly permanent conditions. There are indicators, such as rising rates of suicides in adolescents, that help is surely needed.

To address the unique challenges of being a teenager, Milosavljevic developed a program for ages thirteen to nineteen. The program, which utilizes alternative methods, will give the teen easy, noninvasive tools to feel better and the understanding that feeling better is within their control. This knowledge can then become a lifelong skill.

Milosavljevic put the program into practice at a high school outside Boston in 2011. The positive results generated word of mouth that caused more schools to request the program. In this book, she shares the basics of the program for parents, counselors, and medical practitioners.

> "One of the greatest outcomes of these therapies proved to be one of the most surprising – at least to me. It was a sense of empowerment, control, and confidence the kids gained about dealing with their own health."

The access points for this treatment are the senses: sight, hearing, taste, smell, and touch. All the senses are conduits for external information for our brains to interpret. While the information received can trigger alarm and the fight or flight response, it can also elicit a calming response, which is what the author hopes to achieve through her program.

Milosavljevic begins with an overview for each of the senses that include its development in the brain, historical therapies that have used that sense for healing, and its application to the lives of teenagers today. For example, we learn that hearing involves a complex development process that occurs throughout the brain, not just one location. It begins during the second trimester of pregnancy and does not conclude until about ten years later.

Using sound as therapy goes back centuries and found its way into accepted practice in the United States through the National Association of Music in Hospitals, which was founded in 1926. After World War II, the US War Department recognized its calming and supportive role in healing soldiers with emotional and psychological problems and issued a bulletin in which the Office of the Surgeon General outlined its use.

Music is a large part of the lives of adolescents today. The author notes that their average listening time for music is about four-and-a-half hours every day. Studies have shown they are actually reducing their stress levels and anxiety through their listening.

Milosavljevic's program was developed to address many of the problems facing teens including stress, fatigue, low mood, sleep difficulty, focus and attention, headache, and substance abuse. Each condition is described using a patient case. The description of the condition includes symptoms

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that a parent or health professional can identify. With some of the conditions, professional evaluations are necessary to determine if there is a more serious issue such as depression or physical causes of symptoms such as headaches and fatigue, which may be best treated using conventional means. Finally, with an understanding of the problem, Milosavljevic outlines a "senses" treatment plan.

The touch in the program uses acupressure points. The points are clearly identified in drawings where the person will press with a finger and rotate for a few minutes. The sense of smell calls for using suggested plants, herbs, and essential oils in one's living environment. Herbal tisanes and teas can be made from the recommended plants for taste. Sight is addressed through specific yoga poses and hearing offers the teen appropriate music selections. In addition to the senses protocol, the author offers other supportive therapies that may include acupuncture, biofeedback, and cognitive-behavioral therapy to name just a few.

The secondary theme of this book is the author's desire to "do away with the bright line" that separates conventional medicine from alternative medicine. There could not be a better example of such a need as illustrated in this book. The standard paradigm of the passive patient in a doctor's office can be improved with the therapies that teach the patients methods to reduce stress, thereby offering control over their own health – a true confidence builder.

My first thought when I saw the words *holistic health for adolescents* was – good luck with that. I thought I would be reading about healthy diets and exercises that would fall on deaf ears. Instead I read about a lifeline being thrown to young people who are experiencing more stresses than ever before. Some of these young people are finding their own coping mechanisms through alcohol and drug use, befriending strangers over the internet, aggressive behavior, and over eating. They **will** treat their own discomfort with what is available. Milosavljevic offers a program that first of all cares about the teen and teaches them constructive coping skills. If only all schools had such resources.

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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.

Eat Fresh Vegetables from Your Garden Year-Round

review by Craig Soderberg

Four-Season Harvest: Organic vegetables from your home garden all year long by Eliot Coleman
Chelsea Green Publishing Company, White River Junction, Vermont
©1999; 236 pp; $24.95

The book presents a way to eat the best food – garden fresh and chemical-free – all year long, with little effort or expense.

Four-Season Harvest presents a way to eat the best food – garden fresh and chemical-free – all year long, with little effort or expense. Most gardeners know some season-extending techniques; but this book is not merely about season extension. It is about how to garden and harvest in each of the four seasons. Four-season harvest leads to more freshness, variety, quality, and simplicity.

Coleman's year-round harvest follows two practices: succession planting and crop protection. Succession planting means sowing vegetables more than once, at one- to three- week intervals during the growing season. Crop protection means vegetables under cover.

Coleman also encourages his readers to harvest the vegetables in their youth – before they are fully-grown. In addition to enjoying greater variety, you will also experience far fewer pest and disease problems.

The easiest way to start a four-season garden is with *cold-frames*, which are glass-covered, bottomless wooden boxes, eight feet long and four feet wide. Coleman grows some thirty different crops that survive freezing temperatures with no problem as long as they are provided with a little protection from the wind, which is the real outdoor plant killer in winter.

Fertile soil is the key to growing garden vegetables and compost is the key to a fertile soil. The first step in the four-season harvest is learning to make good compost. Compost consists of two categories: green and brown. Green ingredients are mostly young, moist and fresh materials like various kitchen wastes. Brown ingredients are older and drier and they decompose more slowly. Examples include dried grass stems, old cornstalks, dried pea and bean vines, reeds and old hay. Coleman explains how to balance these two compost categories in chapter two of his book.

Coleman also explains how to adjust soil pH, soil slope, soil hedge (windbreak), soil structure (degree of compaction), and soil aeration. Coleman classifies and discusses different types of green manures based on whether they are legumes or non-legumes and based on whether they are hardy, half-hardy, or tender.

Coleman then discusses the three factors that affect the success of seed germination: soil temperature, seed depth, and moisture. The seed depth and moisture are more able to be directly controlled by the gardener. A general rule of thumb for depth of planting is to cover the seeds to three or four times their diameter. Thus a small seed, such as a carrot, which measure about 1/16 inch in diameter, should be covered with 1/4 inch of soil. However, a corn or pea, which is 1/4-inch-diameter should be covered by soil of about 1 inch.

Coleman's favorite *garden helpers* are ducks. He likes ducks because they do not scratch and fight like chickens to, they are not noisy like chickens, and they lay their eggs at night so the basis for a fresh omelet awaits us in the morning when we let them out of their shelter. They lay more eggs than chickens, and the eggs are bigger, richer, and better tasting. Ducks lay eggs at a reasonable rate during the winter without fancy housing or supplementary light. Even if fed on a homegrown diet of garden and kitchen scraps, instead of the expensive mixed feeds that chickens require, ducks will lay at about 60 percent of the summer rate. However, Coleman really likes ducks because they eat garden slugs. Coleman provides a simple illustration with measurements for how to build a simple duck shelter.

As we begin to think about establishing a winter garden, there are other benefits as well. Vegetables harvested in the winter have higher levels of soluble proteins and reduced sugar, making winter greenery even more nutritious and digestible than hot-season plants.

In terms of vegetable selection, Coleman found that dandelion, escarole, leeks, mizuna, mustard greens, parsley, sorrel, tatsoi, and turnip greens all met the chilling-resistant criterion in his area in Maine. But the hardy souls in Zones 3 (the frigid mountains of Vermont) will find that these five crops - spinach, scallions, mache, claytonia, and carrot - will be dependably harvested all winter from a cold frame, and only mache during the coldest periods.

For those readers who would like to go a step further and ensure the quality and quantity of an even wider harvest of winter vegetables, Coleman offers his experience with a second layer of crop protection - greenhouses and high tunnels.

Coleman also discusses creating a root cellar. Why root cellars? Whereas compost provides the energy to grow the food and the winter protection from frames and tunnels provides a snug home for cold-season greenery, the root cellar is your winter home for the rest of the garden's bounty. In this chapter, Coleman discusses how to create a root cellar, how to control the temperature, how to control the humidity, how to control the darkness level, and what type of storage containers to use in the root cellar.

In the section on garden pests, Coleman notes that chemical fertilizers and pesticides are not necessary. There are natural ways to disadvantage the insects, such as trapping, releasing ladybugs and other predators, time of plantings to avoid hatching periods, and most importantly, strengthening the natural immunity of the plant with optimum growing conditions, adding micronutrient fertilizers, and using ideal growing conditions.

Appendix A was helpful because Coleman provided about 50 pages of information on various vegetables that can grow in cold climates.

This book was well written and easy-to-read. It included eight pages of color photographs of various crops and garden tools. The most helpful tables to me were succession planting, example of crop rotation, green manures, and planting dates for extended harvest. The book does not discuss heat pumps, thermal mass, solar gain, or R-factors because they are too complicated. The author rightly believes that simpler is better, especially where simpler has been time-tested. ◆

The Year in Review and Some Predictions About Next Year, Part One: Stem Cells

It's time to look back at what happened this year and make some predictions about next year. Part One will focus on stem cells.

We started 2017 awaiting the FDA's final guidance documents on HCT/Ps ("stem cells"). In late August, the FDA foreshadowed the guidance documents by issuing warning letters to two of the most high-profile (or infamous) stem cell clinics in the country. Both clinics were warned that their use of HCT/Ps were in violation of the FDA trifecta (unapproved new drug, misbranding, and adulteration), and that their facilities were not in compliance with applicable good tissue and manufacturing practices. (See my September 22, 2017 blog post: http://rickjaffeesq.com/2017/09/22/sleeping-giant-awakens-fda-starts-final-push-eliminate-practice-medicine-stem-cell-clinics/)

Within two months of the warning letters, the FDA published the final guidance documents. They were at least as bad (from the perspective of these clinics and the patients who seek out non-FDA approved stem cell treatments) as the draft guidance documents. See my prior post analyzing the final guidance document: http://rickjaffeesq.com/2017/11/17/big-surprise-fdas-final-stem-cell-guidelines-threaten-existence-stem-cell-clinics/.

On the other hand, two states passed stem cell legislation. California passed a meaningless law aimed at providing informed consent to patients. See http://rickjaffeesq.com/2017/10/05/california-enacts-new-stem-cell-law-wont-change-anything/. Texas passed a stem cell law which could allow patients to use both autologous and allogenic stems cells therapeutically (or in FDA parlance, "non-homologously").

The law won't open-up the floodgates because of the relatively high barriers to entry (i.e., the cost of an ambulatory surgical center, and the big-time IRB requirements): but as I've said, as long as the Texas Medical Board doesn't mess it up, Texas could become the Mecca for the therapeutic use of stem cells about it (http://rickjaffeesq.com/2017/05/31/landmark-texas-stem-cell-legislation-gets-through-the-texas-legislature/).

And yes, Congress did pass some legislation involving stem cells, but it just deals with supposedly faster approval. It won't cause a single patient to receive stem cell treatments in 2018, or so is my prediction. The bill was just a tactic to get stem cell advocates off of Congress folks' backs.

Finally, last week, a civil lawsuit was filed against the Florida clinic, which has become the poster child of the "greedy and evil" for-profit, heretofore unregulated stem cell industry. These are the folks that had a nurse practitioner inject HCT/Ps in the eyeballs of patients and allegedly caused blindness or reduced vision. That's bad news for them and all the stem cell clinics in the intermediate term. It's going to take a while for the case to reach any meaningful result. But the institutional stem cell Mafioso will surely keep banging the drums about this case to keep the pressure on the FDA to do more.

What's Going to Happen in 2018 in the Stem Cell Field?

For sure, the FDA will try to pick-off a few more clinics by starting the process of inspections, issuing 486 field reports, and then following-up with warning letters. I expect to see one or more of the recipients of these warning letters to be involved in litigation with the FDA. However, I don't expect any court rulings until at least mid- to late-2018. As I said before, if the first case decided involves the Florida clinic involved in eyeball injections, the stem cell field won't like the result.

Are Private Stem Cell Clinics Going to Disappear from the US in 2018?

Absolutely not! If anything, I think 2018 will bring more options to patients in terms of use of their own stem cells and even umbilical cord stem cells and other HCT/Ps. You might ask how I can possibly think this in light of the final guidance documents and the FDA's recent warning letters?

I think the delivery of these new therapies is going underground. My read is that more and more physicians are quietly using HCT/Ps in their practice. Therefore, I think that in 2018 and beyond, more people will have access to these treatments, but not necessarily through the large, high-profile stem cell only clinics, because some of them will be mired in legal battles with the FDA.

Won't the FDA Shut All These Stem Cell Docs Down?

I don't think so because the FDA doesn't have the resources or infrastructure to eliminate the clinical use of stem cells. More doctors are using stem cells in their clinical practice. The FDA isn't equipped to go after all these practitioners, because its structure, resources, and operations are geared towards drugs, not the practice of medicine. (And the practice of medicine just happens to be the best defense these docs have, albeit, not recognized by the one case in which it was raised, but more about that another time).

Equally important, patient demand is too great, and more and more physicians are seeing the dramatic benefits of these treatments. I predict that many more docs will start using stem cells because of these two factors, and FDA be damned. Ultimately, I predict that the popularity and the anecdotal evidence of success will prevail over the FDA and the stem cell Mafioso. So, while the FDA may pick-off a few of the large, high profile, or infamous clinics, I think there will be as good, if not better access to these innovative treatments in 2018. That is my prediction and hope.

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Healing with Homeopathy

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

Lingering, Invisible Symptoms Post-Injury

Head injury, traumatic brain injury, post-concussive syndrome – these are the diagnoses of our patients who come for homeopathic help, usually months, or even years, following the accident. The head injuries that we present here are not life threatening. However, patients complain that the symptoms linger, interfering significantly with their thinking, functioning, and normal life. They share with us their dilemma: the accident has passed, they look normal, but they *are not*. Those around them, and they themselves, expect that the injury has passed, but the dysfunction and limitations persist. These patients are typically frustrated and fear they will never fully recover. We have seen consistently excellent results with homeopathy, regardless of the specific symptoms.

If you ask anyone familiar with homeopathy which are *the* most common remedies for head injuries, they will likely tell you *Arnica* and *Natrum sulphuricum.* And, indeed, it is a great idea to take *Arnica* internally in the highest potency that you have immediately following a head injury. We even recommend it immediately after a stroke. *Arnica* 1M will have a more powerful effect than just a 30C potency. But these patients, and others, responded very well to other remedies.

Christina

Christina, thirty-two, was referred by her mom, who is also a patient. She recounted:

> I've suffered two head injuries over the past nine months. First I ran into a plastic slide. It wasn't serious, but I felt depressed afterwards. My chronic back pain got markedly worse, too, after I hit my head. The dizziness and nausea lasted for two weeks. Then, six months later, two months before she began homeopathy, she had a car accident. I experienced a severely reduced capacity to think… to do any cognitively complicated tasks. Like reading. Walking and talking at the same time were difficult. Driving was impossible. I couldn't watch videos. I still can't listen to music without feeling dizzy. After three to four weeks, what doctors consider normal concussion symptoms resolved. I had no dizziness, photophobia, memory loss. I'll feel fine for hours. Then I need to do a task with a high cognitive load, like helping to prepare tax returns, since I'm a bookkeeper, and I'll hit the wall. Everything just kind of powers down.
>
> My functioning improved a lot after I took a vacation, but I still can't function at 100% capacity. When I hit that wall, I can't form any new thoughts. Moving my body feels weird. Sometimes I get dizzy. It is difficult at those times to deal with uncertainty or with the frustration and negative emotion of others. It is difficult to take on projects because I get so anxious about completing them. It's hard to express the scope of it.
>
> My body starts to feel heavy. As if messages from my brain to my body are communicated too slowly. I become lightheaded. This past month I've ended the day with a pretty significant headache. I imagine it's all part of the post-concussion stuff.
>
> My thinking will go in circles. I'll start to cry. Or just want to go to sleep. I almost fall asleep. Lately it's so bad that I can nod out in class. I have to pinch myself or bite my tongue to stay awake. When I feel anxious, I lose track of the foundations of my life and of reality. I lose some sense of my body. I won't notice my feet, my arms. I know they're there, but I stop feeling them. Stop paying attention. Instead of walking on solid ground, I'm walking on a platform supported by tethers and the tethers start to snap. For three to four weeks, I couldn't close my eyes without feeling weird. I wasn't sure I was standing up straight anymore. I'd close my eyes and things would start to tilt. Feel swimmy, unsteady. The way your body feels in water. I didn't know where my head was situated. After the head injury, I would forget the shape of the room around me… which way my head was pointing. I didn't know what was going on outside of me. Where's the door? Where's the wall? My senses would go hazy, disintegrate. Where am I in the world?

We chose *Nux moschata* (nutmeg) for Christina. Like other members of the Magnoliadae family, there is a general feeling of bewilderment and confusion. A blankness, floating, stupefied sensation. *Nux moschata* is well known for experiencing an overpowering sleepiness, such as one sees in narcolepsy. The terrific anxiety that Christina experienced about her disorientation is described in the Sensation of Plants by Rajan Sankaran: "Something strange, bewildering, and confusing must be solved immediately. Once the situation is tackled, she is at ease. Feeling of being lost, like a child." Interestingly, Christina loved spices: "My favorites are cinnamon, fenugreek, cumin, and cardamom. I used to have a spice-of-the-month subscription. Every month they

would send freshly ground spices." Because Christina was highly sensitive, we prescribed *Nux moschata* LM3 to take daily.

Christina's next follow-up visit was a month later:

> I had a really interesting experience a couple of weeks ago. It seemed like another part of my brain came back online. Now I can watch videos… I'm able to work longer hours and to hold my mind in multiple projects, like several tax returns. A month ago, I would have forgotten one project once I started on the next. I'm not sensitive to bright colors anymore. I feel like things in my head are more crisp. In higher definition.

We prescribed a single dose of *Nux moschata* 200C and Christina continued taking the LM3 potency daily.

Six weeks later: "The bigger dose of the remedy was amazing! I remember saying it was like I had a whole new brain. More clear-headed and capable by a really large margin." We gave Christina another dose of *Nux moschata* 200C, to hold in case she needed it in the future, and instructed her to continue the LM3 potency daily.

Four months later: "Cognitively I've improved by leaps and bounds. I'm working ten to fifteen hours a day since it's tax season. The last dose of the *Nux moschata* set my tilt right again." We told Christina to take the 200C dose she was holding and gave her a 1M dose to hold.

Ten months later: We last spoke with her 10 months after her first appointment (12 months following the car accident). She has taken *Nux moschata* 1M twice. The *Nux moschata* has made a dramatic difference in her post-head-injury symptoms. Who would think nutmeg could have such a powerful effect with head injuries?

Maya

We first treated Maya off and on, along with her mom and brother, when she was seven to eighteen years old for ADHD. Her mom again suggested that she contact us for homeopathy when she was twenty-two.

> I was involved in a car accident eight months ago. There was a deer in the road. I swerved and flipped the car. It was totaled. I had a pretty bad concussion. I had to go back to school a week later for student teaching. I've been seeing a physical therapist since then, but I still don't feel completely right. Everything is a whirlwind. I have difficulty focusing and concentration. Light bothers my head. It gives me migraines. Sometimes at night I have trouble looking at a screen. The other night the noise of a highlighter on a book was driving me crazy. Emotionally it's been hard, too. Socially. too.
>
> I was coming home from a friend's house when I saw the deer in the road. It was too late. I went off the road at night. There was blood all over me. They put eleven staples in my head. I don't remember anything after that. I was in complete shock. I didn't even know where I was. I hit my head so hard that it cut the top of my skull and middle of my forehead. I did miss the deer but lost control of my car and ended up in a ditch.
>
> Initially I was diagnosed with a concussion and whiplash. The headaches were very severe. I had trouble sleeping because of the neck and back pain. Light would trigger a headache. Then I would need to lie down in a dark room. The same was true with loud noises. I still struggle with my neck being very sore. When I'm in the car, I can't listen to music or look out the window or it makes my head spin and triggers a headache. I have trouble focusing. All of this has caused a negative attitude and a feeling of instability. I get irritable quickly and lose my patience.
>
> I was doing so well before my accident. Then my life got turned upside down. I ended up getting a Staph infection in the site of the stitches. It seemed never ending. I have not felt the same since. My upper shoulders and back ache. I have difficulty lifting heavy things. I can't walk on the treadmill. Daily tasks and working out have been very hard. I have a hard time thinking, processing, controlling my emotions. Everything shuts down. Everything is just too much to handle. The headaches completely limit me. I just want to be in a closed room by myself with the lights off. It all fell apart at once. The accident was very traumatic to me. It's scary even to be in a car sometimes.
>
> I only remember bits and pieces of what happened. I hit my head so hard. It's hard to believe that I even lived. The headaches are splitting pain that radiates all over my head. It's almost like a fog comes over. A blur. I'm not all there. Sounds are amplified. I get overwhelmed if people get too close to me. And I still dream about being in the accident.

We prescribed *Helleborus (black hellebore)* 200C and LM4 daily for Maya. It is a member of the buttercup family. Those needing remedies from this family can be highly sensitive, as if their nerves were raw. They experience a variety of pain sensations, including sharp, stabbing, stitching, and splitting. However, the other side of this exquisite sensitivity and pain is a numbness or blunting. Maya described this as a fog or blur.

One month later: "I've been good. I'm feeling a lot more relaxed. Not as much anxiety. The headaches have gone down a lot. I'm not experiencing as much light and noise sensitivity as before. The light really hasn't been bothering me. Driving is better. My back is getting better also. I still have soreness in my shoulders and neck. I'm sleeping better. And I feel a lot happier." We suggested that Maya continue the *Helleborus* LM4 daily.

Two months later: "Things are going well. The headaches have decreased even more. I'm able to focus and get my work done without feeling so stressed. I'm not so anxious and on edge about everything." We sent Maya one dose of *Helleborus* 1M, and she continued the LM4.

Three and a half months later: "I've been doing well. I am really busy with my internship. I would like to work with special ed kids. I haven't felt much anxiety. I've really been able to focus…. I've been more able to focus. Now I can work out at the gym and run again. I think the remedy has really helped. I'm not getting flustered like I was before. I can mentally de-stress myself." We repeated the *Helleborus* 1M and continued the LM4.

These are just two of a number of head injury cases we have treated successfully. It is good to remember that homeopathy can be extremely helpful and to seek out care as soon as possible following the head injury. It is very compatible with chiropractic, physical therapy, and whichever other modalities you may be using. Homeopathic care is gentle yet powerful. And, as you can see from these cases, it is highly individualized, depending on the specific symptom picture. And highly effective.

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Functional Gastroenterology Bolus

by Steven Sandberg-Lewis, ND, DHANP

The Grey Areas in GI Health and Disease

Common thought processes about the pathophysiology of septicemia, appendicitis, and diverticulitis tend toward black and white concepts. Either the patient has one of these acute conditions - or they don't. I would like to explain my observations on the continua at work in these three conditions and how thinking outside the box can allow holistically oriented health practitioners to recognize the grey areas in diagnosis. This article will focus on septic shock.

Naturopathic medicine's philosophy is, in large part, based on the concept of unity of disease causation. The theory is that most diseases are due to accumulation of "morbid matter." Under conditions of healthy functioning, these toxins are removed by the emunctories – exhalation, perspiration, defecation and urination. When toxic metabolites accumulate in levels beyond the capacity of the emunctories, inflammation goes to a higher level, eventually triggering "vicarious elimination." This form of detoxification involves suppuration and other exudates, skin lesions, fistulae, respiratory congestion and discharge, diarrhea, vomiting, urinary casts, etc. Standing on the shoulders of the giants of naturopathic philosophy, I agree that this accumulation of "morbid matter" is, in fact, the cause of many diseases. We used to invoke the edict "death begins in the colon." Seen with a broader scope, we might also say that dysfunction and autoimmunity begin in the digestive tract as a whole.

According to Medscape:

> The pathophysiology of septic shock is not precisely understood but is considered to involve a complex interaction between the pathogen and the host's immune system. The normal physiologic response to localized infection includes activation of host defense mechanisms that result in the influx of activated neutrophils and monocytes, release of inflammatory mediators, local vasodilation, increased endothelial permeability (in part though the zonulin pathway), and activation of coagulation pathway.[1]

The present focus in research on the effects of the GI microbiota is bringing us to a better physiological explanation of the unity of disease theory. Lipopolysaccharide (LPS) derived mostly from the outer cell wall of gram negative bacteria, leads to activation of macrophages, neutrophils, and platelets, and triggers the endothelia to release various cytokines (especially tumor necrosis factor and interleukin-1) and other mediators. LPS is also referred to as endotoxin. Peptidoglycans are similar pro-inflammatory substances derived from the outer cell wall of gram positive bacteria. These mediators, along with lipotechoic acid and superantigen, induce Th17 and therefore are significant in the pathophysiology of Crohn's disease, systemic lupus erythematosus, and rheumatoid arthritis.[2]

There are 1 million copies of LPS in each gram-negative microbe and these are released from both living and dead bacteria.[3] Release may also be triggered by antibiotic therapy. Adults have approximately one gram of total gut LPS.[4, 5] When absorbed into the portal vein, LPS is a burden on the liver; and when excessive, LPS serum levels rise and have far reaching effects. Clearly, **intestinal bacteria do not need to cross into the bloodstream to trigger systemic inflammation and even life-threatening pathology.**

As I wrote in a previous *Townsend* article on the gut-brain axis (June 2017), not all bacterial LPS is the same. For example, Enterobacter-derived LPS may be 1000 times more potent than LPS derived from other gram-negative bacteria.[6] Obesity increases the amount of LPS, which may be two to three times higher in the obese population compared to lean individuals.

Many mechanisms are in place to metabolize and remove LPS. In the neonate, LPS is bound and inactivated by a bacterial pattern recognition receptor CD14 found in human breast milk. CD14 is also found in bovine colostrum. Lactoferrin in breast milk also binds to LPS.[3] After weaning, LPS binds to Toll-like receptor 4 (TLR-4) on intestinal epithelial cells; and secretory IgA in enterocytes inactivates LPS. Lowering this endotoxin reduces the NF-KB pathway and its cascade of proinflammatory cytokines interferon, interleukins, and TNF alpha.[7] Mucins (from goblet cells) and antimicrobial peptides such as defensins (from Paneth cells) act on gram negative bacteria and therefore reduce exposure of intestinal epithelia to LPS. Defensins also alter the structure of developing bacterial cell walls to weaken the gram-negative microbes.

Intestinal alkaline phosphatase is another first-line mechanism for removal of LPS. Hepatic alkaline phosphatase helps reduce

LPS arriving via the portal vein. When LPS from gut bacteria is absorbed into the bloodstream at higher levels, the alkaline phosphatase mechanism may not be adequate and serum levels of LPS rise. The ensuing inflammatory cascade has physical, emotional, and cognitive effects.[8]

Recent case reports illustrate that altering GI flora by the use of fecal microbiota transplantation can resolve sepsis and the multiple organ dysfunction associated with sepsis.[9-11] A prospective placebo-controlled trial of elderly patients with intestinal bacterial overgrowth found that use of probiotic food (yogurt) decreased serum LPS and pro-inflammatory cytokines.[12] Another prospective placebo-controlled trial studied the effects of yogurt consumption in premenopausal women. Results included reduced biomarkers of chronic inflammation and reduced evidence of endotoxin exposure compared with a soy-based control food.[13]

The feeding of omega-3 fish oils is a common intervention in nutritional immune support. A multicenter, prospective, randomized, double-blinded, controlled trial showed that the ingestion of omega 3 fish oils and gamma linoleic acid (EPA/GLA) may be beneficial in the treatment of patients in the early stages of sepsis - before organ dysfunction has begun. These oils slowed the progression of sepsis-related organ dysfunction.[14]

Does one need to have life-threatening septic shock in order to have disease-causing LPS levels? The gray area may be those increased levels due to shifts in the gastrointestinal microbiota that induce a spectrum of immune responses. Small intestine bacterial overgrowth – increased levels of commensal flora in a highly absorptive mucosal region - is associated with over 40 major illnesses and provides a major burden of LPS, peptidoglycans, and cytokines. If the mechanisms of secretory IgA, toll-like receptors, intestinal and hepatic alkaline phosphatase, defensins and mucins fail to inactivate and remove these inflammatory triggers, vicarious elimination will ensue. All manner of acute and chronic inflammatory diseases may begin in this way.

References

1. misc.medscape.com/pi/iphone/medscapeapp/html/A168402-business.htm**.**
2. Li H, et al. Commercial peptidoglycan preparations are contaminated with superantigen-like activity that stimulates IL-17 production. *J Leukocyte Biology*. 2008; (89): 409-418.
3. Guerville M, Boudry G. Gastrointestinal and hepatic mechanisms limiting entry and dissemination of lipopolysaccharide into the systemic circulation. *Am J Physiol Gastrointest Liver Physiol.* 2016;311(1):G1-G15.
4. Erridge C, et al. A high-fat meal induces low-grade endotoxemia: evidence of a novel mechanism of postprandial inflammation. *Am J Clin Nutr*. 2007;86(5):1286-92.
5. Bested AC, et al. Intestinal microbiota, probiotics and mental health: from Metchnikoff to modern advances: Part I - autointoxication revisited. *Gut Pathog*. 2013;5(1):5.
6. Mayer E. *The Gut-Brain Connection.* New York : Harper-Collins, 2014.
7. Boullier S, et al. Secretory IgA-mediated neutralization of Shigella flexneri prevents intestinal tissue destruction by down-regulating inflammatory circuits. *J Immunol*. 2009;183(9):5879-85. .
8. Grigoleit JS, et al. Dose-dependent effects of endotoxin on neurobehavioral functions in humans. *PLoS One*. 2011;6(12):e28330.
9. Li Q, et al. Successful treatment of severe sepsis and diarrhea after vagotomy utilizing fecal microbiota transplantation: a case report. *Crit Care*. 2015;19:37.
10. Wei Y, et al. Successful treatment with fecal microbiota transplantation in patients with multiple organ dysfunction syndrome and diarrhea following severe sepsis. *Crit Care*. 2016; 20: 332.
11. Li Q, et al. Therapeutic modulation and reestablishment of the intestinal microbiota with fecal microbiota transplantation resolves sepsis and diarrhea in a patient. *Am J Gastroenterol*. 2014; 109(11):1832-4.
12. Schiffrin EJ, et al. Probiotic yogurt in the elderly with intestinal bacterial overgrowth: endotoxaemia and innate immune functions. *Br J Nutr*. 2009;101(7):961-6.
13. Pei R, et al. Low-fat yogurt consumption reduces biomarkers of chronic inflammation and inhibits markers of endotoxin exposure in healthy premenopausal women: a randomised controlled trial. *Br J Nutr*. 2017;118(12):1043-1051.
14. Pontes-Arruda A, et al. Enteral nutrition with eicosapentaenoic acid, γ-linolenic acid and antioxidants in the early treatment of sepsis: results from a multicenter, prospective, randomized, double-blinded, controlled study: the INTERSEPT study. *Crit Care*. 2011;15(3):R144.

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Monthly Miracles

by Michael Gerber, MD, HMD
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Boron – An Important Trace Mineral

An 80-year-old woman with hands distorted by osteoarthritis walked into my office and gave me a big hug. This is the first time she had no pain in her hands for many years. She had been on Borax for a little over one month and was thrilled at the pain relief she experienced. Borax is sodium tetraborate decahydrate; sodium tetraborate decahydrate is basically boron. It is a trace mineral that deserves more attention.

In his landmark book, *Minerals for the Genetic Code*,[1] Charles Walters, one of the founders of organic farming and executive editor of *Acres USA*, wrote thousands of articles on organic and sustainable agriculture and authored or co-authored dozens of books on this subject. He related boron's importance to our genetic code as described by Dr. Richard Olree. Walters was extremely fond of boron and many other trace minerals especially selenium, which he thought was most important to protect us from cancer.

Walters felt that boron was the conservator of magnesium, and that 3 mg of boron per day would stop urine output of magnesium. Boron, he states, is "the fuel for the highest portions of the brain responsible for pure and high ideals and controls the heart meridian." Perhaps it helps to decalcify the pineal gland. Adequate boron levels absorb radiation and were used to control radiation in the Chernobyl disaster. "Truck drivers were paid extra to deliver boron to the disaster site without knowing that supplementing boron would have spared them the radiation toxicity…. Boron stopped the 'China Syndrome' from occurring in Russia."[1]

Boron elevates levels of testosterone and is easily displaced by aluminum. It activates vitamin D, enhances memory, increases alertness, and protects the heart. Deficiency states include ADD/ADHD, osteoporosis, arthritis, reduces short-term memory, and decreases brain function.

The Borax Conspiracy

Walter Last is a German health science writer living in Australia. His paper, "The Borax Conspiracy: How the Arthritis Cure Has Been Stopped," is easily found online and is a definitive guide to delivering boron via borax, which is fortunately inexpensive. Last recounts the story of Rex Newnham, PhD, DO, ND, a soil scientist in Australia who developed arthritis unresponsive to conventional treatment in the 1960s. Newnham's research revealed that countries with low boron levels had high rates of arthritis and vice versa. He began supplying patients with borax as a safe and inexpensive source of boron and took it himself with often dramatic resolution of arthritis. His dose was 30 mg per day. All his arthritic symptoms and pain resolved in three weeks. Within a few years he had standardized the dose and sold 10,000 bottles per month when he asked a drug company to market it. It proved to be a large mistake when the company realized that borax would replace more expense arthritis drugs and influenced the government to designate it a poison in any form. It was outlawed in Australia in 1981. It was subsequently outlawed in the European Union in 2010.

Boron Chemistry

Boron has many health effects. It normalizes the function of cell membranes and signaling across the membranes. Found throughout the body, it is especially prevalent in the parathyroid glands, bone, and teeth enamel and is necessary for bone and joint function. Boron is for the parathyroids as iodine is for the thyroid. Walter Last says:

> Boron deficiency causes the parathyroids to become overactive, releasing too much parathyroid hormone raises the blood level of calcium by releasing calcium from bones and teeth. This then leads to osteoarthritis and other forms of arthritis, osteoporosis and tooth decay. With advancing age high blood levels of calcium lead to calcification of soft tissues causing muscle contractions and stiffness; calcification of endocrine glands especially the pineal gland and ovaries; arteriosclerosis, kidney stones, and calcification of the kidneys leading to kidney failure…. Boron affects the metabolism of steroid hormones, especially the sex hormones. It increases low testosterone levels in men and oestrogen levels in menopausal women. It also has a role in converting vitamin D to its active form, thus increasing calcium uptake and deposition in bone and teeth rather than causing soft tissue to calcify. Other health benefits have been reported such as improvement of heart problems, vision, psoriasis, balance, memory and cognition.

A 72-year-old patient with hypercalcemia and elevated parathyroid hormone levels normalized in about a month of borax therapy. Another patient, a 56-year-old male, who has suffered recurrent kidney stones for years heads off attacks with borax.

Walter Last says:

> The German cancer researcher, Dr. Paul-Gerhard Seeger, has shown that cancers commonly start with the deterioration of cell membranes. As boron is essential for cell membranes and boron deficiency is widespread, this may be an important cause for the initiation for tumor growth. Boron compounds have anti-tumor properties and are "potent anti-osteoporotic, anti-inflammatory, hypolipemic, anti-coagulant and anti-neoplastic agents."[2]

Fungi and Fluoride

Boron is an excellent fungicide. It has been used for athlete's foot and toe nail fungus. Using a handful of borax rubbed on wetted feet stops itching immediately. Boric acid or borax in caps inserted vaginally for two weeks have relieved vaginal thrush.[3] Walter Last says, "Borax, similar to the equally endangered Lugol's solution, can also be used to remove accumulated fluoride and heavy metals from the body. Fluoride not only causes bones to deteriorate, but also the pineal gland to calcify and the thyroid to become underactive. Borax reacts with fluoride ions to form boron fluorides which are then excreted in the urine."

Side Effects and Dosage

Safety studies show that borax is five to ten times safer than table salt, as Last explains. Read "The Borax Conspiracy" online for a full review of toxicity studies. Borax is not appreciably different from USP boron.

The standard dose is 1 teaspoon of borax per liter of water to make a concentrated, stock solution. One tsp of the concentrate has 25 to 30 mg of borax which gives 3 mg of boron diluted in good water or juice. This may be taken once or twice per day.

Of importance, however, one must start patients very slowly. One or two drops of the stock solution in water initially and gradually increase. Detoxification reactions are common such as aggravation of symptoms or the Herxheimer reaction which are usually short lived. Taking borax is best only four or five days per week and/or interrupt for one week each month. I like taking an EDTA chelation weekly when initiating borax therapy, perhaps removing stirred-up calcium or other metals. Last suggests working up to one-eighth, one-fourth, or one-half teaspoon per day in water with a carbohydrate meal for larger patients to treat strong fungal infections, mycoplasmas, autoimmune diseases, cancer, or dementia. The higher doses taste soapy and may be masked by lemon juice, vinegar, or ascorbic acid.

I really like the effects of borax on psyche and body and on patient's general health.

References

1. Walters C. *Minerals for the Genetic Code*. Acres USA. 2013. ISBN 978-0-911311-85-3.
2. Benderdour M, et al. In vivo and in vitro effects of boron and boronated compounds. *J Trace Elem Med Biol.* 1998 Mar;12(1):2-7.
3. De Seta F, et al. Antifungal mechanisms supporting boric acid therapy of *Candida* vaginitis. *Journal of Antimicrobial Chemotherapy*. 1 February 2009;63(2):325–336.

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Cool Beans

by Robin Rose, MD, RN, FNP
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Getting to Know the Uremics: Attending to Early and Moderate CKD Detoxicology

This column''s intent is to deepen primary care vision and understanding of early and moderate chronic kidney disease (CKD). The CKD epidemic is growing. Many patients report their diagnosis was delayed and their care neglectful. While we may offhandedly portray Stage 3 as asymptomatic, patients beg to differ.[1]

Nephrologist Amanda Raff explains that the concept of uremia, historically described as late stage CKD, is expanding. Uremia literally means "urine in the blood." Now, it is understood that uremia begins at the onset of declining glomerular filtration, long before the end stage.[2] *Uremic toxicity is* a systemic syndrome; uremic toxins can affect all tissues - and do so early in the course of the disease.[3]

Uremia, known as a state of chronic inflammation, can cause acute phase reactants to increase (CRP, IL6, fibrinogen, ferritin, serum amyloid A) or decrease (albumin, prealbumin, and transferrin). Gut-Kidney-related dysbiosis – with endotoxin-induced inflammation – contributes to the multifactorial choir of uremic toxic assault on body functions.

Uremic toxemia is fraught with complexity, whether the source of toxins is endogenous or exogenous. Deficient glomerular filtration results in diminished renal excretory capacity. This, combined with disordered renal tubular metabolism and renal endocrine disarray, perpetuates many dysfunctional processes.[3]

Already by Stage 3, elevated solutes (hippuric acid, indole-3-acetic acid, kynurenic acid) may inhibit tubular excretion. These compete for organic anion uptake transporters and efflux pumps, resulting in increased risk of drug interactions and toxicity.[4]

Uremic toxins can induce apoptosis, with nephron-damaging and fibrosis-inviting "epithelial-to-mesenchymal transition" (EMT) in the proximal tubules. With inhibited tubular transport proteins, the excretion of drugs, solutes, and waste products is compromised. So too, is the patients' quality of life compromised - with notable risk for comorbidities.[4]

Engaging preventive uremia thinking, one observes impaired defensive ability and superimposed deficiency states of CKD. There is a synergy of toxins with maladaptive consequences. Many uremic toxins, already elevated in patients with less advanced cases, often go under the radar without astute laboratory exploration.[2] Thus, renal detoxicology.

The European Uremic Toxins (EUTox) Work Group, established by biochemists and clinicians working with uremic toxicity and its therapies, collaborated to develop the Uremic Toxins DATA BASE, an encyclopedic overview of uremic toxins and comprehensive reviews on all uremic solutes.[5]

Sidebar 1. Uremic Toxin Types Based on Pathobiological Mechanisms

Type I: Normally produced endogenous substance, accumulates due to impaired excretion (i.e., urea).
Type II: Excess endogenous production and impaired degradation of normal substance (i.e., PTH, ADMA, urea).
Type III: Exogenous toxin accumulates due to decreased excretory capacity and persistent intake (i.e., aluminum).
Type IV: Normally produced endogenous substance – decreased synthesis, enhanced degradation.

(Normally, there is a combination of more than one.)[2]

Sidebar 2. Uremic Toxins with Similarities

Purine Derivatives: Cytidine, hypoxanthine, xanthine, uric acid

Pyrimidine Derivatives: Thymine, orotic acid, orotidine, uridine

Methyl amine Derivatives: Methylamine, dimethylamine, trimethylamine

Indole Derivatives: Kynurenine, indole-3-acetate, kynurenic acid, melatonin, indoxyl sulfate, quinolinic acid.[6]

Uremic retention solutes are many. Some of these solutes have more recently been recognized as uremic toxins because they negatively impact normal biological functions. Combined with the mal-effects of their toxic metabolites, these toxins cause a broad range of cellular and molecular patho-biological damage.[3,6]

Several sort-systems for categorizing uremic toxins have been proposed. (See Sidebars) This illustrates why primary care can step way beyond the BUN, creatinine, and protein in urine to assess the status of this population.

- Low-molecular-weight, water-soluble uremic toxins (< 500 Da): EUTox found 68 in this group, many familiar: ADMA, SDMA, creatine, creatinine, hyaluronic acid, guanidine, urea, uric acid, oxalates.
- Protein-bound solutes comprise 27.8% of EUTox uremic toxins, < 500 Da. This includes AGEs, cytokines, interleukins, TNFa, homocysteine, indoxyl sulfate, kynurenic acid, leptin, p-cresyl sulfate, etc.
- Middle-molecular-weight molecules (>500 Da); more than 50 found to cause and effect pathophysiology: Adiponectin, cystatin C, leptin, gherlin, prolactin, cholecystokinin, B2 microglobulin, etc.
- Uremic toxins with similar chemical structures – ie Guanidines: small water soluble compounds that resemble urea and creatinine, also urea derivatives like ADMA.[6] Bugnicourt et al. write that these cause neuroexcitation in CKD, increase Homocycreine, and cause cerebral endothelial dysfunction – all associated with the well-recognized CKD cognitive disorder.[7]

Some Examples of Uremic Toxins and Their Effects

AGEs: An example of a familiar uremic toxin is advanced glycation end products – AGEs. These exogenous uremics, absorbed 30% by digestion, are too large for filtration at Bowman's capsule. AGE proteolysis in cells can result in metabolites that are even more toxic. Inadequate removal leads to accumulation; five-times-increased concentrations can be found in mild CKD.[6] Teaching patients to change cooking habits helps decrease this risk.

ADMA, another example, is a highly protein-bound methylated amino acid, increased in uremic plasma. As a potent NOS inhibitor, endothelial damage is the concern (recall CKD's dramatically increased cardiorenal risk). It is the inhibition of kidney-derived metabolizing enzymes – NOT decreased excretion – that causes this facet of uremic inflammation.[2] Lifestyle strategies may offer patients lowered risk for this issue.

Cardio-renal effects. Premature uremic vascular disease is well recognized at all CKD stages. The phenotype of uremia and its complex dysmetabolism presents an imbalanced relationship with DNA methylation; there's a combination of environmental and heritable factors. Manipulating the epigenome in early/moderate CKD with an individualized lifestyle prescription, guided by functional medicine lab explorations, can impact and lessen the assault of this dire morbidity and mortality.[8,9]

Gut-kidney effects. Functional gastroenterology has a place in remediating uremic dysbiosis with its well-honed inflammation awareness.

Uremia is a significant cause of dysbiosis. The gut is an extension of the external environment. The large intestine produces toxic uremic compounds, even from normal dietary macromolecules. Toxic substances ingested with food can affect intestinal bacterial products. Marked disintegration of colonic epithelial barrier structure, significant alterations in the colonic bacterial flora,[10] and disruption of tight junctions occur as a direct result of uremic toxin damage. Endotoxin influx causes systemic inflammation, even without infection. Oxidative stress recruits immune cells. Impaired Nrf2 compromises cytoprotection, disabling natural antioxidants.[11]

Decreased glomerular filtration rate (GFR) leads to increased concentration of urea. Urea influxes into the gut, hydrolyzes to ammonia, then to ammonium hydroxide (increasing intestinal lumen pH), causing mucosal irritation (accompanied by aberrations in uric acid and oxalate). These metabolites, substituting as food for microbes in place of indigestible carbohydrates, cause a shift, disturbing normal symbiotic microbe/host relationships. Pro-oxidant, pro-inflammatory harmful byproducts form. Compromised tight junctions and efflux of toxins ultimately causes the nephron-sclerosing heralding end stage.

Basic Treatment Approach – Renal Detoxicology

The search for therapies to improve removal of toxins has focused on pharmacological strategies to block pertinent pathways. Due to limited space, I can merely point out familiar areas of functional holistic medicine to mitigate CKD metabolic toxic derangements.

Exogenous Detox. Toxic food and environment significantly effect CKD patients. Heavy metals, pesticides, prepared foods, hygiene products, and household, garden and cleaning chemicals are known to harbor uremia-triggering qualities. Initiating the arduous process of encouraging elimination of potentially toxic and common "products" from kitchen, bathroom, garage, garden, and work offers a program with strong secondary prevention benefit.

Stress illustrates another category of toxics. Reducing life and social stresses reduces toxic catecholamines. Stress reduction is medicine: PTSD, abuse, psychopathology, and eating disorders are all appropriate targets.

Diet specifications for early moderate CKD are individualized. Encouraging a shift to organic, non-GMO fare is a start. Using basic labs can provide insight into potential uremic toxins – creatinine, potassium, phosphorus, albumin, bicarbonate levels, etc. – and easily guide renal diet. Begin by optimizing amount (max 0.8 grams of protein per kilo daily) and type of protein (plant-based choices offer CKD benefits). More sophisticated testing provides a more optimal health status: amino acid testing, organic acid testing, nutrient panels, hormone panels, inflammation markers, etc.

Medication awareness and supplement awareness, including binders, incipients etc., is important, as some contribute to renal toxicity.

Endogenous Detox impacts how internally-derived toxins are formed and processed. It includes engaging well-honed

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skills and proactively evaluating and addressing inflammation, SNPs, coagulation, oxygenation, and acidification. Early subtle findings can be used to guide the long-term arduous process of making healthy changes. Practices to aid endogenous detox include the following:

- Prebiotics, dietary resistant starch, and probiotics can support healthy gut microbe symbiosis. Elimination of GMO products, unnecessary antibiotics, steroids, and sugars offer balance to urea-induced dysbiosis. Fermented foods are well-accepted by patients understanding the CKD-dysbiosis association.
- Low-inflammation lifestyle as Rx, with supplement and nutrient support.
- Sorbent therapies such as natural toxin barriers like bentonite clay and activated charcoal have been studied and used to block gut absorption of toxins (i.e., phosphorus) Nutrient monitoring and supplementing might be necessary.
- Prevention of constipation is important as prolonged mucosal contact with gut-microbe-derived toxins exacerbates dysbiosis. Known strategies are useful. Acacia gum, magnesium, and rhubarb root have dual benefits for CKD and gut.

Summary

Uremia starts with early CKD. Lowering the toxic load protects nephrons and offers the potential to slow progression. Diagnosing at Stage 2 CKD can initiate a health-improving journey. Stage 3 patients have multifactorial complaints and symptoms: an excellent portal into which a doctor-patient team can achieve rewarding detoxicology.

References

1. Personal communications.|
2. Raff A, et al. New Insights into Uremic Toxicity. *Current Opinion in Nephrology and Hypertension*. 2008Nov; 17(6);560-65.
3. Glassock R. Uremic Toxins: What are they? An integrated Overview of Pathobiology and Classification. *Journal of Renal Nutrition*. 2008Jan; 18(1); 2-6.
4. van den Brand JAJG, et al. Uremic Solutes in CKD and their Role in Progression. *PLOS ONE*. 2016 Dec; 11(12).
5. Uremic Toxin (EUTox) Work Group. Purpose of EUTox. www.uremic-toxins.org.
6. Lisowska-Myjak B. Uremic Toxins and Their Effects on Multiple Organ Systems. *Nephrology Clin Pract.* 2014;128:303-311.
7. Bugnicourt J-M, et al. Cogitive Disorders and Dementia in CKD: The neglected Kidney Brain Axis. *JASN*. 2013Mar; 24(3); 353-63.
8. Vanholder R, et al. A bench to bedside view of uremic toxins. *J Am Soc Nephrol*. 2008;19(5):863-870.
9. Stenvinkel P, Ekstrom J. Does the Uremic Milieu Effect the Epigenotype. *Journal of Renal Nutrition*. 2009 Jan; 19(1); 82-85.
10. Black AP, Cardozo LF, Mafra D. Effects of Uremic Toxins from the Gut Microbiota on Bone: A Brief Look at Chronic Kidney Disease. *Ther Apher Dial*. 2015 Oct;19(5):436-40.
11. Vaziri, Nosratola, Altered intestinal microbial flora and impaired epithelial barrier structure and function in CKD: the nature, mechanisms, consequences and potential treatment. *Current Opinion in Nephrology and Hypertension*. 2015 Nov; 21(6); 587-92.

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Calendar

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APRIL 5-7: THE FORUM FOR INTEGRATIVE MEDICINE – Treating the Untreatable: Unraveling Complex Chronic Illness in Chicago, Illinois. CONTACT: https://forumforintegrativemedicine.org/

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APRIL 6-8: ENVIRONMENTAL HEALTH SYMPOSIUM 2018 in Scottsdale, Arizona. Effective methods and interventions for reducing toxic load and body burden. CONTACT: 855-347-4477; http://www.EHS2018.com

APRIL 6-8: 13th ANNUAL JOINT AMERICAN HOMEOPATHIC CONFERENCE – Homeopathy: An Affordable Healthcare Solution in Phoenix, Arizona. CONTACT: http://www.homeopathycenter.org/

APRIL 12-14: A4M ANNUAL SPRING CONFERENCE in Hollywood, Florida. CONTACT: https://www.a4m.com/

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APRIL 14-15: CALIFORNIA NATUROPATHIC DOCTORS ASSOCIATION with PsychANP present INTEGRATIVE PSYCHIATRY AND NEURO-IMMUNOLOGY in Torrance, California. CONTACT: http://www.calnd.org/

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APRIL 19-21: 3rd CONGRESO SENMO (La Sociedad Española de Nutrición y Medicina Ortomolecular) in Barcelona, Spain. CONTACT: http://senmo.org/index.php/congresos/iii-congreso-menu/ponentes-iii-congreso-senmo

APRIL 20-21: INTEGRATIVE MEDICINE FOR THE TREATMENT OF TICK-BORNE DISEASES in Baltimore, Maryland. CONTACT: delmarvalyme@yahoo.com; http://integrativelyme.com

APRIL 26-29: 24th CLINICAL APPLICATIONS FOR AGE MANAGEMENT MEDICINE in Orlando, Florida. CONTACT: https://www.agemed.org

APRIL 27-29: ACUPUNCTURE MERIDIAN ASSESSMENT (AMA) TRAINING for Doctors, Dentists & Health Professionals: Detecting Chronic Diseases & Causes in St. Louis, Missouri. With Simon Yu, MD. **CONTACT:** http://www.preventionandhealing.com/

APRIL 27-29: 47th ANNUAL INTERNATIONAL ORTHOMOLECULAR MEDICINE TODAY CONFERENCE in Tokyo, Japan. CONTACT: https://www.isom.ca/omt/

APRIL 29: CONNECTICUT NATUROPATHIC PHYSICIANS ASSOCIATION 10TH ANNUAL CONFERENCE in Cromwell, Connecticut. CONTACT: http://www.events.syncopatemeetings.com/cnpa/

MAY 3-JUNE 10: ORTHOMOLECULAR APPLICATIONS IN INTEGRATIVE PSYCHIATRY – SCHIZOPHRENIA & PSYCHOSIS. Online course presented by the Canadian Society for Orthomolecular Medicine. CONTACT: https://csom.ca/event/schizophrenia-psychosis/

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MAY 19: MNANP ANNUAL CONVENTION & MEETING – Integrative Chronic Infections Assessment and Treatment with Dr. Paul Anderson in St. Paul, Minnesota. 5 CEUs available. CONTACT: http://www.mnanp.org/conference

MAY 19-20: THE GREAT PLAINS LABORATORY, INC. presents GPL ACADEMY PRACTITIONER WORKSHOPS in Charlotte, North Carolina. This workshop will review organic acids testing, toxic chemical testing, and mycotoxin testing. CONTACT: http://www.GPLWorkshops.com

MAY 24-26: AUTISM ONE 2018 CONFERENCE in Chicago, Illinois. CMEs available. CONTACT: http://www.autismone.org/CUTTING-EDGE-AUTISM-CME-PROGRAM

MAY 31- JUNE 2: INSTITUTE FOR FUNCTIONAL MEDICINE ANNUAL INTERNATIONAL CONFERENCE – Solving the Puzzle of Autoimmunity: The Interplay of Gut, Genes, and Environment in Hollywood, Florida. CONTACT: 800-228-0622; https://www.ifm.org/

JUNE 1-4: MEDICINES FROM THE EARTH HERB SYMPOSIUM in Black Mountain, North Carolina. CE credits available. CONTACT: 541-482-3016; http://www.botanicalmedicine.org

JUNE 14-16: HOMEOPATHY RESEARCH INSTITUTE CONFERENCE in London, United Kingdom. CONTACT: https://www.hri-research.org/

JUNE 16-23: CLINICAL & COMPARATIVE MATERIA MEDICA with Dr. Subrata K. Banerjea at Allen College of Homeopathy in Chelmsford, Essex, United Kingdom. CONTACT: http://www.homeopathy-course.com/index.php/training-courses

JUNE 20-23: SOCIETY OF PROGRESSIVE MEDICAL EDUCATION (SOPMed) INTEGRATIVE THERAPY TRAINING AND ANNUAL CONVENTION in Colorado Springs, Colorado. Includes pre-conference events. CONTACT: 517-242-5813; https://sopmed.org/

JULY 6-8: 5th INTERNATIONAL CONGRESS ON NATUROPATHIC MEDICINE – Promoting Excellence in Natural Medicine in London, United Kingdom. CONTACT: + 44 (0)1745 828 400 Email: secretariat@icnmnaturopathy.eu; http://icnmnaturopathy.eu/en/

JULY 12-14: INSTITUTE FOR FUNCTIONAL MEDICINE – HORMONE APM in Portland, Oregon. CONTACT: 800-228-0622; https://www.ifm.org/

JULY 12-14: AMERICAN ASSOCIATION OF NATUROPATHIC PHYSICIANS ANNUAL CONVENTION AND EXPOSITION in San Diego, California. CONTACT: http://www.naturopathic.org/aanp2018

JULY 15-17: INSTITUTE FOR FUNCTIONAL MEDICINE – ENERGY APM in Portland, Oregon. CONTACT: 800-228-0622; https://www.ifm.org/

AUGUST 4-5: THE GREAT PLAINS LABORATORY, INC. presents GPL ACADEMY PRACTITIONER WORKSHOPS in Denver, Colorado. This workshop will review organic acids testing, toxic chemical testing, and mycotoxin testing. CONTACT: http://www.GPLWorkshops.com

AUGUST 10-12: INTERNATIONAL HYPERBARIC MEDICINE CONFERENCE & EXPO – ADVANCING HYPERBARIC MEDICINE GLOBALLY in Denver, Colorado. CONTACT: https://www.hyperbaricmedicalassociation.org/conference-agenda

SEPTEMBER 6-9: 9TH INTEGRATIVE MEDICINE FOR MENTAL HEALTH CONFERENCE (IMMH) in Dallas, Texas. Evidence-based diagnostic and treatment options to reduce symptoms of autism, ADHD, depression, anxiety, Alzheimer's, and more. CONTACT: http://www.IMMH2018.com

SEPTEMBER 14-15: CLINICAL MITOCHONDRIAL AND ENVIRONMENTAL MEDICINE in Heidelberg, Germany. Specialist lectures in English. CONTACT: info@mito-medizin.de; http://www.mito-medizin.de/

OCTOBER 18-22: INTERNATIONAL COLLEGE OF INTEGRATIVE MEDICINE – An Orthomolecular Approach to Cancer in Minneapolis, Minnesota. CONTACT: http://icimed.com/

OCTOBER 19-20: DERMVEDA INTEGRATIVE SKIN CARE SYMPOSIUM in Sacramento, California. CONTACT: http://2018.integrativeskinsymposium.com/

OCTOBER 25-27: INSTITUTE FOR FUNCTIONAL MEDICINE – GASTROINTESTINAL APM in Nashville, Tennessee. CONTACT: 800-228-0622; https://www.ifm.org/

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Ask Dr. J

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

The Fix Is In

The focus for this month's *Townsend Letter* is on allergies. I could write a comprehensive book just on this topic, but I will attempt to limit myself to talking about what I was theoretically taught in naturopathic school and what Fr. Becker taught me in senior English class at St. Ignatius College Preparatory High School in San Francisco: If you want to know what's really happening, pick up the rug and look underneath it. In other words, what's the true underlying cause of our patients' allergies and how can we fix the real reason that they exhibit allergic symptoms?

Unfortunately, most of our patients don't really wish to comprehend the source of their problems and make a core change in their lifestyle. They just want relief from their symptoms. A good example of this is the old commercial for Pepcid AC where the little jingle was "before drinking beer and eating pizza take a Pepcid AC"! Fortunately, Fr. Becker taught me to see through little charades like this. I realize that if pizza and beer don't agree with me then don't consume them, together or singularly, if I'm allergic to one or more of their ingredients.

Of course, people may need to have what should be short-term therapeutic tricks that will quell their allergic symptoms that, more than likely, will be extremely irritating and quite possibly debilitating. The key phrase here needs to be "short-term." If we haven't used our detective abilities and sleuthed the cause of their allergy, then really how are our integrative solutions different from Aleve or other pharmaceutical stop-gap allergy measures?

Robert Whitaker makes a similar comparison in his wonderful book *Anatomy of an Epidemic.* His premise is similar to what I was advocating above for allergies: anti-psychotic drugs should be taken for a short period of time to stabilize the patient psychologically. Then other non-pharmaceutical approaches can be employed where patients could slowly be weaned off the drugs and remain stable with integrative therapies that actually could be changing their brain biochemistries. He gives concrete examples of this occurring with positive results in Finland and compares them to the anti-psychotics used in America, which he says atrophy the brain over time with long-term use.

So where would I start integratively with a patient who comes to me with allergies? After I stabilize them with some phytochemical such as quercetin or nettle leaves, I would follow Fr. Becker's advice and attempt to start looking under the rug to find the root cause of their allergic condition.

Modern organic chemistry has brought us an extensive range of useful products and services that we trust have been tested and are inert or their chemical effects are insignificant. In reality, only a few hundred of the 80,000 chemicals in use today in the US have adequately been tested for safety.[1] In addition, up to 200 chemicals are in the bloodstream of babies before they're born.[2] Some of the major sources of exposure to these ubiquitous chemicals are from the following:

- Supposedly protective substances such as flame retardants in children's clothes, toys, and blankets;
- Agricultural products such as pesticides, herbicides, fungicides, hormones;
- Health and beauty aids such as lipstick and make-up;
- Structural off-gassing from rugs, paint, and cleaning supplies;
- Food loaded with artificial colorings, flavorings, and preservatives and hormones injected into animal products; and
- Industrial sources such as heavy metals, pollution from factories, and electromagnetic radiation releases.

As I've written before, I've been extremely lucky in my life and had multiple positive doors open for me. One large door was receiving a biology degree from University of California-Davis with an emphasis on ecology. For some reason, it just made sense to me that humans should try to live sustainably on this planet of ours. To my never-ending frustration, I appear

to be in the minority. Unfortunately, most people have not taken to heart the following quote by the inimitable Rachel Carson: "The human race is challenged more than ever before to demonstrate our mastery, not over nature, but of ourselves."[3]

It's my belief that you can't live a healthy life on a toxic planet. These 80,000 various chemicals/heavy metals that are endemic in our society are inevitably going to wind up in our bodies. One area that they could have a deleterious health effect would be our immune systems, which could, under the correct conditions, lead to environmental allergies. One glaring problem is that not everyone develops allergies to pollen or trees or cats or whatever is out there. As my son would say, "What's up with that?"

Over 30 years of clinical experience, over 100 seminars attended, and over 300 books read have allowed me to sleuth out several directions in which to look. There is the ever-expanding effect of the person's microbiota on the integrity of their intestinal mucosa and the erosion of this mucosa leading to leaky gut and entry into the bloodstream of foreign substances. There are also genetic issues that compromise the ability of the various Phase I and Phase II enzymes in the liver to effectively eliminate whatever the person has been exposed to.

Basically, Western medicine wrongly assumes people are standard or a one-size-fits-all mentality and tries to correct everyone's allergies with minimal pharmaceutical variation. We are biochemically/genetically unique, and there can be a thousand-fold variability in how people react to various environmental stimuli. Where I wish to focus the rest of this article is what I consider to be the main source of our patients' susceptibility to manifesting environmental allergies, their food intake.

I've written before on my use of NAET/Nambudripad Allergy Elimination Technique. I find it a very effective tool to diagnose a person's food intolerances and then removing the intolerance(s) via a specific acupuncture treatment. NAET is also quite efficacious in removing intolerances to various environmental stimuli. I was taught that you needed to remove the food intolerances before the environmental ones, or the technique didn't work as well. So far, I have mostly observed this to be true.

Basically, I think that by eliminating intolerant foods you are reducing the body's vulnerability to the various environmental stressors by decreasing inflammation and thus leaky gut in their GI tracts. Reducing or eliminating leaky gut provides the stalwart defense that we need in our intestinal mucosa to keep unwanted substances like pollen/mold toxins out of our bloodstream where our immune system can unnecessarily attack and initiate the biochemical cascade that will manifest as allergic symptoms.

Clinical Examples

The first patient is a 62-year-old female with a 30-year history of perennial hay fever. Basically, she said, her nose ran 12 months a year. She initially was diagnosed with the skin prick test, which showed her to be allergic to multiple pollens, coniferous trees, and multiple molds. She has lived most of her life in the high desert of northeastern California, which contains many conifers, including pine and juniper, and various pollens, including sage. Over the years, she has used various over-the-counter and prescription allergy medicines. None of them have eliminated the symptoms. According to her, they allow her to only use half instead of a whole box of Kleenex every day.

I used NAET and found her allergic to only wheat and eggs. Of course, her diet was littered multiple times daily with both foods, singly and in combination: bread, cookies, cakes, bagels, pasta, etc. I explained to her that we needed to clean up her food intolerances before concentrating on her environmental allergies. Fortunately for her and me, she agreed to give it a whirl. She came back two weeks later and couldn't believe what had happened in her body. She now was making a box of Kleenex last three days. Personally, I wouldn't have wanted to be where she was at symptomatically, but for her it was like manna falling from the sky.

Now, I tested environmental substances and found pollen, flowers, and dust to be weak. Over a period of three weeks, I treated her for these, and she basically reached a point where she said she was 80% better. Happy as a clam was an understatement. I attempted to help her go a little deeper

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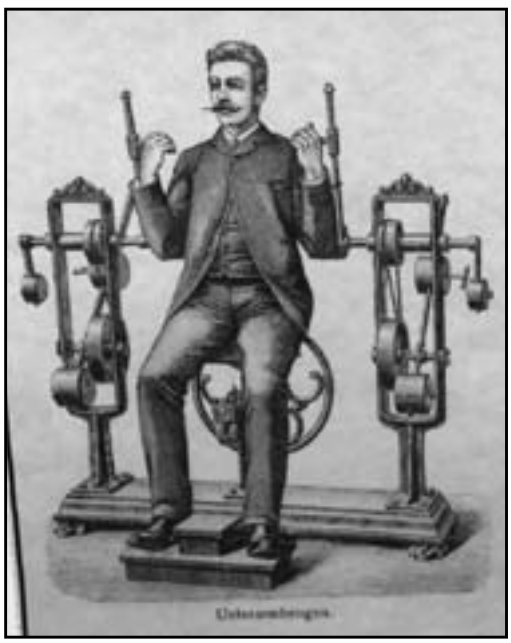
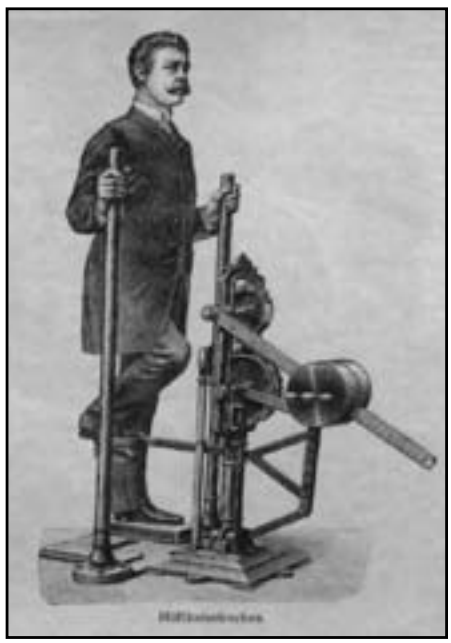
GET EXERCISING!





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in her treatment regimen, but the drainage remedies and supplements I was recommending were just a little too much for her. Now she comes in twice a year, and I tune her environmental allergies up with NAET.

Patient #2 was a 21-year-old female with a long history of respiratory illnesses and allergies since she was six months old. She was not breastfed and had trouble tolerating formulas until she finally was somewhat able to tolerate a soy formula. She was started on semi-solid food at three months, mostly oatmeal and cream of wheat. She had multiple ear infections the first two years of her life that were treated with antibiotics. She then started having several upper respiratory infections a year that would routinely develop into bronchitis but never pneumonia.

When she was five, she was finally tested for environmental allergies and was found to only be extremely sensitive to various molds. Her parents then looked at their house which was completely enclosed in trees and on the north side of a hill. They found mold growing in several places. They proceeded to move to a sunnier house with what they thought was no mold. She slowly started to improve symptomatically and became less debilitated by her allergies and respiratory illnesses. In reality, she still suffered three-to-four incidences of bronchitis every year and would automatically react to any place she entered with mold.

I tested her for food intolerances first. There were eight different ones. For me, when I see this, I have clinically come to the conclusion that there is a severe case of leaky gut. I have found that when the GI mucosa begins to heal most food allergies will disappear also. I explained this to her and her mother and had her start a hypoallergenic diet and use a product I really like to help heal leaky gut called RepairVite™ by Apex Energetics. There are multiple products out there similar to RepairVite, but that is just my choice. I asked her to come back in three weeks, and I would then test her for food intolerances.

Three weeks later, I immediately noticed a color change to her face, and she had suddenly found that she could be energetic. She also couldn't believe that her body actually felt lighter and that her stomach didn't always hurt, which either she had forgotten to tell me or I had forgotten to ask her. She had become a big believer in the "food is medicine" line by possibly Hippocrates.

I then tested her for food intolerances and now found only soy and milk. This allowed me to move on to the mold vials where I found several that she was sensitive to. After a multi-week treatment of these various molds, she came back and told me how wonderful life had become. She didn't dread waking up every morning and falling into the allergy/respiratory symptomatic rut she had occupied for most of her life.

Thus, for me, even allergies seem to have a symptomatic beginning in the GI tract. I use a new expression now with patients which is try not to dig your own grave with your fork and knife. Choosing food that maximizes your own personal biochemistry is amazingly critical to long-term health in every one of your bodily organ systems, including this month's focus on hyperactivity of your immune system.

So, hopefully, the real fix will be in with our allergy patients. It can be maddeningly and frustratingly difficult to find the true cause of our patients' allergies. Additionally, convincing them to not just suppress the symptoms but truly find the source of their allergies can also require considerable skill and effort. The end result will be worth it though when you see the look on their faces that tells you their misery and suffering have been alleviated and the extreme burden they have been carrying has been considerably lightened. It really does make a difference to carry a 50-pound backpack instead of a 200-pound one!

References

1. Kristoff N. New Alarm Bells About Chemicals and Cancer. *The New York Times.* May 5, 2010.
2. A Conversation with Sanjay Gupta, MD. Summer 2011. https://medlineplus.gov/magazine/issues/summer11/articles/summer11pg6-8.html
3. http://www.azquotes.com/author/17642-Rachel_Carson

Jim Cross graduated with a degree in biology from the University of California at Davis in 1975 and with a secondary teaching credential in life science from California State University, Sacramento, in 1976. After beginning to study naturopathic medicine at Pacific College of Naturopathic Medicine in tiny Monte Rio, California, he finished his naturopathic studies at National College of Natural Medicine in Portland, Oregon, in 1984. He later earned his LAc at San Francisco College of Acupuncture in 1989. He has practiced acupuncture and naturopathy in the northern Sierra town of Quincy, California, since 1990. He has also taught anatomy and physiology at Feather River College in Quincy since moving there.

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Curmudgeon's Corner

by Jacob Schor, ND, FABNO
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The Dark Days of the Year – The Winter Solstice 2017

My daughter Sophie and I picked the darkest and longest days of the year to make a road trip north to Canada. If you think the days are short and the nights long in Denver on the Winter Solstice, well they are a whole lot shorter and a whole lot longer the further north you go. Trust me, Denver is downright tropical compared to say, Judith Gap, Montana, during a winter snowstorm.

With this phenomenon of changing day length so in our faces, the idea that there are seasonal influences on physiology and health doesn't seem like a stretch of the imagination. Sure, there are the obvious and quite popular implications that result from changing ultraviolet exposure and the resultant fluctuations in vitamin D levels. These changes may explain the change in prognosis for certain cancers based on season of diagnosis. For example, in a study of almost 6,000 Swedes with diffuse large B-cell lymphoma, "[o]verall survival was significantly better for patients diagnosed ….. during the summer months"[1] Being diagnosed with lung cancer in the Springtime is associated with longer survival as well, the assumption being that increasing vitamin D during the summer is helpful.[2] The idea that changing length of day itself would also have an influence is seemingly obvious.

One must assume that shifting vitamin D levels would be only part of the story. It's changing daylight that seems to be the more striking trigger for biological cycles. Or perhaps we differ totally from other creatures in this world and are unaffected by seasons? I think not and must assume that buried within our evolutionary heritage our biology still responds to shifting seasons that trigger a desire to migrate, breed, or hibernate. We see some evidence of this in the scientific literature.

Depressed people get discharged faster from hospitals when days are longer, that is in the summer. (Or I suppose we could look at that the other way, the cup half empty approach, and say, "depressed people are kept longer in hospital in winter.")[3] Suicide rates, by the way, increase with lengthening daylight hours from winter to spring and reach their peak at about the summer solstice.[4]

A few weeks back one of my favorite medical writers, Dr. Siddhartha Mukherjee, author of *The Emperor of All Maladies: A Biography of Cancer,* wrote a piece published in the *New York Times* Sunday magazine titled "A Failure to Heal." The article describes the challenges of having patients enroll in clinical trials and the desire of all involved to squeeze some useful information out of every study, even from studies that appear to be failures.

Mukherjee isn't a fan of the common practice of reanalyzing data over and over hoping to draw out other associations or lessons from the numbers other than what the study was initially designed to question. As an example, he describes Richard Peto et al's 1988 study that proved aspirin was helpful for preventing heart attacks. Let me quote Dr. Mukherjee:

> …The Lancet agreed to publish the data, but with a catch: The editors wanted to determine which patients had benefited the most. Older or younger subjects? Men or women?
>
> Peto, a statistical rigorist, refused — such analyses would inevitably lead to artifactual conclusions — but the editors persisted, declining to advance the paper otherwise. Peto sent the paper back, but with a prank buried inside. The clinical subgroups were there, as requested — but he had inserted an additional one: "The patients were subdivided into 12 ... groups according to their medieval astrological birth signs." When the tongue-in-cheek zodiac subgroups were analyzed, Geminis and Libras were found to have no benefit from aspirin, but the drug "produced halving of risk if you were born under Capricorn." Peto now insisted that the "astrological subgroups" also be included in the paper — in part to serve as a moral lesson for posterity. I've often thought of Peto's paper as required reading for every medical student. [5]

While I hold Dr. Mukherjee in the highest esteem, this example, while somewhat amusing, strikes this reader as poorly chosen. The astrological signs for all their connotations and associations are after all seasonal markers. They divide the year into segments. Though it's a long stretch to say the month you were born will influence your risk of a heart attack

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a lifetime later, it doesn't seem impossible. [Many of you will recall how Malcolm Gladwell argued that you could predict winning Canadian hockey teams by the birthdays of the team's players….]

In December 2017, a large Danish study reported that "month of birth is associated with subsequent diagnosis of autoimmune hypothyroidism." Looking at data from (n=111565) people diagnosed with autoimmune hypothyroidism, authors Thvilum et al tell us that people born in June have the highest risk of this disease.[6] They could also have said that Gemini's and Cancers have the greatest risk. Low thyroid function is a risk factor for heart disease after all.

A study, published last August 2017, compared levels of antibodies found in cord blood sampled at birth by month. Levels of IgE peak in the winter.[7] Could that tell us something about Capricorns?

Last May, a study of half a million Chinese reported that being born in the summer was associated with a lower risk of type-2 diabetes later in life. Those born in spring, fall, or winter had a 8-9% greater risk of the disease.[8] So being a Cancer or Leo offers some protection at least against DM-2. Type-2 diabetes is a risk factor for heart disease.

In early December a report was published that in South Africa children are born with orofacial clefts significantly more often during the winter months than during the summer.[9]

So Peto's choice to tease the *Lancet* with seemingly implausible astrological associations may now look less unrealistic. Heart attacks though? They don't seem to be directly; a 2023 Danish study couldn't find an association. The authors also reported no impact of "season of birth on risk of type 1 diabetes, cancer, schizophrenia and ischemic heart disease…" but there was a strong trend toward increased risk of pneumonia and multiple sclerosis for those born in the winter months."[10]

It is Mukherjee's argument against mining data from studies on other questions in the hope of finding useful associations after the fact that troubles me the most, far more than his attitude toward astrology. His position strikes me as elitist; I want to say, "written like a medical oncologist" as oncology endures an affluence of research investment that surpasses all other disciplines in medicine. Few other fields have the resources to expect evidence from large cohorts of double-blinded, placebo-controlled trials to inform every decision made in practice the way oncologists do. In choosing treatment decisions, they can usually fall back on statistics from specific and well-conducted trials.

This, of course, is reasonable given the level of toxicity associated with most interventions used in oncology. No sane patient would ever undergo cancer treatment unless absolutely certain that there was a net benefit. No conscientious physician would prescribe treatment. There is an absolute need to be certain of benefit or else the trade off would not be worthwhile.

It is from the privileged world of medical oncology that Mukherjee views the problem when he writes:

> Why do we persist in parsing a dead study — "data dredging," as it's pejoratively known? One answer — unpleasant but real — is that pharmaceutical companies want to put a positive spin on their drugs, even when the trials fail to show benefit. ("But within a subpopulation of subjects, the results were positive." The FDA, though, does not approve drugs based on post hoc data.)
>
> The less cynical answer is that we genuinely want to understand why a medicine doesn't work.[5]

Of course, when Mukherjee thinks of research, he is thinking of pharmaceutical research; and when we think of it, we may be looking at dietary or nutritional interventions. The big difference is that we can use certain adjectives such as safe, non-toxic, low risk, or harmless to describe the interventions we are pondering. Thus, we may not feel the same obligation to prove these interventions efficacious to the same degree of certainty as we do with chemotherapy, before considering using them.

We do not insist on absolute certainty before prescribing naturopathic interventions, less than perfect data can still inform us.

The PREDIMED trial comes to mind. The Prevención con Dieta Mediterránea (PREDIMED) study was the largest prospective randomized controlled experiment examining the effects of a Mediterranean style diet so far conducted. It may be the most important clinical trial on diet yet performed. The primary goal of PREDIMED was to examine the effect of the Mediterranean diet on cardiovascular disease; these main findings were published in February 2013.[11] Conducted in Spain, the study randomly assigned participants, who were at high cardiovascular risk, to one of three diets: a Mediterranean diet supplemented with extra-virgin olive oil, a Mediterranean diet supplemented with a mixture of nuts, or a low-fat control diet. Let's not even talk about the initial outcomes here but instead consider the studies that have resulted from "data-dredging" in the five years since initial publication. PubMed lists an additional 165 studies published using the PREDIMED data. Rather than calling it data-dredging, better we call it data-mining.

A few recent examples of information "mined" from PREDIMED data:

- Dec 2017: Potato consumption does not increase blood pressure.[12]
- October 2017: Choline metabolites increase risk of cardiovascular disease.[13]
- September 2017: Metabolic predictors of fatty liver disease[14]
- July 2017: Inflammatory diet and risk of metabolic disease and risk of obesity[15]
- May 2017: Dietary polyphenols and risk of obesity[16]
- May 2017: Mediterranean diet's effect on cataract surgery outcome. [17]

Those are the most recent. The mining efforts continue to pay-off. Should we ignore all of these findings? Perhaps the results are not the most rigorous from the point of view of die-hard statisticians, but they are nevertheless useful, they advance our understanding of health and disease. They are nothing to scoff at. Unless, of course, you come from a land where all research proposals are paid for. I hate to say it but Mukherjee criticizing data-mining reminds me of Marie Antoinette's comments regarding cake. Yes, some researchers get to design specific trials to answer their exact questions; we common people have to live with data mining. It's not the end of the world. We learn to live within our means.

[Though perhaps we should give the good doctor some slack as the data dredging he probably sees most often comes from drug companies hoping to find excuses for selling expensive drugs to his patients.]

While I am playing curmudgeon, let me bring up another pet peeve. Some days I worry that we have taken the concepts of statistical significance too far. We refuse to admit something is significant unless the p-value is < .05. If it isn't significant, we translate the results as "not true" and ignore the findings.

This brings to mind a study published in 2012 on using metformin as an adjunctive treatment for breast cancer, specifically triple negative breast cancer (TNBC). Researchers from MD Anderson reported that metformin did not improve survival outcomes in diabetic patients. Researchers retrospectively identified 1,448 women treated with chemotherapy for TNBC and grouped them by diabetes status and whether or not they used metformin. At a mean follow up of 62 months, the hazard ratio for patients who did not receive metformin was 1.63 and for non-diabetic patients was 1.62 for distant metastasis compared to patients receiving metformin. In other words, taking metformin appears to have lowered risk of metastasis by about 60%.

When the results are displayed graphically, patients taking metformin had a higher probability of distant metastasis-free survival, a higher probability of relapse-free survival, a higher probability of overall survival, a lower risk of distant metastasis at ten years, a lower risk of recurrence, a lower risk of death, a lower risk of metastasis and a lower risk of recurrence than non-diabetics.[18] These results are all good, yet these results are all what statisticians call trends; they did not reach statistical significance so are not reported as real. The study concludes that there is no significant difference in outcomes between those who took metformin and those who did not.

But seriously, I have yet to find a patient who examines these graphs and doesn't prefer to hope for outcomes in line with the outcomes seen in those taking metformin. Taking metformin is not a sure bet, those benefits could have just been an odd fluke in this patient group, kind of like flipping a coin and getting heads four times in a row. Still, surviving triple negative breast cancer a not a sure bet. Most patients would like to improve their odds. Reliance only on statistically significant human data may be depriving patients of useful and pragmatic advice.[19]

We all crave certainty in life. We want study results that give us confidence in what we tell patients. We want rules to follow in life. We want to safely ignore results from data-dredging or from data that didn't reach statistical significance. Life isn't like that. Life is often too complex to be reduced to black and white rules.

We must learn to work with what we have and sometimes data mined from large studies are helpful. Sometimes insignificant trends can hint us in the right direction. Sometimes we have to work with what life gives us.

References

1. Székely E, et al. Season of diagnosis is associated with overall survival in patients with diffuse large B-cell lymphoma but not with Hodgkin's lymphoma - A population-based Swedish Lymphoma Register study. *Eur J Haematol*. 2016 Oct;97(4):393-8.
2. Oguz A, et al. Season of diagnosis and survival of advanced lung cancer cases--any correlation? *Asian Pac J Cancer Prev*. 2013;14(7):4325-8.
3. Canellas F, et al. Increased daylight availability reduces length of hospitalisation in depressive patients. *Eur Arch Psychiatry Clin Neurosci*. 2016 Apr;266(3):277-80.
4. van Houwelingen CA, Beersma DG. Seasonal changes in 24-h patterns of suicide rates: a study on train suicides in The Netherlands. *J Affect Disord*. 2001 Oct;66(2-3):215-23.
5. Mukherjee S. A Failure to Heal. *New York Times.* November 28, 2017.
6. Thvilum M, et al. Month of birth is associated with the subsequent diagnosis of autoimmune hypothyroidism. A nationwide Danish register-based study. *Clin Endocrinol* (Oxf). 2017 Dec;87(6):832-837.
7. Susanto NH, et al. Effect of season of birth on cord blood IgE and IgE at birth: A systematic review and meta-analysis. *Environ Res*. 2017 Aug;157:198-205.
8. Si J, et al. Season of birth and the risk of type 2 diabetes in adulthood: a prospective cohort study of 0.5 million Chinese adults. *Diabetologia*. 2017 May;60(5):836-842.
9. Sofianos C, Christofides EA, Phiri SE. Seasonal Variation of Orofacial Clefts. *J Craniofac Surg*. 2017 Dec 6.
10. Við Streym S, et al. No effect of season of birth on risk of type 1 diabetes, cancer, schizophrenia and ischemic heart disease, while some variations may be seen for pneumonia and multiple sclerosis. *Dermatoendocrinol*. 2013 Apr 1;5(2):309-16.
11. Estruch R, et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *N Engl J Med*. 2013 Feb 25.
12. Hu EA, et al. Potato Consumption Does Not Increase Blood Pressure or Incident Hypertension in 2 Cohorts of Spanish Adults. *J Nutr*. 2017 Dec;147(12):2272-2281.
13. Guasch-Ferré M, et al. Plasma Metabolites From Choline Pathway and Risk of Cardiovascular Disease in the PREDIMED (Prevention With Mediterranean Diet) Study. *J Am Heart Assoc*. 2017 Oct 28;6(11). pii: e006524.
14. Papandreou C, et al. Serum metabolites in non-alcoholic fatty-liver disease development or reversion; a targeted metabolomic approach within the PREDIMED trial. *Nutr Metab* (Lond). 2017 Sep 2;14:58.
15. Cantero I, et al. Dietary Inflammatory Index and liver status in subjects with different adiposity levels within the PREDIMED trial. *Clin Nutr*. 2017 Jul 6. pii: S0261-5614(17)30238-8.
16. Guo X, et al. Polyphenol Levels Are Inversely Correlated with Body Weight and Obesity in an Elderly Population after 5 Years of Follow Up (The Randomised PREDIMED Study). *Nutrients*. 2017 May 3;9(5). pii: E452.
17. García-Layana A, et al. The Effect of a Mediterranean Diet on the Incidence of Cataract Surgery. *Nutrients*. 2017 May 3;9(5). pii: E453.
18. https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom&p=PMC3&id=3207034_nihms-311520-f0001.jpg
19. Bayraktar S, et al. Effect of metformin on survival outcomes in diabetic patients with triple receptor-negative breast cancer. *Cancer*. 2012 Mar 1;118(5):1202-11.

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Women's Health Update

by Tori Hudson, ND
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Guidelines and Clinical Practice Support for 2017

Blood Pressure Categories for Women

New guidelines for the prevention, detection, evaluation, and treatment of high blood pressure have been updated by the American College of Cardiology (ACG) and the American Heart Association (AHA). According to the new guidelines, blood pressure (BP) is normal if < 120/<80; elevated if 120-129/<80; stage I hypertension if 130-139 or 80-89; or stage 2 hypertension if ≥140 or ≥90. A hypertensive crisis is defined as > 180 systolic pressure or > 120 diastolic pressure. These patients need immediate changes in intervention if there are no other indications of urgent or emergent need for hospitalization, or if there are any symptoms or signs of systemic damage. Compare these new guidelines to the 2003 Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7). See table below:

Systolic Diastolic PB mm Hg	JNC7	ACC/AHA 2017
<120 and < 80	Normal BP	Normal BP
120-129 and < 80	Prehypertension	Elevated BP
130-139 or 80-89	Prehypertension	Stage I hypertension
140-159 or 90-99	Stage I hypertension	Stage 2 hypertension
≥160 or ≥100	Stage 2 hypertension	Stage 2 hypertension

Blood pressure readings should be analyzed by using the average of BP measures taken over several visits as well as BP measurements taken out of the clinician's office.

The results of these new definitions of hypertension will result in about 46% of US adults having high BP and nearly 80% if 65 years and older. For younger adults, it is predicted that those who meet these new definitions will triple in men and double in women if younger than 45 years.

Guidelines for treatment are influenced the patient's underlying risk of cardiovascular disease. For those with stage I hypertension, only patients with clinical cardiovascular disease or an estimated risk of 10% or more would be offered treatment if one were following these conventional medicine new guidelines. Individuals 65 and older would all be treated if stage 1. Others in this stage I group, who do not fit into the just stated groups, should be advised on lifestyle changes, the fundamentals of any treatment plan for elevated blood pressure or any stage of hypertension. This would include weight loss in those who are overweight, the DASH (Dietary Approaches to Stop Hypertension) diet, lower the sodium in the diet to less than 1,500 mg per day, increasing exercise to a minimum of 30 minutes three times per week, and limit alcohol to two drinks or fewer per day for men and one or fewer for women.

The risk of cardiovascular disease continues to slope upwards with this risk starting around 115[1] for systolic BP and around 75 for diastolic BP and from ages 30 to older than 80 in both women and men.[1,2] For each 20 mm rise in Hg in systolic blood pressure and 10 mm Hg rise in diastolic blood pressure, the risk doubles for the risk of death from heart disease, stroke, heart failure, and other vascular illnesses.

It has also been shown that for each 10 mm Hg reduction in systolic BP there is about a 20% reduction in major cardiovascular events, a 17% reduction in coronary heart disease, a 27% reduction in stroke, 28% reduction in heart failure and 13% reduction in mortality due to all causes.[3]

While the risk of hypertension is lower in women than in men until around the age of menopause, blood pressure is greater in later life for women than for men. Other than different treatment guidelines for pregnant women, treatment goals and treatment interventions are the same for women and men.

Whelton P, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation and management of high blood pressure in adults. *Hypertension.* November 13, 2017. (online ahead of print)

2017 Hormone Therapy Position Statement of the North American Menopause Society

The North American Menopause Society (NAMS) is the leading international menopause organization for practitioners. NAMS provides evidence-based and current best

clinical practice recommendations for the use of hormone therapy(HT), calcium, and testosterone therapy in women. Their last position statement on this topic was in 2012 by a panel of clinicians and researchers who are experts in women's health and menopause. New data since 2012 include results from long-term randomized, clinical trials and observational studies. I highly recommend a full and thorough read of the entire document but here are the overall benefit-to-risk issues and conclusion:

- Hormone therapy is the most effective treatment for vasomotor symptoms (VSM) and genitourinary symptoms of menopause (GSM) and has been shown to prevent bone loss and fracture.
- Risks of HT differ for women, depending on the type, dose, and duration of HT use, the route of administration, the timing of when it is initiated and whether a progestogen is needed. Treatment should be individualized using the best available scientific evidence to maximize the benefits and minimize the risks. Periodic reevaluations should be done (likely yearly) to assess the benefits and risks of continuing HT.
- For women aged younger than 60 years, or are within the first 10 years of menopause onset and have no contraindications to HT, the benefit-risk ratio is favorable for the treatment of moderate to severe VMS and for those at elevated risk of bone loss or fracture due to osteoporosis. Longer duration of use may be more favorable for estrogen only rather than for estrogen plus progestogen.
- For women who initiate HT more than 10 years from menopause onset or when aged 60 years or older, the benefit-risk ration appears less favorable than for younger women because of the greater absolute risks of CHD, stroke, venous thrombolic embolism and dementia.
- For GSM symptoms not relieved with over-the-counter or other therapies, low-dose vaginal estrogen therapy is recommended.

To truly enhance menopause and hormone prescribing skills, a full understanding of the benefits and risks and key points on all menopause/aging issues is vital to safe, effective prescribing and menopause management.

The 2017 Hormone Therapy Position Statement of the North American Menopause Society. *Menopause*. 2017; 24(7):728-753.

Screening Mammograms

One screening exam, many opinions. Keep in mind that these guidelines apply to average-risk women. You are considered average risk if all of the following are true:

- No personal history of breast cancer.
- No known genetic mutation increasing risk for breast cancer (i.e. BRCA).
- No history of chest radiation.

The major purpose of mammograms is to detect cancerous lumps before they can be felt and start treatment sooner, with the hope that earlier detection and treatment will save lives. Unfortunately, it appears women die at a similar rate whether breast cancer was detected early by mammogram or later by breast exam. In addition, screening mammograms lead to healthy women receiving unnecessary

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	Starting Age	Ending Age	Frequency
American College of Obstetrics & Gynecology (ACOG)	Offer at 40 If decline, start at 50	Discuss at 75	Every 1-2 years, depending on patient preference
American Cancer Society (ACS)	45	When life expectancy is < 10 years	Annually if 45-54 Every other year if > 55
US Preventive Services Task Force (USPSTF)	50	74	Every other year
European Model	50 (option to start at 40)	69	Every other year (annually if 40-49)
Finland Model	50	59	Every other year

Liposomal Glutathione Elevates Glutathione and Immune Function Markers

Glutathione is a critical antioxidant in human metabolism. Therefore, it is critical that glutathione levels in the body are adequate to combat oxidative stress and chemical exposures**. A clinical trial using Tri-Fortify™ liposomal glutathione showed efficacy in raising reduced glutathione levels (GSH) along with natural killer cell function while also decreasing oxidative stress markers**:

Abstract

Background/Objectives: Glutathione (GSH) is the most abundant endogenous antioxidant and a critical regulator of oxidative stress. Maintenance of optimal tissues for GSH levels may be an important strategy for the prevention of oxidative stress-related diseases. We investigated if oral administration of liposomal GSH is effective at enhancing GSH levels in vivo.

Subjects/Methods: A one-month pilot clinical study of oral liposomal GSH administration at two doses (500 and 1000 mg of GSH per day) was conducted in healthy adults. GSH levels in whole blood, erythrocytes, plasma and peripheral blood mononuclear cells (PBMCs) were assessed in 12 subjects at the baseline and after 1, 2 and 4 weeks of GSH administration.

Results: GSH levels were elevated after one week with maximum increases of 40% in whole blood, 25% in erythrocytes, 28% in plasma and 100% in PBMCs occurring after two weeks ($P<0.05$). GSH increases were accompanied by reductions in oxidative stress biomarkers, including decreases of 35% in plasma 8-isoprostane and 20% in oxidized:reduced GSH ratios ($P<0.05$). Enhancements in immune function markers were observed with liposomal GSH administration including natural killer (NK) cell cytotoxicity, which was elevated by up to 400% by two weeks ($P<0.05$), and lymphocyte proliferation, which was elevated by up to 60% after two weeks ($P<0.05$). Overall, there were no differences observed between dose groups, but statistical power was limited due to the small sample size in this study.

Conclusions: Collectively, these preliminary findings support the effectiveness of daily liposomal GSH administration at elevating stores of GSH and impacting the immune function and levels of oxidative stress.

Sinha R, et al. Oral supplementation with liposomal glutathione elevates body stores of glutathione and markers of immune function. *European Journal of Clinical Nutrition*. 30 August 2017.

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Women's Health Update

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breast biopsies and even cancer treatment; Cochrane Review estimates that for every life saved by mammography, 10 women receive unnecessary breast cancer treatment.

So why bother with mammograms at all? Consider the following:

- Early detection of breast cancer with mammograms may spare women from more aggressive treatment regimens, improving quality of life for women diagnosed with breast cancer.
- We know that women who get breast cancer before age 50 tend to have more aggressive cancers. Delaying screening mammograms to age 50 or later may result in a more aggressive cancer in a younger woman being missed.

Increasingly, the medical community is giving weight to the individual risk factors and informed choice of women in the decision of when and how often to screen for breast cancer using mammography. In fact, population studies in Switzerland found that opportunistic screening (mammograms only when requested by doctor or patient) worked as well as uniform screening (mammograms at specified intervals) in identifying breast cancer.

The above document was compiled by Jennifer Johnson, ND, LAc.

References

1. Rapsomaniki E, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet.* 2014;383 (9932):1899-1911.
2. Lewington S, et al. Prospective Studies Collaboration. *Lancet.* 2002;360 (9349):1903-1913.
3. Ettehad D, et al. Blood pressure lowering for prevention of cardiovascular diseases and death: a systematic review and meta-analysis. *Lancet.* 2016;387 (10022):957-967.

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Klaire Labs (SFI USA) Announces Availability of Target gb-X™

The first commercially available gut-brain focused probiotic blend for clinically-demonstrated mood support

Klaire Labs (SFI USA) today announced availability of Target gb-X™ with Ecologic BARRIER, a unique nine-strain blend to support positive mood. This shelf stable, 5B CFU probiotic was specifically designed to influence the gut-brain axis through defined mechanisms including strengthening of the gut barrier function, modulation of cytokines and inflammatory response, neuroprotective metabolite production, and HPA axis.

Target gb-X™ was formulated and developed in partnership with Winclove Probiotics (Amsterdam, NL), a company that researches, develops and manufactures evidence-based probiotics.

"Target gb-X™ is a clinically-researched, safe, and effective way to support patients with mood-related concerns," said Jeremy Appleton, ND, Vice President of Regulatory Affairs at Klaire Labs. "This product is the first in a line of Klaire Labs' targeted, indication-specific probiotics. We are very excited to continually support our practitioner partners with innovative, evidence-based products."

The product will be launched officially at the Integrative Healthcare Symposium (IHS) in New York, 22-24 Feb. Klaire Labs will be sponsoring an evening symposium discussing the mechanisms, the clinical evidence, and one psychiatrist's experience with the formulation.

Target gb-X™ is currently available for pre-order. This formulation is available as shelf-stable, hypoallergenic*, non-GMO, single serving sachets. For more information and product updates, visit meetklaire.com or stop by the Klaire Labs booth (100) at IHS.

*Free of the following common allergens: milk/casein, fish, shellfish, tree nuts, peanuts, wheat, gluten, and soybeans. No artificial additives, colors, flavorings, preservatives, sugar, or salicylates are used. Contains corn.

About Klaire Labs

Klaire Labs has been formulating and manufacturing premium, hypoallergenic supplements sold through healthcare practitioners for nearly half a century. Our mission is to develop and manufacture the purest, most potent nutraceuticals possible, thereby empowering clinicians with consistently reliable performance.

Klaire Labs is located in Reno, Nevada. It is owned by Soho Flordis International, a privately held nutraceutical company based in Sydney, Australia.

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

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Glutamine and Sickle Cell Disease: Another Example of Why Healthcare Is So Expensive

On July 7, 2017, the US Food and Drug Administration (FDA) approved Endari™ (Emmaus Life Sciences; Torrance, CA) for the treatment of sickle cell disease (SCD). Endari is the only FDA-approved treatment for children with SCD and is the first new treatment in 20 years to be approved for adults. While effective new therapies for difficult-to-treat diseases are always welcome, it is unsettling to see that, for a typical dosage of Endari (10-30 g per day, depending on body weight), insurance companies will be shelling out around $28,000 per year for a natural substance that can be obtained over the counter for about 5% of that price.

Endari, you see, is nothing more than glutamine (L-glutamine), an amino acid that is synthesized in the body and is present in a wide variety of foods; an amino acid that has been available as a dietary supplement for more than 60 years. Glutamine has a wide range of biochemical effects and numerous clinical indications, including treating acquired immunodeficiency syndrome, alcohol addiction, burns, gastroenteritis, pancreatitis, and peptic ulcer, and preventing infections that follow intense physical exercise.

Interest in glutamine as a potential treatment for SCD was triggered by an observation in the 1990s that glutamine could reverse *in vitro* the sickling of red blood cells obtained from a patient with SCD. In addition, oral administration of glutamine (30 g per day for 4 weeks) to patients with SCD decreased the adhesion of red blood cells to endothelial cells, an effect that has the potential to prevent the microthrombi that are associated with organ damage in sickle cell crises. FDA approval of Endari was based on two double-blind trials. In the first trial, 81 patients received glutamine or placebo for one year. At 24 weeks, the mean number of painful crises was 55% lower (2.5 vs. 5.5; $p < 0.06$) and the mean number of hospitalizations was 38% lower (0.8 vs. 1.3; $p < 0.04$) in the glutamine group than in the placebo group. Adverse events were similar between groups. In the second study, 230 adults and children at least five years of age received (in a 2:1 ratio) glutamine or placebo for 48 weeks. The mean number of painful crises (3.2 vs. 3.9; 18% reduction; $p < 0.005$) and the number of days of hospitalization (2 vs. 3; not clear whether this was median or mean; $p < 0.005$) was significantly lower in the glutamine group than in the placebo group.[1]

Currently, the mainstay of treatment for SCD is hydroxyurea, which has been shown to decrease the number and severity of painful crises and to increase survival time. However, hydroxyurea can cause numerous side effects, some of which are serious, such as anemia, myelosuppression, and leukemia. Treatment with glutamine might obviate the need for hydroxyurea in some cases, allow for a reduction of the hydroxyurea dosage in other cases, and provide an alternative for patients in whom hydroxyurea causes intolerable side effects or is ineffective. However, because of the high price of Endari, insurance companies are taking steps to limit its use. Blue Cross, for example, will not pay for Endari unless the patient has already tried hydroxyurea and experienced treatment failure. Patients with SCD can purchase glutamine without a prescription and pay for it out of pocket, but many are unable to afford it.

One would assume that insurance companies would be less restrictive if they were paying $1,400 per year for generic glutamine (an amount only slightly more than the cost of hydroxyurea), rather than $28,000 per year for Endari. However, it is the policy of most insurance companies not to pay for most dietary supplements, even though these companies will pay for the same substance at a much higher price if it is approved by the FDA as a prescription drug. The people who created this budget-busting policy attempt to justify it in part by arguing that pharmaceutical companies would have no incentive to develop drugs for rare diseases if they did not have a way to recoup their investment. In 1983, Congress passed the Orphan Drug Act, which provided financial incentives to encourage the development of "orphan drugs" for rare diseases. These incentives included research grants, tax credits for money invested in research, and the exclusive right to sell the product for the approved indication for seven years, beginning on the day the drug is approved.

These incentives might seem reasonable for diseases that are truly rare, but SCD is not a rare condition: about 100,000 Americans and about 25 million people worldwide are affected. For reasons that are not clear, Congress amended the Orphan Drug Act in 1984 by expanding the definition of "orphan drug" to include products for any disease or condition that affects less than 200,000 people in the US. By that definition, an estimated 20-25 million Americans have a "rare" disease.[2] It seems wrong to grant a drug company a monopoly on a natural treatment for a disease that affects so many people, when all the company had to do was sponsor a couple of medium-sized clinical trials that were partially funded by grants and tax credits.

We need to find ways to encourage and support research into natural substances without unnecessarily raising the cost of healthcare.

Alan R. Gaby, MD

References

1. Wilmore DW. Food and Drug Administration approval of glutamine for sickle cell disease: success and precautions in glutamine research. *JPEN J Parenter Enteral Nutr*. 2017;41:912-917.
2. Seoane-Vazquez E. Incentives for orphan drug research and development in the United States. *Orphanet J Rare Dis*. 2008, 3:33.

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