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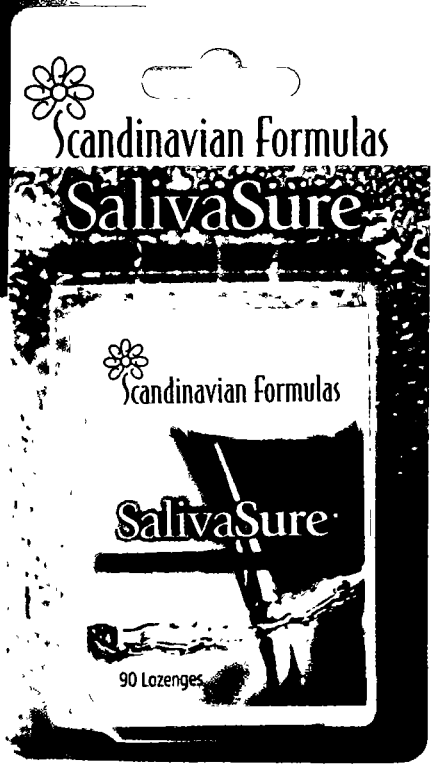

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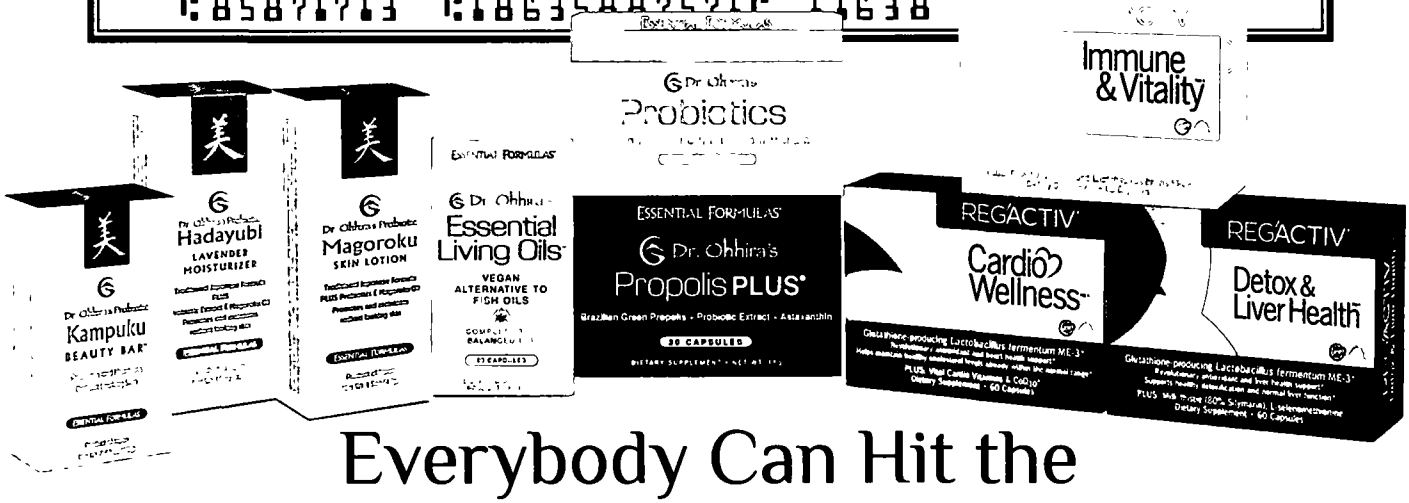

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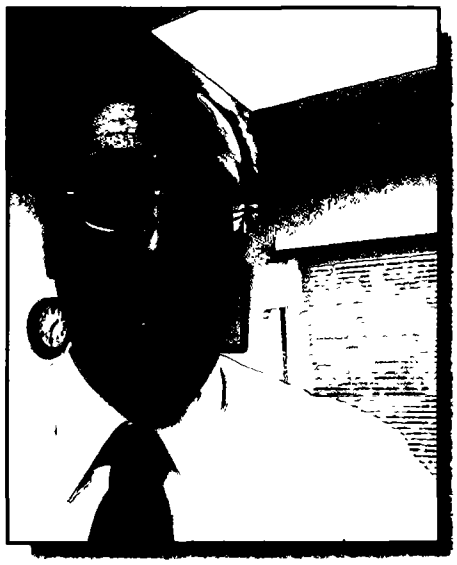

From the Publisher

Follow-Up: Theranos Lab-on-a-Chip Testing Halted Temporarily for Lab Deficiencies

In my February/March 2015 *Letter*, I reported on a Silicon Valley company founded by a 19-year-old Stanford chemical engineering student, Elizabeth Holmes, that sought to innovate routine lab testing performed from finger-prick blood specimens. After 10 years of research and development, last year Theranos launched patient blood-drawing sites in more than 40 pharmacies with testing done by two laboratories, one in Newark, California, and one in Arizona. Theranos acquired major funding from investors and attracted a stellar board of directors, including former Secretary of State George Schultz, former Secretary of State Henry Kissinger, and Cleveland Clinic President Delos Cosgrove, MD. The testing methodology, proprietary and patented, is based on "lab-on-a-chip" microfluidics. Microfluidics is a technological science combining physics, chemistry, biochemistry, biology, robotics, material science, and computer processing. As discussed in Wikipedia, microfluidics employs automation and robotics to analyze reduced volumes of blood or other fluids. One of the exciting aspects of microfluidics is high-speed-throughput (HST) enabling the study of hundreds or thousands of sample droplets managed robotically. Theranos laboratory diagnostics feature a growing array of basic and more complex lab testing procedures, using lab-on-a-chip technology, requiring only some drops of blood easily acquired at a lab stations in the pharmacy. Unfortunately, Medicare (CMS) has recently found problems in the testing procedure at the Newark facility, necessitating a cessation of lab testing, according to the Jan.

continued on page 8 ➤

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From the Publisher

➤ *continued from page 6*

30 *Wall Street Journal*. However, Holmes is confident that the "lab irregularities" were a minor problem and testing will be operating as usual within the next several weeks.

Part of the reason that Theranos lab testing has its critics is that it has not yet been given FDA approval, nor has it completed peer-review testing compared with conventional lab testing using venipuncture specimens. However, the fact that testing will not necessarily require a physician's order will enable consumers to monitor their health without routine doctor appointments. New health apps are appearing that enable consumers to monitor their health status by inputting their heart rate, blood pressure, and other variables measured through their phone or related devices. Adding the results of laboratory testing that one can obtain conveniently at a local pharmacy will enable "real-time" assessment of one's health. Additionally, consumers may opt to input their lab assessments in big-data input apps that will presumably draw correlations between lab results and risk for developing disease.

Probe of Herbalife Business Practices Halted

In my January 2016 *Letter*, I wrote about the growing concerns of multilevel-marketing (MLM) companies that are being scrutinized for operating fraudulently. When Amway Corporation was accused of this years ago, it vigorously defended itself and was found not to be a pyramid scheme. Over the past three years, a hedge-fund billionaire, William Ackman, and his fund, Pershing Square Capital Management, have short-purchased more than $1 billion in Herbalife stock, according to the Jan. 30 *Wall St. Journal*. Ackman claimed that Herbalife was a pyramid scheme needing investigation. The FBI and U.S. Attorney's Office in New York did study Herbalife's business practices and concluded that there was insufficient evidence for prosecution. Ackman thought that if the agencies could prove that there was a pyramid scheme, Herbalife stock shares would tank and his hedge fund would profit handsomely.

Instead, since the initial accusation by Ackman, Herbalife stock prices that had fallen 40% in 2012 not only have recovered from the drop but have nearly doubled in price. Meanwhile Herbalife countered that Ackman attempted to manipulate the stock price and should be investigated. The SEC and other agencies did not find there to have been sufficient evidence of criminal activity by Ackman. The investigations have stopped for both parties.

Are Injectable Manufacturers Following Shkreli's Action Plan?

Hedge fund manager Shkreli, the former CEO of Turing Pharmaceuticals, who infamously raised the price of Daraprim from $13.50 to $750 per tablet, recently "took the Fifth" while testifying before Congress. Following the meeting, he

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From the Publisher

➤ *continued from page 8*

commented to the press that he could not believe that "these idiots represent us in Congress." Shkreli is unrepentant about the price gouging that he authorized.

Over the past year, other drug company executives have followed in Shkreli's footsteps and steeply increased the price of pharmaceuticals. Perhaps not surprisingly, the manufacturers of injectable B vitamins have pursued similar tactics. Vitamin B complex, an injectable that includes vitamins comparable to an oral B vitamin tablet, has recently been priced between $100 to $200 per 30 cc vial. I was shocked to discover that in the last month, cyanocobalamin, the commercial form of vitamin B12 that has been manufactured inexpensively for the past 50 years, has now been priced at $140 per 30 cc vial.

This may not be upsetting for most readers. However, as I prefer to treat patients who experience stress, anxiety, depression, and related mood disorders, as well as fatigue and cognitive dysfunction, with vitamin B12, it is a personal blow. I recommend that vitamin B12 be used frequently compared with the conventional advice to administer once weekly – I advise patients to inject vitamin B12 1 to 3 times weekly. When cyanocobalamin was reasonably priced at $25 per vial, this prescription recommendation was not only a boon to the patient, but well within the budget. I remember that in the 1980s cyanocobalamin could be acquired wholesale for 85 cents per vial. To be told that it is now to cost $140 wholesale is outrageous. This is price gouging based on greed, pure and simple. There is no justification for this pricing – there is no shortage of raw materials, no difficulty in the manufacturing process, no lack of customers wanting to purchase vitamin B12.

If this price escalation – and it can't be called volatility, as the price only goes in one direction, up – is now "business as usual," integrative and naturopathic medicine will no longer be reasonably priced treatment. As a patient recently expressed to me, "We are now going to have to choose between getting treatment and putting food on the table." I would expect this sort of behavior from street dealers selling me oxycodone, not from responsible drug companies manufacturing injectable vitamins.

Prenatal Fluoride and Autism

Two hundred million people in the US drink fluoridated water; that is good news for the more than 100 million who do not, but not such good news for those who do. Of course, the ADA and public health authorities would have you believe the opposite: that the folks drinking fluoridated water not only benefit by getting fewer cavities but experience other medical

continued on page 19 ➤

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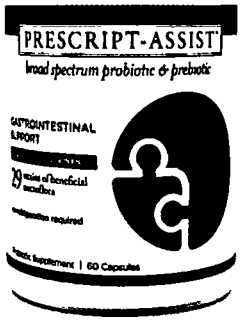

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[1] Pennisi, E. (2011). Body's Hardworking Microbes Get Some Overdue Respect. *Science, 330* (December 2010), 1619

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Brain Health Conference: Listening to the Gut

by Bob Frost

Brain health connects to the gut, teeth, and eyes. That's a take-away message from the NeuroRegeneration Conference conducted by the Academy of Comprehensive Integrative Medicine (ACIM) in Orlando last October.

Some 100 attendees – mostly alternative-minded practitioners – gathered for two days at the Florida Hotel and Conference Center and heard presenters speak about topics ranging from the gut lining to root canals to the retina, and how various systems connect to the brain.

For example, Zach Bush, MD, said: "If you stop stress from the gut, the brain improves." And this from David Minkoff, MD: "If you've got neurological illness, and you've got root canals, you've got to have your root canals pulled out."

Here are some highlights from the conference gleaned from presentations and follow-up interviews. Some quotes have been lightly edited for clarity. The ACIM website is acimconnect.com.

Tight Junction Injury

Tight junctions in the body are being injured by toxins, according to Bush.

Also called *zonulae occludentes*, tight junctions are proteins found in gut linings and other places in the body. They hold cell layers together – rather like Velcro. They affect the health of the microbiome, the brain, and other systems, and they are "incredibly vulnerable to some of the things we eat these days," said Bush.

Gluten, for example: "Gluten sensitivity is now affecting at least 18 million Americans," Bush said. "We think the number is far greater than that. In our laboratories, when we test epithelial linings of guts, we have yet to find a single lining that doesn't respond negatively to the gliadin in gluten." Tight junctions are also vulnerable to damage from the common herbicide Roundup (glyphosate), Bush said.

Tight junction problems in the gut – that is, intestinal epithelial barrier dysfunction – are an early step in the pathogenesis of many chronic inflammatory and autoimmune diseases, Bush said, including neurological conditions. In the last several years, scientists have established strong links between microbiome health and disease outcomes, he noted. When researchers began publishing these papers, the studies were widely regarded as "crazy talk," but today "we all talk about the microbiome. If you stop stress from the gut, the brain improves."

So what's the root cause of all this trouble?

"Destruction of the soil," said Bush.

Since World War II, petroleum-based, nitrogen-rich fertilizers have proliferated, and this, he said, has contributed to the depletion of soil bacteria in farmland. Destruction of soil bacteria has led to damaged root systems in plants, which in turn has hurt the ability of plants to gather nutrients from the soil. For example, kale in stores today is not as nutritious as it was in 1940.

There's a link, he said, between (a) loss of soil bacteria, (b) loss of bacteria in plants, (c) loss of bacteria diversity in the gut microbiome, and (d) increased gut vulnerability. The latter connects to many health issues, including neurological conditions such as dementia and depression.

Bush is founder and CEO of Biomic Sciences Ltd., which makes a gut-healing product called Restore.

Teeth

David Minkoff, MD: "If you've got neurological illness, and you've got root canals, you've got to have your root canals pulled out. You won't get better without it, and you won't get better with a redo, in my experience. The root canal problem is so often missed by practitioners. I'm not saying that everyone who has a root canal is sick with it, but it's a very important toxic load in nearly all the chronically ill patients I see, and it has to be dealt with."

Stuart Nunnally, DDS: "Some people tolerate root canals. People handle toxicities in different ways; everyone has to be treated individually. But if there's a bizarre change in your health, and no one has a solution to it, I am here to tell you, oftentimes it's what's going on in the mouth that is causing other systemic health issues." Nunnally added: "Regarding chelation for patients with amalgams – I think it's best not to chelate when they have mercury in their mouths; have them see a biological dentist first." (Related books and an article: *The Toxic Tooth: How a Root Canal Could Be Making You Sick*, by Robert Kulacz, DDS, and Thomas E. Levy, MD [2014]; this book provides a fresh examination of root canal data. *It's All In Your Head: The Link Between Mercury Amalgams and Illness*, by Hal A. Huggins, DDS [1993]; the late Huggins is a legend in alternative dentistry and health care. An article by Nunnally titled "*In Vitro* Enzymatic Inhibition Associated with Asymptomatic Root Canal Treated Teeth: Results from a Sample

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Listening to the Gut

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of 25 Extracted Root Fragments" [*Journal of Orthomolecular Medicine*. 2012;27(3)].)

The Eye

Thomas J. Lewis, PhD, spoke about the eye as a diagnostic tool. His company, Real Health Systems, uses relatively simple, noninvasive techniques for examining several aspects of health (including brain health) via the eye. His presentation was a highlight of the conference for several observers. He commented, "Eye pathologies, particularly in the retina, correlate to neurogenerative and cardiovascular disease." Real Health Systems opened its first clinic in October. Lewis is coauthor, with Clement L. Trempe, MD, of *The End of Alzheimer's? A Differential Diagnosis Toward a Cure* (2014).

Depression

Many researchers blame low serotonin levels for depression, but this model is incomplete, said Suruchi Chandra, MD, a psychiatrist in Silicon Valley, who noted that there's no consistent body of evidence showing that depleting serotonin leads to depression. Also, she said, a meta-analysis of antidepressant use found that these drugs are no more effective than placebo for cases of mild or moderate depression (i.e., most cases).

Chandra identified an "emerging view" of depression – that it's a "whole-body illness" with "many pathways" to healing. She puts a great deal of emphasis in her practice on the gut, which she studies and ponders "much, much more" than serotonin.

"The microbiome," she said, "has a relationship to how the brain functions and even how the brain develops – especially in patients with microbiome disturbances from frequent or prolonged antibiotic use." The basics of her gut protocol include diet, probiotics, prebiotics, and fermented foods.

She often helps patients deal with stress with adaptogenic herbs including rhodiola, ashwagandha, and astragalus, which have a "growing body of literature" for how they work and a long history of use in traditional cultures. She also uses minerals, including lithium, magnesium, zinc, and copper, and a variety of other approaches.

"Depression is not just in the head," she said. "When patients understand that, it gives them a lot of hope. They may think, 'I'm taking an SSRI and I'm not getting any better!' and get discouraged. The idea that depression is something that can be addressed in many ways, and that treatment can be individualized, gives them hope." (A book mentioned by Chandra is *The Emperor's New Drugs: Exploding the Antidepressant Myth*, by Irving Kirsch, PhD [2010].)

A Few Quotes from the Podium

"It's very rare to find a patient nowadays who doesn't have a chronic infection somewhere in their body." – W. Lee Cowden, MD, conference moderator.

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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.

"There's no chance for good health unless we repair the microbiome." – Jim Lemire, MD.

"Everybody's toxic. Neurotoxins are everywhere – we are exposed to hundreds if not thousands every day. The vast majority of patients we see in our clinic are neurologically impaired in some form or another and have major gut dysfunction. Few neurologists are thinking about what is really happening in the nervous system from the point-of-view of *cause*. It's all, "Use medications to suppress tremors and seizures" – never investigation into "*Why* is this happening?" While a seizure disorder does have to be treated, *why* it is occurring is the second most important thing. The patient wasn't born this way. This is not, by and large, genetic. The symptoms that one sees are the result of toxins and infections." – David Minkoff, MD.

"Evidence-based medicine is not just double-blind placebo-controlled studies. It also includes careful, collective clinical observations." – Suruchi Chandra, MD. (Related article: "Evidence Based Medicine: What It Is and What It Isn't," by David L. Sackett, MD, et al. [*British Medical Journal*. January 13, 2006].)

"We do testing with our patients to find out what they're missing, nutritionally, but also to *show them* what they're missing. Because otherwise they won't believe you! They believe they're eating well but they're not! I like hair analysis from Trace Elements and the RBC Mineral Test from Genova. SpectraCell has a great test that looks for nutrients inside immune system cells." – Carol Roberts, MD.

"You've seen just the tip of the iceberg in these presentations. We can do *so* much." – Garry Gordon, MD.

Water

"Dehydration is at least 50% of the aging process." – Zach Bush, MD.

"Chronic dehydration is *very* common." – Steve Hines, ND.

"Adding molecular hydrogen to water – creating hydrogen-infused alkaline water – is an exciting area of research. Hydrogen has been shown to be therapeutic in 150 human and animal disease models." – Tyler LeBaron, executive director of the Molecular Hydrogen Foundation. LeBaron noted that hydrogen infusion of water is well known and accepted in Japan but still pretty much under the radar in the US.

"There's a lot you can do with water. Hydrogen is going to be the next big topic." – Garry Gordon, MD.

"Hydrate by drinking 2 ounces of water every 15 or 20 minutes, all day, depending on your activity level. If you're exercising, every 10 minutes. Drinking a quart of water at a time doesn't hydrate, it just goes straight through you. – W. Lee Cowden, MD.

The Coca Pulse Test

The basic version of this food allergy test was described by several conference attendees: Relax for 5 minutes. Measure your pulse. Eat a food. Stay at the table for 15 minutes. Measure your pulse again; if it has gone up 15 beats or more, you almost certainly have an allergy to that food. If it's gone up 10 to 14 beats, possibly an allergy. If it's gone up 9 or less, probably not an allergy.

Listening to the Gut

The test is examined in detail in *The Pulse Test*, by Arthur F. Coca, MD (1994, revised ed.). The first edition of the book is available free online at the Soil & Health Library (an extraordinary resource located at soilandhealth.org; to search titles, go from the home page to "About" and then to "The Library" and scroll down the right-hand column). Another route to the free PDF of the book is via a Google search for "coca pulse public domain."

Lithium

Cowden said that his favorite type of lithium is Lizyme Forte from Biotics Research. Chandra noted that several good forms of the mineral are available, including Lizyme Forte, ionic lithium liquids, and lithium orotate – all of which, she said, are used at much lower dosages than pharmaceutically prescribed lithium carbonate. When used at low doses, she said, lithium is generally well tolerated and doesn't present anywhere near the toxicity of the carbonate form of the mineral.

Pain Relief

"Gallixa topical cream is the most incredible pain remedy you've ever seen." – Steve Hines ND.

GMOs (Genetically Modified Organisms)

"GMOs cause leaky gut and antibiotic resistance in everybody who ingests them. We're inundated with these foods." – David Minkoff, MD.

"GMO is the plague of our times." – Jim Lemire, MD.

Two Therapeutic Methods

The King Method, an energy exercise system, was warmly endorsed by several conference attendees. Information is available at kinginstitute.org. The Masgutova Method also won praise; see masgutovamethod.com.

Books

Many books received favorable mention at the conference podium, including these:

- *TOX-SICK: From Toxic to Not Sick*, by Suzanne Somers (2015).
- *Radical Healing: Integrating the World's Great Therapeutic Traditions to Create a New Transformative Medicine*, by Rudolph Ballentine, MD (2011, 2nd ed.). "This is a great book," said presenter Carol Roberts, MD, "it really woke me up." (Roberts is author of *Good Medicine: A Return to Common Sense* [2010].)
- *Dr. Neal Barnard's Program for Reversing Diabetes*, by Neal D. Barnard, MD (2007). "I trained at the third-best endocrinology program in the world," said Bush, "and no one mentioned you could reverse type 2 diabetes. I read this book one night, woke up the next morning, went to the chair of medicine, and said, 'Why didn't I know about any of this?'"
- *Oxygen Multistep Therapy*, by Manfred von Ardenne (1987, 4th ed.).
- *Curing the Incurable: Vitamin C, Infectious Diseases, and Toxins*, by Thomas E. Levy, MD (2002).
- *Detox With Oral Chelation*, by David Jay Brown and Garry Gordon, MD (2009).
- *One Answer to Cancer*, by William Donald Kelley, DDS (1974, revised ed.). Kelley is also author of *Cancer: Curing the Incurable Without Surgery, Chemotherapy, or Radiation* (2000).

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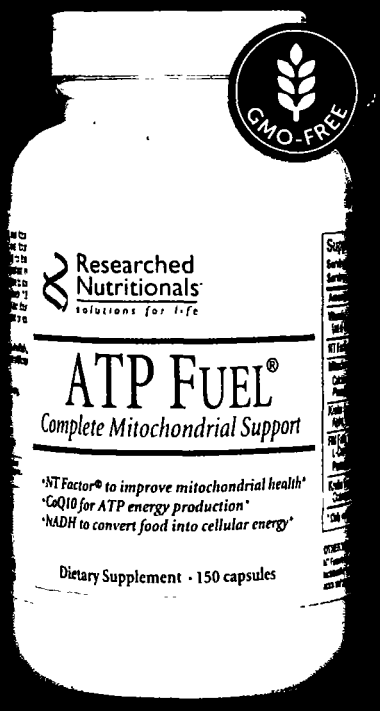

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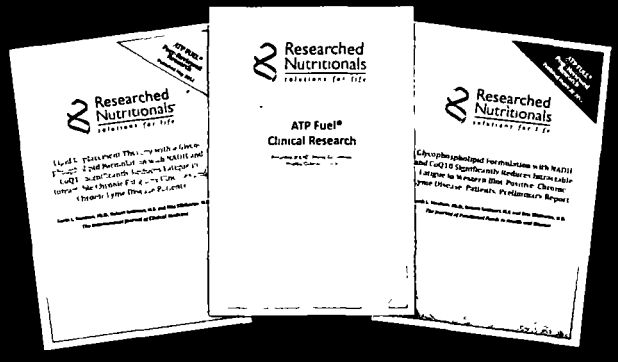

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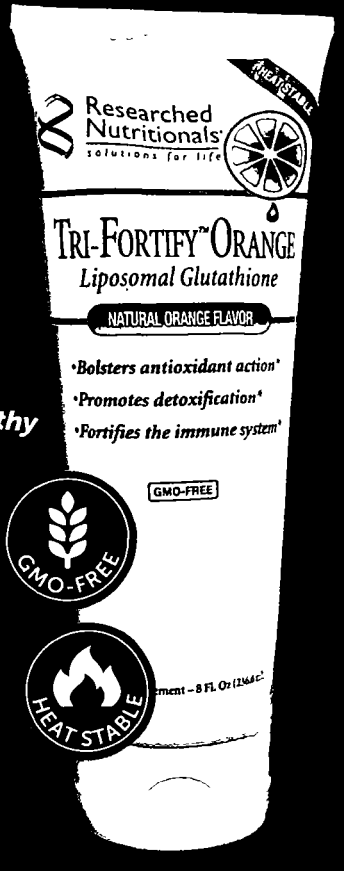

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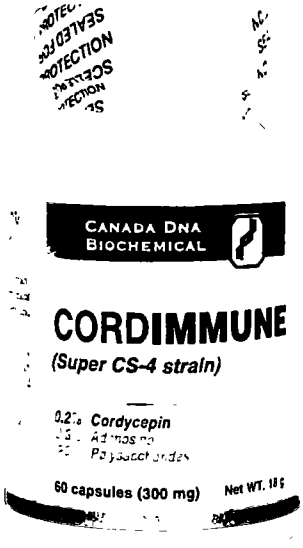

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➤ continued from page 10

benefits by not having as many infected teeth and periodontal disease, a risk factor for heart disease. The campaign to make all communities provide fluoridated water is never ending. Fortunately, every municipal water system is permitted to independently decide whether to fluoridate or not. It almost appears to be a random process when a city decides to fluoridate, as though the decision is introduced by a new set of commissioners. Once the city initiates the process, however, those who want to keep fluoride out of the water are generally overruled. Experts are called in to testify, and almost uniformly they proclaim that fluoridation is safe, with no proven side effects when provided within safe limits – the only worries occur when system operators overfluoridate the water supply. Of course, these experts minimize the highly studied and widespread problem of dental fluorosis. If antifluoridation experts testify about the medical risks of fluoridation, their opinions are typically disregarded. Yet there is a growing literature on the dangers of fluoride to human health, and public health authorities have turned a deaf ear to this research.

The days of a shrill group of health nuts complaining about fluoridation are past. Well-done research in animals and humans on the health effects of fluoride, while somewhat limited, is demonstrating adverse effects of fluoride on the central nervous system. In 2013, John D. MacArthur reported on the association of fluoride and copper in Alzheimer's disease.[1] One of the mechanisms by which fluoride insults the brain is by its accumulation in the calcified pineal gland. When there is a high level of fluoride in the pineal, the production of melatonin declines.[2] However, melatonin is a major protectant against fluoride-induced neurocellular damage. Depletion of melatonin contributes to reduced antioxidant functioning.[3] Fluoridation contributes to neurologic damage indirectly; when excess fluoride is pumped into a water system, there is corrosive damage to the pipes, causing lead to leach out into the water supply.[4,5] MacArthur argues that fluoride increases the neurochemical damage of copper to the brain, raising the risk for developing Alzheimer's disease.

In 2015, MacArthur reviewed the risks associated with fluoride in pregnancy – how bioaccumulation of fluoride in the placenta increases the risk of developing preeclampsia.[6] In the current issue, MacArthur examines the role prenatal fluoride has on the fetus, changing the neurophysiology associated with developing autism. MacArthur cites recent German research demonstrating that the major antimicrobial activity of fluoride in preventing caries is the weakening of bacterial adhesion forces.[7] Bacteria depend on adhesion forces to successfully colonize human tissues including dentition. The weakening of the adhesion forces prevents *Streptococcus mutans* from colonizing the enamel responsible for dental infection. However, the same fluoride antimicrobial activity affecting teeth also affects the microbial population in the gastrointestinal tract. For the developing fetus, fluoride will exert weakening of bacterial adhesion forces on essential bacteria such as bifidobacteria and Bacteroides organisms, at the expense of hardier bacteria such as *Klebsiella* or *Clostridium*. The failure of the fetus to develop a healthy intestinal microbiota, MacArthur argues, not only weakens the newborn's immune functioning but also interferes with normal genomic expression. The resultant abnormal biochemistry and neurophysiology pose a risk for improper brain development and functioning, contributing to autism risk.

For those who have felt squeamish about resisting the profluoride lobby, MacArthur's article cites numerous studies showing the relationship between fluoride bioaccumulation and adverse effects on human health. MacArthur's previous articles in the *Townsend Letter* and this article will serve well when supporting antifluoridation efforts.

Jonathan Collin, MD

Notes

1. MacArthur JD. Overdosed fluoride, copper, and Alzheimer's disease *Townsend Lett.* 2013,363 63–70
2. Luke J Fluoride deposition in the aged human pineal gland *Caries Res* 2001; 35(2):125–128.
3. Bhart VK, Srivastava RS. Effect of pineal proteins at different dose levels on fluoride-induced changes in plasma biochemical and blood antioxidants enzymes in rats *Biol Trace Elem Res.* 2011,141(1–3).275–282.
4. Robb J Lead levels in Thurmont water drop *Frederick Post* Feb 3, 1994.
5. Personal communication to MacArthur from the director of the lab that test NYC water. Feb. 6, 2008
6. MacArthur JD. Placental fluorosis. fluoride and preeclampsia *Townsend Lett.* 2015,382 74–79.
7. Loskill P, Zeitz C, et al Reduced adhesion of oral bacteria on hydroxyapatite by fluoride treatment. *Langmuir* 2013, 29(18) 5528–5533

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Listening to the Gut

➤ *continued from page 15*

- *Summary of the New Medicine*, by Ryke Geerd Hamer, MD (2000). Hamer's work is fundamental to EVOX therapy, which today is a major aspect of the company Zyto.
- *Grain Brain* (2013) and *Brain Maker* (2015) by David Perlmutter, MD, with Kristin Loberg.
- *Gutbliss*, by Robynne Chutkan (2013).
- Three recent books by W. Lee Cowden, MD, and Connie Strasheim: *Foods That Fit a Unique You* (2014), *Create a Toxin-Free Body & Home Starting Today* (2014), and *BioEnergetic Tools for Wellness* (2015). (Strasheim is author of several authoritative books on Lyme disease.)

Who Was Li Ching-Yuen?

He was a Chinese herbalist who lived a very long life (perhaps an incredibly long life, according to some sources) and died in 1933. Among his health practices, as noted by Cowden: fo-ti root tea, ginseng, speed walking, reishi mushrooms, gotu kola, rice wine, and daily exercise with qigong and *baguazhang*.

And Who Is Sarah Kavanagh?

She is a teenager in Mississippi (mentioned at the conference) who read an article in *Scientific American* in 2012 about the dangers of bromine. (Possible bromine side effects include neurological disorders, reduced fertility, and altered thyroid hormones.) She launched a petition drive at Change.org, hoping to persuade PepsiCo to get bromine out of Gatorade. Amazingly enough, soon thereafter, Gatorade removed brominated vegetable oil (BVO) from its sports drinks (although PepsiCo never publicly mentioned Kavanagh). US testing for BVO is "abysmal," says the Center for Science in the Public Interest, and the European Union has long banned it. (Incidentally, a 32-ounce bottle of Gatorade contains more than a dozen teaspoons of sugar, according to Internet sources.)

A Powerful Tool

"The most important tool I've ever learned in medicine is Autonomic Response Testing. It allows me to zero in on the core issue *right now* for *this* patient." – David Minkoff, MD.

An Inexpensive Light Source That Might Save Someone from a Fall

The topic of sleep was discussed at the podium and in the hotel lobby: the importance of having a completely dark room at night, avoiding placing a clock radio close to the head, and not turning on any bright lights in the night, in order to avoid disrupting sleep patterns. "If you need a light at night to get to the bathroom safely," said one attendee, "it should be a dim red light" – for example, a red laser pointer, available online for $30 or $40, kept on the nightstand.

An Inexpensive Product Mentioned Favorably at the Podium

The Sunpentown Healthy Swing Machine with Swivel Disk (a chi machine): $100.

A Pricey Product Mentioned Favorably

Celergen, a marine cell therapy supplement: $350 a month.

A *Very* Pricey Product That Got Rave Reviews

The HOCATT Ozone Steam Sauna got serious attention and major praise from a number of conference goers, who lined up to give it a try. It's a modern-day sweat lodge. You sit in it, encased, like you're in an eggshell with doors. It can provide a range of useful stuff all at once – hyperthermia, ozone treatment, electrical therapy, color therapy, carbonic acid treatment, aromatherapy, and other modalities. It's noninvasive and easy to use. It's said to be very helpful for athletic performance. HOCATT stands for Hyperthermic Ozone and Carbonic Acid Transdermal Therapy. The device is manufactured and distributed by Signature Health; the price is in the neighborhood of $18,500.

More Cool Products and Books

Tom Butler and Mark Squibb of the Whole Health Network (and the company LiveO2) presented a talk on oxygenation and exercise-with-oxygen equipment.

Garry Gordon, MD, presented on the preventive benefits of the herb *Pueraria mirifica*.

Damon Miller, MD, discussed macular degeneration and other retinal dystrophies and mentioned the books *Amazing Grace: Autobiography of a Survivor*, by Grace Halloran (1993) and *The Body Electric: Electromagnetism and the Foundation of Life*, by Robert O. Becker, MD, and Gary Selden (1985).

E. Michael Molnar, MD, presented on stem cell transplantation. He is author of *Stem Cell Transplantation: A Textbook of Stem Cell Xenotransplantation* (2006, revised ed.), *Forever Young: The Practical Handbook of Youth Extension*, (1985, 2015), and two books published in 2015: *Diseases and Genocide Are Not Our Destiny* and *Treatment of Incurable and No Longer Treatable Disease*.

Kyl Smith, DC, discussed cognitive health and longevity; he is the inventor of the multi-ingredient product MemoryWorks and author of *Brighter Mind* (2007).

Arzhan Surazakov, PhD, presented on the benefits of MIL (magnetic infrared laser) therapy and described a hand-held therapeutic device, the Delta Medical Terminal.

Awards

The ACIM gave Lifetime Awards to Victor Marcial-Vega, MD, and David Steenblock, DO.

Don't Forget This ...

The value of exercise was emphasized by many attendees. The vast majority of Americans don't exercise regularly, noted Carol Roberts, MD, – a fact perhaps overlooked by some practitioners.

W. Lee Cowden, MD: "Exercise with oxygen therapy – 'EWOT' – is one of the best ways to get toxins out. I recommend it for everybody in this room and all your patients."

And, of Course, You Must Remember This ...

"Don't forget the emotional side. Kisses and hugs help people feel better." – David Minkoff, MD.

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Seasonal Allergies are No Match for Colostrum-LD®

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As potent immune system modulators, Proline-Rich Polypeptides (PRPs) in bovine colostrum have the ability to suppress an overactive immune system, as with seasonal allergies, preventing the immune system from over-reacting to otherwise harmless, foreign antigens. PRPs act on T-cell precursors to produce helper T-cells and suppressor T-cells and induce the growth and differentiation of B lymphocytes. PRPs also stimulate the production of cytokines, including IL-10, an anti-inflammatory cytokine. The anti-inflammatory action is key to returning the body to a homeostatic state. PRPs are abundant in bovine colostrum, and along with lactoferrin, have been shown to eliminate or improve the duration and symptoms of seasonal allergies.[1] Lactoferrin increases the quantity and activity of T and B lymphocytes as well as Natural Killer (NK) cells. It also stimulates the release of anti-inflammatory cytokines and the production of immune cell receptors.

Bovine Antibodies: Not Just for Cows

Antibodies against ryegrass pollen, house dust mites, Aspergillus mold and wheat proteins have been identified in bovine colostrum.[2] Numerous other antibodies are present in bovine colostrum which cross-react with allergens of importance to humans, including antibodies against pathogenic invaders, such as E. coli, Candida, H. pylori, salmonella, and many others.

The IgE and IgE inhibitors present in colostrum are believed to be responsible for regulating the allergic response; together, they inhibit the allergic response by limiting the histamine response.[3]

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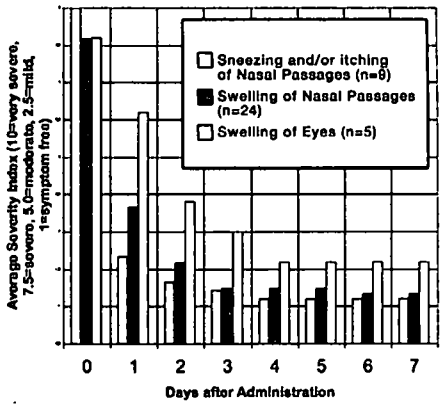
Visit www.ColostrumTherapy.com (for professionals) or www.CenterForNutritionalResearch.org (for consumers).

1 Keech, A. *Unpublished results.* 2007.

2 Collins AM, et al. *Bovine milk, including pasteurised milk, contains antibodies directed against allergens of clinical importance to man.* International Archives of Allergy and Applied Immunology 96(4):362-7 (1991).

3 Milgrom, H *Attainments in atopy: special aspects of allergy and IgE.* Advances in Pediatrics 49:273-97 (2002).

For Seasonal Allergy Symptoms



Patients suffering from seasonal allergies were given the IRM® formula in 2 ml doses over a seven day period. All showed significant improvement in allergic symptoms compared to placebo over the test period. Symptoms included sneezing and/or itching of the nasal passages (allergic rhinitis), swelling of the nasal passages (allergic sinusitis) and swelling of the eyes.[1]

Returning the immune system to homeostasis is welcome relief for seasonal allergy sufferers.

Medical professionals may receive professional pricing by registering on www.ColostrumTherapy.com or call Sovereign Laboratories at 928.202.4031.

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Pathways to Healing

by Elaine Zablocki

LightHearted Medicine Engages Deeply with Patients

Molly Roberts, MD, MS

"We are creating an environment where we can connect with patients and explore what's going on for them on the many levels of their existence as human beings: physical, emotional, mental, and spiritual," says Molly Roberts, MD, MS, the cofounder of LightHearted Medicine, in San Francisco. "We want to look together at what is working/isn't working in their lives, and see what needs our attention and support the most." Roberts is board certified in family medicine, integrative holistic medicine, and nutritional medicine, and is a psychotherapist as well. She started the clinic together with her husband, Bruce Allen Roberts, MD, who is board certified in family medicine, psychiatry, and integrative holistic medicine.

They looked for a location that would support their health-care vision and found a building surrounded by green space, where they can walk from downtown along the Embarcadero piers to their office. "It's a beautiful, festive commute to work every day," Roberts said. "My room has a floor-to-ceiling window looking at two mature trees, rolling hillocks of grass, and the San Francisco Bay. Birds come right up to the window to look in."

She uses a sit/stand desk, sometimes with a treadmill so that she can work and walk at the same time. The practice schedules outdoor educational sessions for groups of patients, so that they can walk and stay active while learning about health-care issues. (Sometimes, for fun, the group walks to explore San Francisco's neighborhoods and history together.) Patients can come in for the typical medical visit sitting across from the practitioner in chairs, or they can schedule individual "walk your talk" sessions, in which both patient and doctor walk during their scheduled visit. "We have purposely created an environment and a structure that lets us expand the times when we are physically active and engaged," Roberts said. "As we visualized our goals for this practice, we found ways to walk our own talk and model the active lifestyle we advocate for others."

Listening Attentively on All Levels

LightHearted Medicine opened in October 2015. During the first decade of the century, the Robertses were based in Tucson, working through Canyon Ranch Health Resort as well as their private medical practice. However, the financial crisis toward the end of the decade hit Tucson very hard. In 2009 they transitioned to the Sutter Health Institute for Health & Healing in San Francisco.

At Sutter, Roberts worked on a team that also included acupuncturists, chiropractors, nutritionists, psychologists, and massage therapists. "It was a great team, and I can't say enough wonderful things about them. That was the aspect I liked the most," she says. "However, working within the insurance system limited our ability to help our patients in that deeper way that we felt was most healing."

Roberts was part of the Sutter system for more than five years. During that time, she experienced pressure from the insurance system to shorten interaction times with each patient. She practices the functional medicine model of care, and, "In that model you need time to figure out what is really going on with the patient," she says. "You form a partnership with the patient to find the next inroad to their health and happiness. You also need enough time for an educational process, so they understand what's going on inside their body and so we can talk about how to get their lives into better balance."

In addition to the limits on time spent with patients, she also found that she was responsible for a great deal of administrative work without enough time set aside in her schedule to accomplish it. "Anything like responding to patient phone calls or e-mails, or contacting another health provider – all of that had to happen after hours," she says. "Especially during an initial visit, I would focus solely on listening deeply to the patient's story but then would have to spend extra time at the end of the day entering their data into the electronic medical record system. It was my choice to not do data entry during their first visit, but it felt like the right one to make for their care."

A typical first visit at LightHearted Medicine takes 90 minutes, and Roberts focuses on listening attentively to the patient's story. Often, by the end of that initial conversation,

she has an idea of the most important issue for this person. It may be physical or emotional; it may be an individual issue or relate to the family as a whole.

She is able to have the type of wide-ranging, interconnected conversation with patients that rarely takes place in more conventional settings, partly for lack of time but also due to a lack of experience in addressing both the physical and psychospiritual issues of any illness, Roberts says. "I often feel like a detective, looking at the puzzle pieces and asking how they connect. If someone has a thyroid problem along with headaches and GI symptoms, how are they all related?" There's a range of possibilities. One person may have an inflammatory process under way. In other people, the GI system can be a common underlying source of problems. Others may have a hormonal imbalance or emotional stressors in their life. For some, it may be all of the above.

Between the first and second visits, Roberts writes a fairly long letter summarizing the discussion and the options available for potential treatments. At the second visit, "We go over the options as partners in care and set priorities. We typically order labs during that second visit, and we schedule another visit after the labs come back. These follow-up visits may look different if individual or family counseling is the first focus of our attention."

LightHearted Medicine does not bill insurance. Patients do receive a copy of their superbill so that they can deal directly with their insurance company, and they generally receive between 20% and 50% reimbursement for services if they have a PPO policy. In addition, patients who have a health savings account can make use of those funds.

LightHearted Medicine also offers a "Pledge to Yourself" option. Patients can sign up for 3, 6, or 12 visits. The more visits they pledge, the less they are charged per visit. "We created 'Pledge to Yourself' because we wanted to get away from the traditional idea of a 'pill to the ill' visit," Roberts said. "People sometimes come in saying 'I've got this symptom, so give me something to make it go away.' We take a more comprehensive and long-term approach, seeking the root causes of problems so that we can better address current symptoms while also avoiding other problems down the road.'

While many patients at the clinic are fairly healthy and want to stay healthy, many others are coping with either chronic or serious illness. "Throughout my career I've worked with people who were pretty ill, who've seen a lot of other doctors and weren't sufficiently helped and so they came to see me," Roberts says. "Because I am partnering with the patient to search for the underlying physical and emotional imbalances contributing to illness, we often can get pretty far in helping the person to feel better."

Maintaining a Light Heart in Difficult Circumstances

When you visit the LightHearted Medicine website, its "About Us" page says, "Come join us to explore how to bring vibrant health, love, joy, vitality, and connection into your life."

When I first saw those words, I wondered whether this might be a clinic designed to serve people who are already healthy. I wondered if LightHearted Medicine might have unrealistic expectations about how healthy we can all be.

It turns out that Roberts has developed this approach based on her own profound experiences with life-changing illness. At one point she experienced a serious neck injury and could not use her arms. She did various mental/emotional exercises to explore her situation and find peace with her circumstances. "At one point, I did an exercise where you write as fast as you can to dialogue with your problems and I found myself talking to the pain. The pain said, 'You don't love me.' I wrote back, 'How can I love you, you hurt me all the time.' Internally I perceived this response: 'When you're hurting, don't you want someone to love you?' This was a way to connect with my own inner wisdom. I learned that when I was in pain, instead of saying, 'Damn, here it comes again,' I needed to put my hands on my heart and say to the pain, "Oh honey, what do you need from me?'"

Roberts found she was able to stop fighting the pain and reached a point of acceptance where she felt that everything is as it should be, however it is. "And I don't mean that you clasp your hands and don't do anything about the situation," she clarifies. "This is deeper than that. It's about going with the flow of whatever comes in your life and finding your way to a light heart even in the midst of hard times."

About 10 years after her neck injury healed, she lifted a heavy piece of luggage the wrong way and injured a disk and the membrane surrounding her spinal cord. She was fixed into a 90-degree position and had tremendous pain with any movement. For months she could barely walk, and she slept sitting up in a chair. "There was a point where I didn't know if I would ever get out of a wheelchair again," she recalls. "I realized how much I had learned from my past experience with my neck, because I was able to move very quickly into that space of, 'OK, here we are now, so what's the next best thing I can do?' I was in a lot of physical pain but instead of suffering, my main emotions were of gratitude and love for the family and friends who supported me during such a difficult time in my life."

"My goal today, as a healer, is to create a safe space to explore everything that is going on for my patients, physically, emotionally, mentally, spiritually," she says. "Everything is related. Just as I can't separate out the GI tract and the headache, I can't separate out mind, body, emotions, and spirit, because they're all interlocking. Because of this, there is a treasure trove of healing ability within every person. We can all use various aspects of ourselves to shore up the parts that are struggling. When you see that happening in someone, it's beautiful."

Resources

For more information about the clinic, go to:
http://www.lightheartedmedicine.com
http://www.lightheartedmedicine.com/#!this-is-us/ctz4

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

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Shorts

briefed by Jule Klotter
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Computer Vision Syndrome

Reading text on hand-held computer devices or flat-panel monitors for extended periods is more likely to produce blurred vision and other symptoms of eyestrain than reading hard copy. These symptoms, which also include dry eyes, eye irritation, redness, burning, headache, and neck and shoulder pain, are diagnosed as computer vision syndrome (CVS) by the American Optometric Association. "[S]ome 90% of the 70 million U.S. workers using computers for more than 3 hours a day may experience CVS," say Jamie Klamm, BSN, RN, and Karen Gahan Tarnow, PhD, RN, in their 2015 CNE article. Good ergonomic positioning of the computer screen and exercises can mitigate neck and shoulder pain. Eye strain, however, requires less time staring at the computer – a difficulty for workers and students who need to finish their tasks.

Reading is an intense workout for the eyes and the orbicularis oculi muscle that controls squinting and blinking, as Jim Reedy and Kevin Larson explain in their 2008 article "Blink: The Stress of Reading." Glare, small text, and light-colored or gray text make the eye muscle work harder, contributing to eye strain. In addition, we blink less when reading. Less blinking means reduced tear film and less protection from irritants. As a result, symptoms of dry eye – redness, irritation, burning – arise. Although the mean blink rate between reading hard-copy text and computer text does not significantly differ, Christina A. Chu and colleagues observed "a significantly higher percentage of incomplete blinks" when subjects were reading from a computer (7.02% for computer vs. 4.33% for hard copy; $p = 0.02$) in their 2014 study. "Decreased blink rates and incomplete blinks [also] occur with both fast-paced and slow-paced computer games," Klamm and Tarnow write.

Klamm and Tarnow offer several recommendations for preventing computer vision syndrome. First, eliminate glare and reflection from the computer screen by adjusting room lighting and using an antiglare cover or coating on the screen. The computer screen should be positioned at least 20 to 24 inches away, as eye muscles have to work harder when text is too close. Klamm and Tarnow also recommend blinking often, closing the lids completely, and taking short breaks by looking about 20 feet away for at least 20 seconds every 20 minutes. Over-the-counter eye drops for the redness and irritation caused by dry eyes are another suggestion. I have also found enlarging the text size and using a darker font, such as Comic Sans MS, to be helpful.

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DHA and Photooxidative Damage

Is it possible that too much docosahexaenoic acid (DHA), an omega-3 fatty acid found in fatty fish and fish oil supplements, increases the risk of photooxidative damage to the retina? It seems counterintuitive, since DHA is known to be essential for vision development. The membranes of light-detecting rods in the retina have a high DHA content. Recent laboratory studies, however, indicate that high DHA levels in the retina exacerbate the damaging effects of intense light. In addition to fish oil, the body can obtain DHA from alpha (α)-linolenic acid, an essential fatty acid found in flaxseed oil (richest source), walnut oil, hemp oil, and totally unrefined canola and soybean oils.

A 2014 in vitro study, led by Y. Liu, looked at the effects of DHA on retinal pigment epithelium (RPE) cells. DHA promoted RPE proliferation under dark conditions. In the presence of high-intensity light, however, DHA "inhibited cellular proliferation, destroyed cell membrane integrity, enhanced cellular senescence, increased vascular endothelial growth factor (VEGF) release, and decreased phagocytic function."

A 2009 in vivo study, led by Masaki Tanito, also found that the combination of intense light and higher DHA levels leads to increased lipid peroxidation and retinal damage. The researchers gave wild-type mice (controls) and mice genetically modified to convert omega-6 to omega-3 polyunsaturated fatty acids an omega-3-deficient safflower-oil-rich diet. The

researchers found severe functional and morphological damage in the retinas of animals with low omega-6/omega-3 ratios (i.e., more omega-3 DHA than omega-6) that had been exposed to intense light. The authors discuss "the ying and yang roles of [omega-3 polyunsaturated fatty acids] and DHA in retinal physiology and pathology," pointing out the absolute necessity of DHA for visual acuity and its contradictory role in retinal damage.

Only a few human studies have investigated the effect of omega-3 supplementation on retinal degeneration. The Cochrane Collaboration reviewed two controlled clinical trials involving 2343 people with high risk of developing age-related macular degeneration. Cochrane researchers say, "Omega-3 supplementation ... for periods up to five years did not reduce the risk of progression to advanced [age-related macular degeneration (AMD)] or the development of moderate to severe visual loss." The relationship between intense light exposure and omega-3 supplementation was not investigated in these studies.

Both omega-3 supplementation and the increase in intense-light exposure are recent phenomena. The human eye is now exposed to intense light from televisions, smartphones, iPods, and other computers. The light from these sources is bright enough to be used like a flashlight. Would we think of staring into a flashlight for hours on end? Of course, in vitro and animal studies do not necessarily indicate risks for humans, but they do indicate a need for more research.

Enig M G *Know Your Fats* Silver Spring, Maryland, Bethesda Press: 2000 246.

Lawrenson JG, Evans JR Omega 3 fatty acids for preventing or slowing the progression of age-related macular degeneration [abstract] *Cochrane Database Syst Rev* 2015, Issue 4, Art Nos CD010015 Available at http //onlinelibrary.wiley com/doi/10 1002/14651858 CD010015 pub3/abstract Accessed February 4, 2016.

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Tanito M, Brush RS, Elliott MH, Wicker LD, Henry KR, Anderson RE High levels of retinal membrane docosahexaenoic acid increase susceptibility to stress-induced degeneration *J Lipid Res* 2009,50(5).807–819. Available at www jlr org/content/50/5/807.full Accessed February 2, 2016

Light Stress and Retinal Damage

High-energy visible light, particularly blue light with a wavelength from 450 to 495 nm, is known to damage the retina and contribute to the development of age-related macular degeneration and retinitis pigmentosa. Blue light energy has a much greater ability to remove electrons from molecules and create reactive oxygen species than other visible light. "The increased risk of mitochondrial damage induced by blue light has been demonstrated in many experimental models," write Professor Peep V. Algvere, MD, and colleagues. "For example, red light of a certain intensity is insufficient to induce retinal damage, whereas blue light of the same intensity will cause retinal injury. Deep blue light has been described as 50-80 times more efficient at causing photoreceptor damage than green light." Sources of this high-energy light include sunlight, fluorescent light, and light-emitting diode (LED) light emitted by energy-saving light bulbs and electronic devices. Several natural compounds protect against light-induced oxidative retinal damage.

The American Academy of Ophthalmology recommends a nutrient formula that was tested in the Age-Related Eye Disease Studies (AREDS I & II). The first AREDS clinical trial investigated antioxidant and mineral supplementation (vitamin C 500 mg, vitamin E 400 IU, β-carotene 15 mg, zinc 80 mg, and copper 2 mg) in 3640 participants at risk for advanced age-related macular degeneration. "At 5 years, the estimated probability of progression to advanced [age-related maculopathy] (neovascular ARM, geographic atrophy) was 28% for those assigned to placebo, and 20% for those assigned to antioxidants plus zinc," according to Algvere et al.

Because β-carotene has been linked to an increase in lung cancer in people who smoke, the second AREDS investigated lutein (10 mg) and zeaxanthin (2 mg), two carotenoids found in leafy, green vegetables, as alternatives. Lutein and zeaxanthin are found in the eye lens and retina. A lower level of zinc (25 mg) and omega-3 fatty acids DHA and EPA were also tested. Although the omega-3s showed no effect, the carotenoids did lower the risk of advanced age-related maculopathy, particularly in those who don't usually eat leafy green vegetables. Also, the lower dose of zinc (25 mg) was as effective as the 80 mg dose.

Other nutrients have also shown protection against blue light damage. Bilberry extract and lingonberry extract and their active components protect the retina against blue LED light-induced retinal photoreceptor cell damage, according to a 2014 in vitro study. The Japanese study used a bilberry ethanol extract containing anthocyanins and a lingonberry ethanol extract containing trans-resveratrol and proanthocyanidins. Kenjirou Ogawa and coauthors report that the extracts "exert not only antioxidant effects but also inhibitory effects against stress response proteins induced by blue LED light exposure."

Fucoxanthin, found in the marine alga *Laminaria japonica*, is another compound that protects the retina from blue-light damage, according to in vitro and in vivo research. In their 2016 study, Y. Liu and colleagues report that fucoxanthin provided better retinal protection against light damage than lutein in vivo. In vitro, fucoxanthin "exhibited better bioactivities than lutein, zeaxanthin, and blueberry anthocyanins in inhibiting overexpression of vascular endothelial growth factor, resisting senescence, improving phagocytic function, and clearing intracellular reactive oxygen species in retinal pigment epithelium cells."

Radiofrequency waves (RFW) emitted by wireless technology also cause oxidative stress and produce eye damage, according to a 2013 study. Gholamali Jelodar and colleagues found that exposing adult male rats to RFW from a base transceiver station antenna used to transmit wireless communication (900 MHz RFW) decreased antioxidant enzymes activity (glutathione peroxidase, superoxide dismutase and catalase) and increased malondialdehyde, an oxidative stress marker, compared with control ($p < 0.05$). The exposed group that received vitamin C (200 mg/kg of body weight/day by gavage) showed better antioxidant activity and lower malondialdehyde levels, compared with untreated RFW-exposed rats ($p < 0.05$). The abstract does not say that vitamin C totally negated the effect of RFW exposure.

The widespread use of light-emitting diodes (LEDs), computers, and widescreen mobile phones makes it even more

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urgent to find natural ways to protect vision beginning early in life, particularly if a familial history of macular degeneration is present.

Algvere PV, Marshall J, Seregard S Age-related maculopathy and the impact of blue light hazard *Acta Ophthalmol Scand* January 23, 2006,84 4–15. Available at http://onlinelibrary.wiley.com/enhanced/doi/10.1111/j.1600-0420 2005 00627 x. Accessed January 20, 2016.

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Liu Y, Liu M, Zhang X, et al Protective effect of fucoxanthin isolated from *Laminaria japonica* against visible light-induced retinal damage both in vitro and in vivo [abstract]. *J Agric Food Chem* January 4, 2016 Available at http://www.ncbi nlm nih gov/pubmed/26708928 Accessed January 20, 2016

National Eye Institute For the public. what the AREDS means for you. May 2013. Available at https.//nei nih gov/areds2/PatientFAQ Accessed February 9, 2016

Ogawa K, Kuse Y, Tsuruma K, et al Protective effects of bilberry and lingonberry extracts against blue light-emitting diode light-induced retinal photoreceptor cell damage *in vitro. BMC Complement Altern Med* April 2, 2014,14 120 Available at www ncbi nlm nih gov/pmc/articles/PMC3992157 Accessed January 20, 2016

Moisturizing Creams and Skin Cancer

Are moisturizing creams contributing to skin cancer? Yao-Ping Lu and US colleagues performed a study that showed a connection between UVB exposure during early life and topical applications of moisturizing creams and skin cancers in high-risk mice. Initially, they intended to test topical caffeine compounds' ability to prevent sunlight-induced skin cancers. As a preliminary step, the research team decided to test the skin moisturizer that they wanted to use as a base (Dermabase). To their surprise, mice exposed to the moisturizer developed more skin cancers than the control. They then decided to test other commonly used commercial moisturizers.

In their 2009 study, albino SKH-1 mice, which have a high risk of developing skin cancer, were exposed to UVB twice a week for just 20 weeks early in life. The researchers then randomized the mice into seven groups. One group received no treatment, and the others received daily applications (5 days/week for 17 weeks) of Dermabase, Dermavan, Eucerin, Vanicream, a custom-blend, or water (active control) applied with a Q-tip. The custom blend cream, prepared at the researchers' request by Johnson & Johnson (Skillman, NJ), contained purified water, propylene glycol, stearyl alcohol, cetyl alcohol, polysorbate 20, isopropyl myristate, C12-15 alkyl benzoate, benzoic acid, glycerin, and sodium hydroxide. Sodium lauryl sulfate, a known skin irritant, and mineral oil, which stimulates skin tumors in the presence of UVB radiation, were specifically excluded from the custom blend cream. All of the commercial creams except Vanicream contain mineral oil.

All four commercial creams showed increased tumor activity compared with controls. Dermovan-treated mice had the highest tumor volume per mouse (51.3 ± 14.0 mm^3), and Eucerin was the lowest (40.6 ± 16.1 mm^3). The tumor volume per mouse in the custom blend group was 26.2 ± 9.8 mm^3. In comparison, tumor volume was 32.0 ± 12.6 mm^3 in untreated mice, 23.2 ± 6.6 mm^3 in water-treated mice, and 27.3 ± 6.9 mm^3 in the combined control. Oddly, tumor volume in the water-treated mice was much lower than the untreated group. Also, mice exposed to Vanicream, which contains neither mineral oil nor sodium lauryl sulfate, developed more tumors and greater tumor volume than mice exposed to Eucerin, which contains mineral oil. Did stroking mice with a Q-tip have a stress-relieving effect? Does Vanicream contain a tumorigenic ingredient comparable to mineral oil? Did unconscious bias affect the results since the researchers were not blinded?

The authors caution that their results cannot be generalized to humans. Mice in general have thinner and more permeable skin than humans; and the mice in this study have a high genetic risk of developing skin cancer. However, most commercial creams and ointments – with or without UVB exposure – are not tested for carcinogenic activity, according to the authors. Skin care product safety testing usually looks for evidence of irritation and sensitization.

Lu Y-P, Lou Y-R, Xie J-G, et al Tumorigenic effect of some commonly used moisturizing creams when applied topically to UVB-pretreated high-risk mice. *J Invest Dermatol* February 2009;129(2)468-475 Available at http //www ncbi.nlm nih.gov/pmc/articles/PMC2630214 Accessed January 20, 2016.

Sublingual Immunotherapy and Allergies

Sublingual immunotherapy (SLIT) is a safe and effective alternative to monthly subcutaneous immunotherapy injections for the treatment of allergic rhinitis due to seasonal and house dust mite allergies, according to a 2015 review article by Pascal Demoly and colleagues. In SLIT, specific allergens are delivered in drops or a quick-dissolving tablet placed under the tongue each day. Initial treatment begins with a low dose (e.g., 30 IR) and gradually increases to the maintenance dose of 300 IR (index of reactivity). IR refers to the wheal size that occurs during skin prick-testing on 30 subjects who are sensitized to the corresponding allergen source. In addition to short-term relief, SLIT provides long-term efficacy (tested up to 2 years posttreatment) when given seasonally for 3 years.

Aging has no effect on SLIT's efficacy, according to a 2012 placebo-controlled, double-blind Polish study led by A. Bozek. People, aged 60–75 years, with confirmed house dust mite allergy were given SLIT (Staloral 300 IR made by Stallergenes) or a placebo. The total nasal symptom score for the active group ($n = 47$) decreased by 44% compared with a decrease of 6% for the placebo group ($n = 48$) after 3 years. The active group also showed a significant decrease in the use of other symptom-relief medications (e.g. antihistamines). Three patients in the active group experienced local adverse reactions (oral itching and facial flushing), which resolved spontaneously.

SLIT is considered safer than subcutaneous treatment, but adverse events (AEs) do occur. Oral pruritus, burning sensations, lip or tongue swelling, gastrointestinal symptoms, rhinoconjunctivitis, and asthma have all been reported. The more serious AEs are most likely to occur when the maintenance dose is initiated too quickly or when a patient switches to a different SLIT preparation during allergy season. In a letter to *Pediatric Allergy and Immunology,* Australian allergy specialists Kuang-Chih Hsiao and Joanne Smart report a severe allergic reaction in one of two allergy patients who switched over to a different SLIT preparation when their original preparation became unavailable from the manufacturer. They write: "We believe that manufacturers and suppliers of allergen immunotherapy extracts need to acknowledge the significant clinical impact of treatment interruption and have

a responsibility to ensure that allergen immunotherapy extract supply disruptions are minimized."

Bozek A, Ignasiak B, Filipowska B, Jarzab J House dust mite sublingual immunotherapy. a double-blind, placebo-controlled study in elderly patients with allergic rhinitis *Clin Exper Allergy* 43 242–248 Available at EBSCOhost. Accessed January 20, 2016.

Demoly P, Passalcqua G, Calderon MA, Yalaoui T. Choosing the optimal dose in sublingual immunotherapy Rationale for the 300 index of reactivity dose *Transl Allergy* 2015;5·44. Available at http://www.ncbi nlm nih.gov/pmc/articles/PMC4689001. Accessed January 20, 2016.

Hsiao K-C, Smart J. Comment on 'Anaphylaxis caused by in-season switchover of sublingual immunotherapy formulation' *Pediatr Allergy Immunol* 2014, 26·92 Available at http // onlinelibrary.wiley.com/doi/10 1111/pai.12329/full. Accessed January 20, 2016

Editor's note: See also "Allergy and Immunotherapy,"by Diego Saporta, MD, FAAOA, on page 34.

Zinc and Skin

Zinc supplementation improves atopic dermatitis (eczema) in some patients, according to research and empirical clinical evidence. Zinc, an essential trace element, takes part in numerous physical processes, including normal cell growth and immune response. Zinc deficiency can lead to dry skin and lesions. It also contributes to chronic inflammation, according to Dr. Ananda S. Prasad, whose studies on zinc deficiency were used to establish an RDA for zinc in 1974.

Korean researcher Jeong Eun Kim and colleagues sought a correlation between hair zinc levels, zinc supplementation, and atopic dermatitis (AD) in 58 children with AD and 43 controls (age range 2–14 years). "At baseline, the mean zinc level was significantly reduced in AD patients (113.1 µg/g vs. 130.9 µg/g, p=0.012)," say the authors. AD patients who received 12 mg/day of zinc for 8 weeks showed significant improvement and increased hair zinc levels compared to AD patients who did not receive zinc. In commenting on this study, Dr. Alan Gaby says, "The concentration of zinc in hair does not appear to be a reliable indicator of zinc nutritional status, and it is not clear whether patients with atopic dermatitis need to be zinc-deficient in order to benefit from supplementation." Gaby reports clinical benefit when using zinc along with essential fatty acids (sunflower oil, safflower oil, flaxseed oil) to treat atopic dermatitis (AD) in children.

Kirk Hamilton, PA-C, founder of Clinical Pearls Publications, says, "That small dose of 12 mg of elemental zinc makes sense in children. In adults it would be in the 25-50 mg/day range." Dr. Ananda S. Prasad told Hamilton, "If zinc is administered in amounts greater than 50 mg/d, we recommend that 1 mg of copper daily should be also administered to prevent copper deficiency."

Gaby AR. Zinc for atopic dermatitis (eczema). *Townsend Lett.* July 2015,32

Hamilton K Aging, antioxidants, anti-inflammation and zinc interview with Dr. Ananda S Prasad July 2015 Available at www vitasearch com/CP/experts/p2experts htm. Accessed February 10, 2016.

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Kim JE, Yoo SR, Jeong MG, Ko JY, Ro YS Hair zinc levels and the efficacy of oral zinc supplementation in children with atopic dermatitis *Acta Derm Venereol.* 2014,94.558–562. Available at EBSCOhost Accessed January 20, 2016

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Literature Review & Commentary

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

Vitamin D for Eczema

One hundred seven Mongolian children (aged 2–17 years) with winter-related atopic dermatitis were randomly assigned to receive, in double-blind fashion, 1000 IU per day of vitamin D or placebo for 1 month. All children received emollients. The mean score on the Eczema Area and Severity Index improved to a significantly greater extent in the vitamin D group than in the placebo group (31% vs. 16%; $p = 0.04$).

Comment: In this study, vitamin D supplementation improved winter-related eczema in Mongolian children, a population likely to have vitamin D deficiency in the winter. Other research has also found that vitamin D supplementation improves eczema in people with low 25-hydroxyvitamin D levels (mean, 7.4 ng/ml; Samochocki Z et al. Vitamin D effects in atopic dermatitis. *J Am Acad Dermatol*. 2013;69:238–244). In contrast, in a double-blind study conducted among individuals with mostly normal or low-normal 25-hydroxyvitamin D levels at baseline (mean, 28.4 ng/ml), supplementation with 4000 IU per day of vitamin D for 3 weeks did not improve eczema (Hata TR et al. A randomized controlled double-blind investigation of the effects of vitamin D dietary supplementation in subjects with atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2014;28:781–789.). Possible explanations for these negative results are that vitamin D is beneficial only for people with vitamin D deficiency, or that it takes longer than 3 weeks for vitamin D supplementation to improve eczema.

Camargo CA Jr et al. Randomized trial of vitamin D supplementation for winter-related atopic dermatitis in children *J Allergy Clin Immunol* 2014,134.831–835 e1

Sunflower Oil for Eczema

Forty-eight adults (mean age, 24 years) with chronic, severe atopic dermatitis (eczema) were randomly assigned to receive, in double-blind fashion, 3 g/day of linoleic acid from 4.76 g/day of sunflower oil; 2 g/day of eicosapentaenoic acid (EPA) and 1.3 g/day of docosahexaenoic acid (DHA) from fish oil; or placebo (olive oil) for 12 weeks. Disease severity was assessed by the Rajka score, which takes into account disease extension, course of eczema, and itch intensity. The mean Rajka score improved in the sunflower oil group by 73% after 6 weeks and by 80.6% after 12 weeks. The improvement was significant compared with the changes in the fish oil and placebo groups ($p < 0.0001$ for each) and compared with baseline ($p < 0.01$).

Comment: There is evidence that patients with eczema have reduced activity of the enzyme delta-6-desaturase, which plays a role in the conversion of linoleic acid to gamma-linolenic acid (GLA). Researchers have postulated that a deficiency of GLA could play a role in the development of the skin lesions in patients with eczema. A number of studies have examined whether supplements that contain GLA (such as evening primrose oil and borage oil) are beneficial for eczema patients. Some studies have shown benefit, whereas others have not. Surprisingly, evening primrose oil was more effective than borage oil, even though the daily dose of GLA in the evening primrose oil studies was less than that in the borage oil studies.

These studies do not provide strong evidence that reduced activity of delta-6-desaturase is a major contributing factor to the skin lesions in patients with eczema. Another defect in fatty acid metabolism in these patients is an impaired capacity to incorporate linoleic acid into cell membranes. Perhaps this impairment is of greater importance than the reduced activity of delta-6-desaturase. Supplying additional linoleic acid might (by mass action) overcome the impaired uptake by cell membranes, potentially ameliorating the skin lesions. Both evening primrose oil and sunflower oil contain about 70% linoleic acid, whereas the linoleic acid content of borage oil is much lower.

Gimenez-Arnau A et al. Effects of linoleic acid supplements on atopic dermatitis. *Adv Exp Med Biol* 1997;433.285–289

Oral Niacinamide Prevents Nonmelanoma Skin Cancer

Three hundred eighty-six Australian individuals (mean age, 66 years) with at least 2 nonmelanoma skin cancers in the previous 5 years (mean, 8; range, 2–61) and a mean of 47 actinic keratoses at baseline (range, 0–214) were randomly assigned to receive, in double-blind fashion, 500 mg of niacinamide orally twice a day or placebo for 12 months. Participants were evaluated by dermatologists at 3-month intervals for 18 months. At 12 months, the mean number of new nonmelanoma skin cancers (basal cell and squamous cell carcinomas) was significantly lower by 23% in the niacinamide group than in the placebo group (1.8 vs. 2.4; $p = 0.02$). The number of prevalent actinic keratoses was 11% lower in the niacinamide group than in the placebo group at 3 months ($p = 0.01$), 14% lower at 6 months ($p < 0.001$), 20% lower at 9 months ($p < 0.001$), and 13% lower at 12 months ($p = 0.001$). During the 6 months after the treatment was discontinued, the mean number of new nonmelanoma skin cancers was 0.8 in each group, indicating that the benefits of niacinamide did not persist after the treatment was discontinued. No noteworthy safety issues occurred with niacinamide.

Comment: Basal cell and squamous cell carcinomas are among the most common types of cancer. Photoimmunosuppression (suppression of immune function by sunlight) plays a key role in the transformation of actinic keratoses into skin cancers. Niacinamide has been shown to prevent photoimmunosuppression in humans and photocarcinogenesis in mice. In the present study, oral administration of niacinamide decreased the number of actinic keratoses and decreased the number of new basal cell and squamous cell carcinomas in people with a history of these skin cancers. Although there have been occasional reports of hepatotoxicity from large doses of niacinamide (3000 mg per day or more), doses such as 500 mg 3 or 4 times per day are usually well tolerated and rarely cause elevations of liver enzymes.

Chen AC et al A phase 3 randomized trial of nicotinamide for skin-cancer chemoprevention. *N Engl J Med* 2015,373·1618–1626.

Omega-3 Fatty Acids for Dry Eyes

A meta-analysis was conducted on 7 randomized controlled trials (including a total of 790 patients) that examined the effect of omega-3 fatty acids in the treatment of dry eye syndrome. A meta-analysis of the 5 studies that reported data in mean values revealed that the tear breakup time increased significantly by 1.58 seconds ($p = 0.007$). This increase signifies that the tears became less susceptible to evaporating. Omega-3 fatty acids also significantly improved the results of Schirmer's test, an indicator of the rate of tear production ($p = 0.001$). In the three trials that reported the Ocular Surface Disease Index, there was a nonsignificant improvement with omega-3 fatty acids, compared with control ($p = 0.09$).

Comment: The results of this meta-analysis suggest that omega-3 fatty acids are beneficial in the treatment of dry eye syndrome. In most of the individual clinical trials, the beneficial effect could be described as moderate. Most of the studies used fish oil or the omega-3 fatty acids present in fish oil, in dosages equivalent to 2 g per day or more of fish oil, for treatment periods of 1 to 6 months. One study used flaxseed oil, but it is not clear whether flaxseed oil is as effective as fish oil. Omega-3 fatty acids may work by an anti-inflammatory mechanism.

Liu A, Ji J Omega-3 essential fatty acids therapy for dry eye syndrome a meta-analysis of randomized controlled studies *Med Sci Monit*. 2014,20 1583–1589

Human Milk for Diaper Rash

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

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

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

Lutein and Zeaxanthin May Help Prevent Cataracts

Some 4203 individuals (mean age, 73 years) participating in the Age-Related Eye Disease Study 2 (AREDS2), who were at risk of progression to advanced age-related macular

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degeneration (because of the presence of bilateral large drusen or large drusen in 1 eye and advanced macular degeneration in the other eye), were randomly assigned to receive, in double-blind fashion, daily supplementation with lutein (10 mg) plus zeaxanthin (2 mg), omega-3 fatty acids (650 mg of EPA and 350 mg of DHA), both treatments, or placebo. During a median follow-up period of 4.7 years, the risk of progression to cataract surgery was nonsignificantly lower by 4% in the lutein/zeaxanthin group than in the no lutein/zeaxanthin group. When the analysis was restricted to participants in the lowest quintile of dietary lutein/zeaxanthin intake, lutein/zeaxanthin supplementation significantly decreased the risk of progression to cataract surgery by 32% ($p = 0.03$). Omega-3 fatty acids had no effect on the need for cataract surgery.

Comment: Observational studies and clinical trials suggest that lutein (and possibly the related carotenoid zeaxanthin) can prevent the development and slow the progression of age-related macular degeneration. In the present study, lutein/zeaxanthin supplementation also showed potential for slowing the progression of cataracts in the subset of participants who had low dietary intake of these carotenoids. Although the mechanism of action is not certain, lutein and zeaxanthin might help prevent cataract progression by decreasing photooxidation of lens proteins. Good food sources of lutein and/or zeaxanthin include spinach, kale, other dark green leafy vegetables, egg yolks, corn, grapes, oranges, squash, and zucchini.

Chew EY et al Lutein/zeaxanthin for the treatment of age-related cataract AREDS2 randomized trial report no 4 *JAMA Ophthalmol.* 2013,131:843–850

Curcumin for Radiation Dermatitis

Thirty women (mean age, 58 years) with non-inflammatory breast cancer or carcinoma in situ who were undergoing radiation therapy without concurrent chemotherapy were randomly assigned to receive, in double-blind fashion, curcumin (2 g 3 times per day) or placebo during the course of radiation therapy. Radiation dermatitis was assessed by the Radiation Dermatitis Severity (RDS) score, a 4-point scale, with 0 indicating no dermatitis and 4 indicating severe dermatitis. At the end of the treatment period, the mean RDS score was significantly lower in the curcumin group than in the placebo group (2.6 vs. 3.4; $p < 0.01$).

Comment: Radiation dermatitis occurs in approximately 95% of patients receiving radiation therapy for breast cancer. Curcumin is a compound present in turmeric that has anti-inflammatory activity, and may also have anticancer effects. The results of the present study indicate that oral administration of curcumin can decrease the severity of radiation-induced dermatitis in women with breast cancer.

Ryan JL et al. Curcumin for radiation dermatitis a randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients *Radiat Res* 2013,180.34–43.

Nightshade-Free Diet for Itchy Scars

Chronic pruritus occurs in most scars that form after serious burns, and in some surgical scars and keloids. Some patients have observed that intake of certain foods exacerbates their postburn pruritus. Based on patients' reports, the authors of this study advised a woman who had had postburn pruritus for 6 months to avoid nightshade foods (i.e., potato, tomato, eggplant, and peppers). The pruritus disappeared completely within 1 week, and the woman remained symptom free except on 1 occasion when she ingested tomato soup. Subsequently, the authors recommended a 1-week trial of a nightshade-free diet to 15 patients with pruritus of postburn scars ($n = 7$), surgical scars ($n = 6$), or keloids ($n = 2$) that had been refractory to antihistamine treatment. Three patients did not follow the recommendation and experienced no improvement. Among the 6 patients with postburn scars who followed the recommendation, 4 experienced 100% relief and the other 2 experienced 80% to 90% relief. Among the 5 patients with surgical scars who followed the recommendation, 3 experienced 100% relief, 1 experienced 50% relief, and 1 had no improvement. The 1 patient with keloids who followed the recommendation reported 95% improvement.

Comment: Nightshades contain solanine alkaloids, which have been found anecdotally to be a triggering factor for joint pain in some people with osteoarthritis, as well as a cause of various other symptoms in susceptible individuals. The mechanism by which these alkaloids might cause pruritus in scars is not known.

Alonso PE et al Solanaceae-free diet for scar pruritus *Burns* 2013,39:534–535.

Topical Silymarin Cream for Melasma

Ninety-six patients (aged 28–55 years) with melasma (disease duration, 2–6 years) were randomly assigned to apply, in double-blind fashion, silymarin cream (7 mg or 14 mg of silymarin per ml) or placebo cream to the affected areas twice a day for 4 weeks. Eighty-three percent of the patients were female; pregnant and nursing women were excluded. The patients were advised to avoid sun exposure and to use topical sunscreen. Significant improvement in the Melasma Area and Severity Index score was seen after 1 week in both active-treatment groups. The lesions cleared completely in all patients after 4 weeks of treatment with low-dose silymarin and after 3 weeks of treatment with high-dose silymarin. No significant changes were seen in the placebo group. No side effects were observed.

Comment: Melasma is a brown hyperpigmentation that occurs on the face and other sun-exposed areas. Silymarin was investigated as a potential treatment for melasma, because it has been shown to prevent melanin production. Other treatments that have been shown to be effective for melasma include topical vitamin C, topical niacinamide, and topical azelaic acid.

Altaei T The treatment of melasma by silymarin cream. *BMC Dermatol.* 2012,12 18.

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Optimizing Metabolism

by Ingrid Kohlstadt MD, MPH
www.INGRIDients.com

The Proof and the Pudding: Using What We Know About the Human Microbiome

April welcomes Earth Day, when scintillating research findings inspire us to save the Earth one ecosystem at a time. This column takes a broad approach to saving our most intimate ecosystem – the microbiome.

All fields of science are turning up evidence that the human microbiome sways human health in complex and profound ways. For example, this edition of *Townsend Letter* covers the health topics of seasonal allergy disorders, skin disease, and eye health, and published research supports the assertion that all of these medical conditions are entwined with the health of the microbiome.

Microbiome research is causing us to rethink long-held scientific assumptions about the origins of disease. Even so, most published papers draw that well-known conclusion, "More research is needed." I want to start seeing an equally valid conclusion. "More implications for medical and public health practice are needed." The evidence about the microbiome is so compelling that we need to use it.

If you know the expression "The proof is in the pudding," you catch my sentiment. The expression dates back to Medieval England. I imagine that it started when an argument arose among the royal court when they were boasting about the upcoming holiday festivities. Tired of the banter, one noble lord insisted: "Enough talk about the holiday plum pudding, my lady. When I can taste it, I'll believe how good it is." Then the court jester stepped in to smooth tensions, "Ah, indeed. The proof is in the pudding."

So how do we get to "pudding" prevention into practice?

What Does Proof Look Like for Biologic Systems?

For one, you can't hammer a chiffon pie into the wall. We shouldn't delay a decision for a patient or public health, in order to await hard-and-fast evidence. Rather we should use the best evidence we've got at the time, even if it wiggles like gelled pudding.

Our present medical model tends to compare all clinical evidence to randomized double-blind, placebo-controlled trials. That may be appropriate for clinical drug research; however, living ecosystems are not studied the same way as a chemical compound. It's not that the epidemiologic output from microbiome research is stronger or weaker, just that it's

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different. What's important from a prevention perspective is how accurately the data correlate with patient symptoms. From that vantage point, the research findings on the microbiome are compelling.

Why Would Something Taste Good If It's Bad for You?

Like pudding, prevention is a matter of taste. And asking patients about their taste perceptions often provides clinically useful clues about their metabolism. For example, rather than telling patients to eat less sugar, health-care providers facilitate their patients' health more effectively by exploring with them the cause of unrelenting carbohydrate cravings. Often a microbiome out of balance is a sort of medical smoking gun.

How Do We Improve Uptake of Foods That Nourish the Microbiome?

You can make holiday plum pudding with prunes, but don't ever call them that. To illustrate my assertion, let me share some intriguing statistics from a youth nutrition program that I developed. Only a few children who liked raisins ever tried dried grapes, and prunes usually get half as many "likes" as dried plums. From a public health perspective, we could do a lot more to market these foods. Some of them need a complete makeover.

Microbiome research is a neon highlighter. It makes the importance of the dietary *F*s – Fiber, Fermented foods, and Phytonutrients too visible to overlook. It's also proven that there's no such thing as a "smart cookie." Sugar, fake sugars, and synthetic trans fats are food for microbial sluggards.

Based on the microbiome research, we shouldn't assume that the live active cultures in cultured dairy products are indeed "pro"biotics; that is, beneficial to our health. Milk is the growth medium for the bacteria that digest the milk and turn it into yogurt. If the growth medium contains 0% fat, high-intensity sweeteners, added sugar, or all of the above, how do I know that the beneficial microbes will be the ones that grow?

The Microbiome's Relevance to Food Safety

Plum pudding used to be more popular for holiday parties than it is now. For public health departments around the country, that's a relief, because improperly prepared pudding frequently leads to foodborne illness.

I write this in fond memory of Dr. Leon Gordis (1934–2015), longtime chair of epidemiology at Johns Hopkins University. Imagine an 8 a.m. lecture that filled the hall by 7:50 because so many students wanted to watch 2 × 2 epidemiologic tables spring to life.

The 2 × 2 tables are a back-of-the-napkin way to tally who of those who did or didn't eat the plum pudding got sick at the holiday party. By going through each food, one can calculate the most likely causative one. What was interesting was that not everybody who got sick ate the pudding and not everyone who ate the pudding got sick, even though the pudding was the cause. When I directed a local health department, the outbreaks that I investigated followed this pattern too, because everyone's microbiome differs. Outbreaks aren't usually a question of whether the infectious agent is present, but in what concentrations relative to the microbiomes of the people exposed.

Insights into Why Eradication Seldom Works

Unless your name is President Jimmy Carter and the organism that you want to eradicate is *Dracunculus medinensis* (Guinea worm), you may want to reconsider eradication as a medical treatment strategy. Prescribing pharmaceutical commandos to assassinate pathogens usually results in reinfection and relapse of symptoms. Microbiome research is confirming that peaceful cohabitation may be as effective, and easier to achieve especially alongside nutritional strategies.

As a medical student in 1990, I traveled to Peru and sampled holiday pudding called *mazamorra morada*, which is purple – not from plums but from purple corn. Although the pudding was exceptional, my travel was for the "proof," an introduction to the microbiome. I researched how *H. pylori* exposure during infancy might influence gastrointestinal physiology in adulthood.[1] A leader in the *H. pylori* research, Dr. Marty Blazer, commended my student paper and encouraged me not to forget the conclusions during my clinical training. "Eradication of *H. pylori* isn't the answer," he emphasized. Now 25 years later, Marty is furthering his claim with compelling evidence that the way antibiotics change the microbiome actually contributes to obesity.

How Do You Regulate Probiotics and Other Microbiome Therapies?

Most of us aren't on the edge of our seats about how the FDA is regulating probiotics. Yet it's a practical application of the microbiome research. Probiotic capsules are regulated as dietary supplements. That seems straightforward even if diet isn't the primary source of the microbiome. But if the capsules are added to boiled milk to culture yogurt, then they are regulated instead as a food ingredient. The ultimate in probiotics are treatments for *C. difficile* infection, and these therapies are regulated as biologics. But when it comes to public safety and probiotics, it's the pharmaceutical regulators who are appropriately the most concerned. That's because of the potential for probiotics to create antimicrobial resistance. Based on microbiome research, more attention is being given to reusable medical devices and how they are sterilized between patients.

Conclusion

Microbiome research is providing real-time applications for medical and public health practice. These include prioritizing what is important on food labels, personalizing medical treatments to include gut health, and responding to the findings with public health foresight. Another important conclusion is that a thank-you is in order – happy Earth Day to the health professionals and clinical researchers who are caring for the planet one ecosystem at a time!

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Faculty Associate, Johns Hopkins Bloomberg School of Public Health
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Editor, *Advancing Medicine with Food and Nutrients* (CRC Press; 2013)

Notes

1 Kohlstadt I, Antunez de Mayolo A, Gastrointestinal Physiology Working Group, Ramirez-Icaza C Parietal cell antibodies among Peruvians with gastric pathology *Scand J Gastroenterol.* 1993

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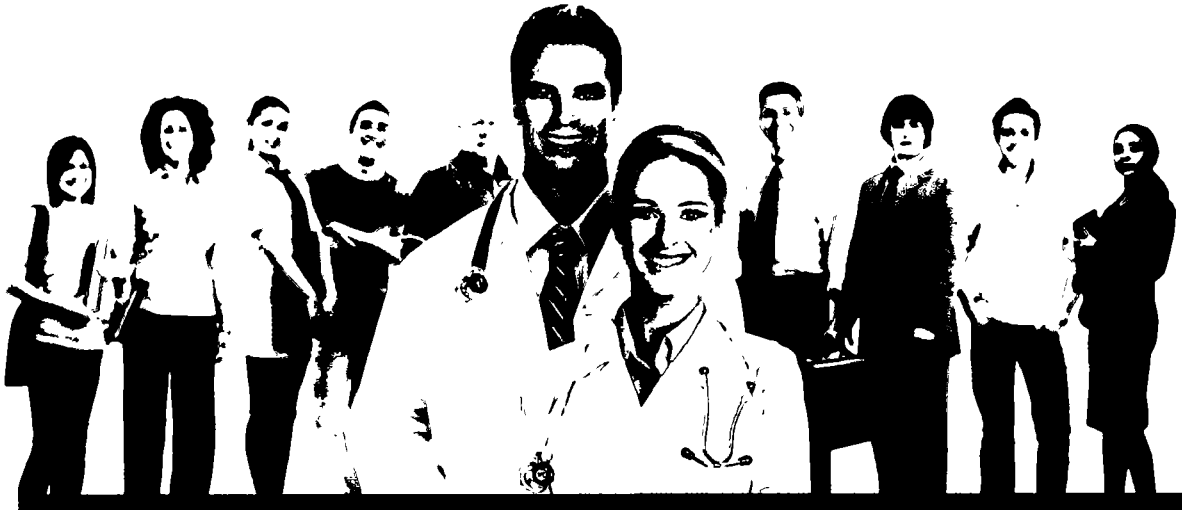

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Allergy and Immunotherapy

by Diego Saporta, MD, FAAOA

Introduction

The word *allergy*, derived from two Greek words, *allos* (different) and *ergos* (mechanism), was coined by von Pirquet (circa 1905) to describe a state of altered reactivity.[1] This concept remained in use until IgE was discovered by Johansson and associates in Sweden and finally characterized by Ishizaka and associates in the US.[2] After IgE's discovery, allergy was considered a phenomenon related to the presence of IgE. Early on it was observed that IgE was elevated in patients with asthma.[3] With the introduction of in vitro technology, the idea that IgE caused the allergic reaction was strengthened and led to the notion that a skin test only diagnosed IgE-related phenomena, even though the hypersensitivity reactions described by Gell and Coombs involved four different types of immunological reactions.[4–6]

The allergic reaction affects the whole body. Nasal allergies, allergic conjunctivitis, asthma, dermatitis (eczema or urticaria), some cases of migraine, and others are different manifestations of the allergic condition.

Allergy Management

The management of allergic conditions is based on the use of environmental modification maneuvers, use of medications, or administration of immunotherapy.

Environmental modifications: They are important, as allergen avoidance will obviously decrease or even eliminate the symptoms, but they will not alter the potential for reactivity of the immunological system.

Medical management: prevents the bioactive chemicals generated during the allergic reaction from activating the receptors of the effector cells. When effective, the symptoms will not be produced but the allergic reaction will continue unimpaired.

Immunotherapy: modifies the dysfunctional immunological system, shifting it from a Th2 weighted system into a Th1 nonreactive system, leading into symptom resolution.[7]

Diet modifications, vitamins, supplements, and optimization of hormonal levels can strengthen the altered immunological system, but immunotherapy is the only treatment that elicits a long-standing improvement of the altered immunological system.[8]

Immunotherapy

Immunotherapy consists in the repeated administration of small but increasing amounts of the allergen(s) responsible for symptom production, leading into a change in reactivity of the immunological system.[7] The responsible allergens are diagnosed with an allergy test. If immunotherapy is successful, the patient will stop reacting to those allergens.

Allergy Tests

Charles Blackley described the first allergy test. He applied a drop of pollen over abraded skin. The resultant wheal and flare led him to conclude that exposure to pollen elicited hay fever. Skin tests eventually developed into three different modalities:

Scratch test: A drop of allergen is applied to the skin. A lancet is used to excoriate the skin through the drop of allergen. Reactive cases are called positive; nonreactive, negative. This type of test was found to be unreliable. In 1987 the AMA advised not to use this test anymore.[10]

Prick test: A drop of allergen is applied to the skin and an instrument is used to prick the skin without piercing it. Initially this was done with a needle; therefore, it required a certain amount of dexterity to avoid injuring the skin. At the present time this test can be done with the Morrow Brown needle (single prick device) or with a device that holds several prongs called the multiprick device, which has the advantage of allowing several allergens to be tested at the same time. Application takes seconds and requires minimal training.

Intradermal test: A small amount of allergen is injected into the dermis which is heavily populated with mast cells.[11] This explains why this test potentially can elicit severe reactions. The diameter of the skin wheal is measured immediately, and 10 to 20 minutes after the injection. A growth in wheal diameter implies that the test is positive.

Allergy tests can also be run in a sample of the patient's blood (without risk to the patient). In vitro technology became commercially available in 1967.[4] Specific immunoglobulins (sIg) that bind to an antigen are measured. Measurement depends on using a "labeled" anti-sIg antibody. The

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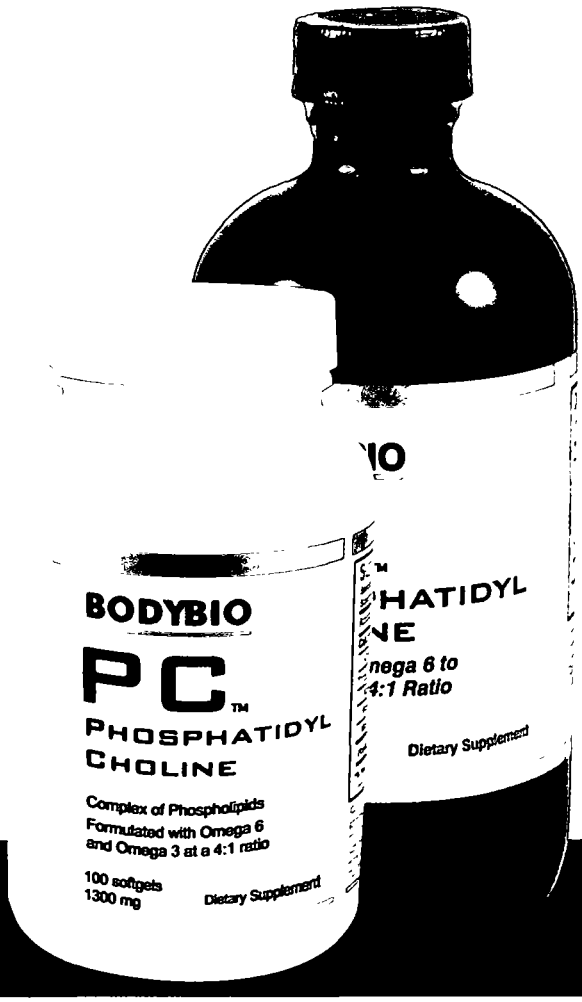

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prototype of in vitro testing is the radioallergosorbent test (RAST), which uses radioactive anti-sIg antibodies.[4] Modern "RAST-like" tests use nonradioactive technologies.

Is There a Better Test?

There is a long-standing controversy as to which test is better. The skin prick test (SPT) is the most commonly used allergy test. Guidelines advise that negative SPTs are followed by an intradermal test.[12] According to the same guidelines, intradermal tests are more sensitive and permit identification of a larger number of clinically reactive patients, especially those with lower skin test sensitivity (i.e., a higher-potency concentration of the allergen is required to elicit a skin response), and they are also useful in evaluating skin sensitivity to low-potency allergenic extracts (i.e., diluted allergen which implies that there is a state of higher skin reactivity). SPTs are sensitive enough to detect clinically relevant IgE antibodies when potent extracts, such as grass and cat, are used. Other allergens may require intradermal tests for diagnosis.[13]

The problem with intradermal tests is the potential danger of a severe reaction.[14,15] This would be an exceptional occurrence with SPTs. While the reason for this difference is not clearly explained in the literature, it is likely related to the mast cells being present mainly in the dermis, but rarely in the epidermis.[11] The intradermal tests place the allergen immediately next to the mast cells, but the SPT does not penetrate the skin; therefore, the allergen will not easily interact with the mast cells.

There are 2 types of intradermal tests:

Intradermal test with one single dilution: Usually a 1:1000 weight/volume dilution of the allergen is injected, and if reactive, the result is considered positive.[12]

Intradermal Dilutional Test (IDT): Serial dilutions of the same allergen are injected, starting with a weak dilution (weaker than 1/1000 wt/vol), and advancing to more concentrated allergen (potentially to 1:100 wt/vol) until either one of the dilutions react (positive result) or none react (negative result).[10] Because the IDT starts by injecting a dilution that has been clinically established over many years to be safe, advancing to stronger concentrations only if there is no reaction to the previous injection, the test is inherently safe and the possibility of a severe reaction during testing is small.[10,16]

If the diagnostic power of the SPT is compared with the IDT, it appears that the SPT will only diagnose cases of high reactivity. These cases would elicit a reaction on an IDT with very diluted allergen (1:12,500 wt/vol to 1:312,000 wt/vol).[12,17]

There are also problems with the RAST-like tests. It is a common observation that their results do not match the clinical diagnosis. For example, a patient clinically reactive to cat may show a negative RAST test. Because of the assumption that allergy is exclusively related to the presence of IgE, a negative RAST result is often interpreted as "patient has no allergies."[18] The activating mechanism via IgE requires that an allergen bridges two IgE molecules in the surface of the mast cell, but IgG-allergen immune complexes can also activate mast cells.[11,20] A negative RAST test simply means that the specific immunoglobulin being measured for that allergen (usually IgE) is not present. In support of this statement, in vitro tests simultaneously measuring different immunoglobulins give results more consistent with the clinical presentation and more in agreement with the IDT.[21]

Over the years, the author has observed that RAST tests fail to match the clinical presentation and that SPT usually diagnoses only a few of the allergens to which the patient reacts but the IDT can identify the majority. The clinical implications of this observation become clear when patients with persistent symptoms while on immunotherapy based on SPT and/or single dilution intradermal tests come for consultation, and improve when additional allergens diagnosed by IDT are added to the treatment vaccine.

Administration of Immunotherapy

Immunotherapy is the administration of increasing quantities of the allergens to which the patient is reactive, producing immune tolerance and improving allergic symptoms. The involved mechanisms are complex, including inducing a shift from the Th2 proallergic system toward a Th1 nonreactive system, with an increase in T-regulatory cells, which through IL-10 secretion inhibit IgE production, increase IgG_4 and promote suppression of T-effector cell function.[22,23]

Immunotherapy can be administered as injections (subcutaneous injection immunotherapy; SCIT) or orally (sublingual immunotherapy; SLIT). The key to a successful treatment is based on the ability to diagnose the majority of the allergens responsible for patients' symptoms and mix them into a vaccine to be administered at short intervals with increasing dosages. When an aggressive dose advancement is pursued (beyond the symptom-relief dose), and a maintenance dose is administered for a total time of 3 to 5 years, long-term effects will be observed upon discontinuation.[24] The author has observed that longer treatments (5–6 years) give more consistent long-term effects after discontinuation.

There are two different therapeutic approaches: either the patient is treated with only a few clinically relevant allergens, or all the reactive allergens are included in the treatment vaccine.[12,25] By utilizing all positive allergens, the treatment results are better as more of the patient's allergic load is treated. The type of test utilized for diagnosis plays a role in this difference, as the SPT or even the intradermal test with a single

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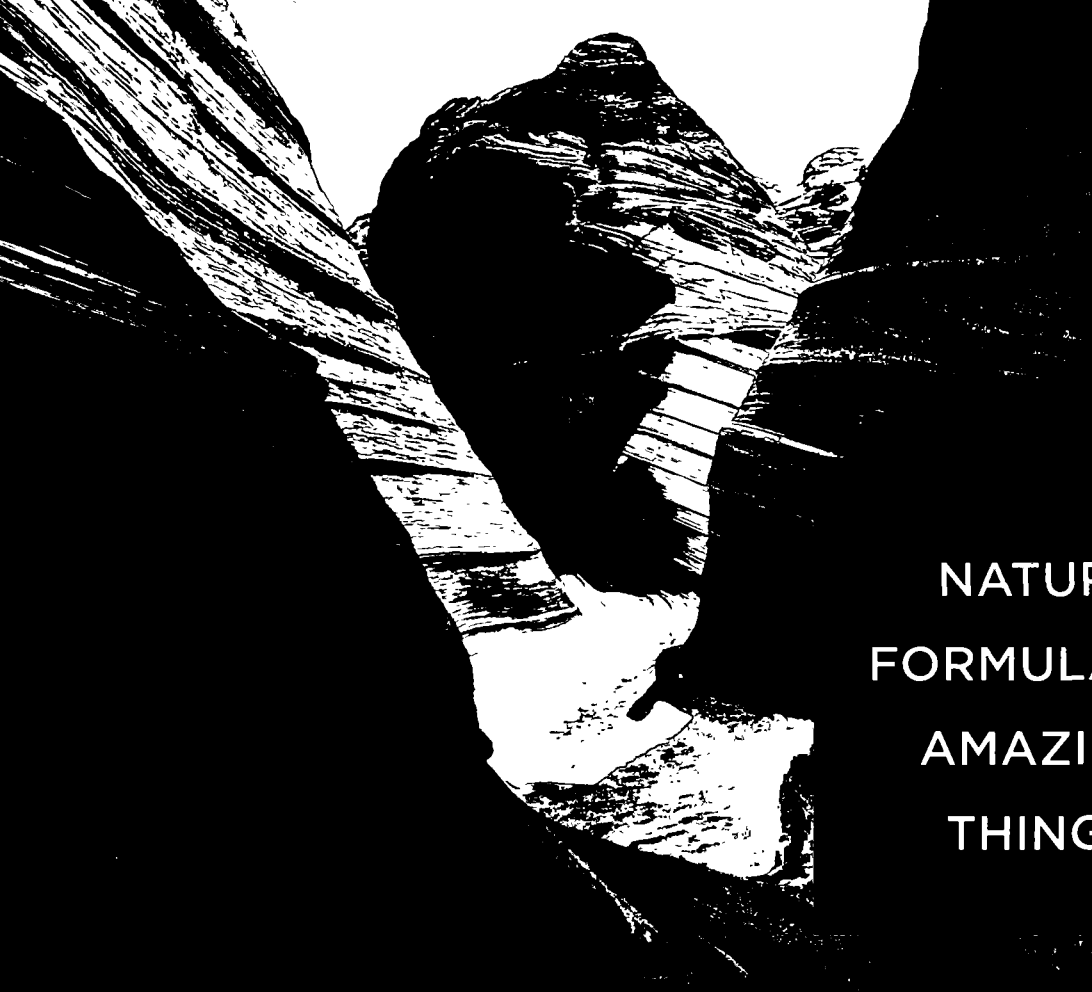

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dilution will not be able to diagnose all the allergens to which the patient is reactive.

A patient whose skin reacts only to more highly concentrated (potent) allergens will be misdiagnosed as "negative" unless an IDT is used. While the significance of allergens diagnosed with potent (concentrated) doses is controversial, when these results are taken into consideration there is a significant clinical improvement.[26] The author's personal experience is in agreement with these findings.

An important advantage of the IDT is that it establishes the strongest safe starting dose for immunotherapy; therefore clinical improvement occurs from the beginning of treatment and the risk for a reaction is minimized.[27]

SCIT

The injectable route requires weekly injections. This treatment modality has risks, as any injection can elicit a reaction, potentially severe, including anaphylaxis and death.[14,15] Some practitioners do not advance beyond the symptom-relief dose. While this is safe, the patient will not attain long-term relief.[24]

For safety reasons, it is recommended that SCIT be administered at the doctor's office exclusively. Patients should wait 20 to 30 minutes following intradermal tests or injections and an adrenaline autoinjector should be prescribed, as the risk for a reaction persists up to 24 hours after the injection.[13,25]

SLIT

The sublingual (oral) route has unique advantages: It is efficacious, safe, and easy to administer. There are no efficacy differences between SCIT and SLIT, but SLIT is inherently much safer. SLIT is ideal for the management of the young and/or asthmatic patient.[28–33] Given its great safety, the patient does not need to come to the office, making it an ideal "home-based therapy." There are a few reports of severe reactions after SLIT administration.[34–37] These patients were predominantly asthmatics treated with a rush advancement protocol. The author successfully uses a SLIT protocol with daily drop-administration that never elicited a severe reaction.[38,39] Problems with this technique do not occur often, probably because the dose is advanced very slowly and it is reduced if symptom provocation occurs.[39]

There are multiple protocols for SLIT administration. It is now advised that drops be administered daily.[40] SLIT is widely used and accepted in Europe.[41,42] In the US, SLIT is not FDA approved. Insurance companies do not reimburse for it. Yet SLIT should be considered an important tool for the management of the young child with allergies, more so if asthmatic.[28,31–33,44] SLIT is safe during pregnancy, even for treatment initiation.[45]

A variation of SLIT is the use of allergy tablets (AT) introduced by pharmaceutical companies that have recently been approved by the FDA.[46–48] These tablets deliver a few allergens only at one constant concentration, which is a flaw in treatment effectiveness.[49] The prescribing information includes a boxed warning to inform that severe allergic reactions may occur, and the label insert advises carrying an adrenaline injector.[50]

Low-Dose Allergen Immunotherapy (LDA)

This treatment modality, while being effective, does not conform to "usual" immunotherapy. With LDA, allergens are diluted to the order of 10^{-6} to 10^{-17}. A major controversy about this treatment is a lack of understanding about its mechanisms. An attempt to get approved by the FDA failed.[51] LDA efficacy information is mostly anecdotal. It uses proprietary information in its formulation, and there is only one source for the treatment sets.[52] LDA reportedly uses all allergens present in the environment as well as foods. Immediately before administration these allergens are mixed with the enzyme beta-glucuronidase.

Knowledge of LDA stems mainly from observations of Dr. Leonard McEwen, a British allergist who realized that beta-glucuronidase had antiallergenic properties. The treatment was popularized in the US by Dr. Welman Shrader.[51] The most remarkable fact about LDA is that it works. LDA is administered initially once every 2 months. It takes usually 12 to 18 months to attain a 2-month improvement, at which time the interval between administrations is increased. Eventually the patient can be managed with treatments once a year or longer.[51]

LDA advantages:

Administration is based on a clinical diagnosis of the allergic condition. An allergy test is not necessary because:

a. All allergens are covered; therefore there is no need to diagnose which are the responsible allergens.
b. The administered dose is so diluted that it will never give a reaction as can happen with SCIT; therefore the concept of "safe dose to start immunotherapy" does not apply.

The cost of this treatment decreases over time, since the number of administrations diminishes as the patient improves.

LDA administration treats hypersensitivity to not only inhalant allergens but also foods. The prevalence of food reactivities is on the rise worldwide. The patient with allergies commonly reacts to one or more foods. There are no FDA-approved therapies for food allergy.[53] The standard of care consists of allergen avoidance and, if needed, prompt treatment of allergic reactions after accidental ingestion. Oral and sublingual food immunotherapy are being evaluated, and reports are optimistic.[53,54] LDA offers another option for the management of food allergies and reactivities.

Anecdotal information suggests that LDA is effective.[51] In a study comparing results of patients treated with LDA or with standard immunotherapy, no statistical differences between the

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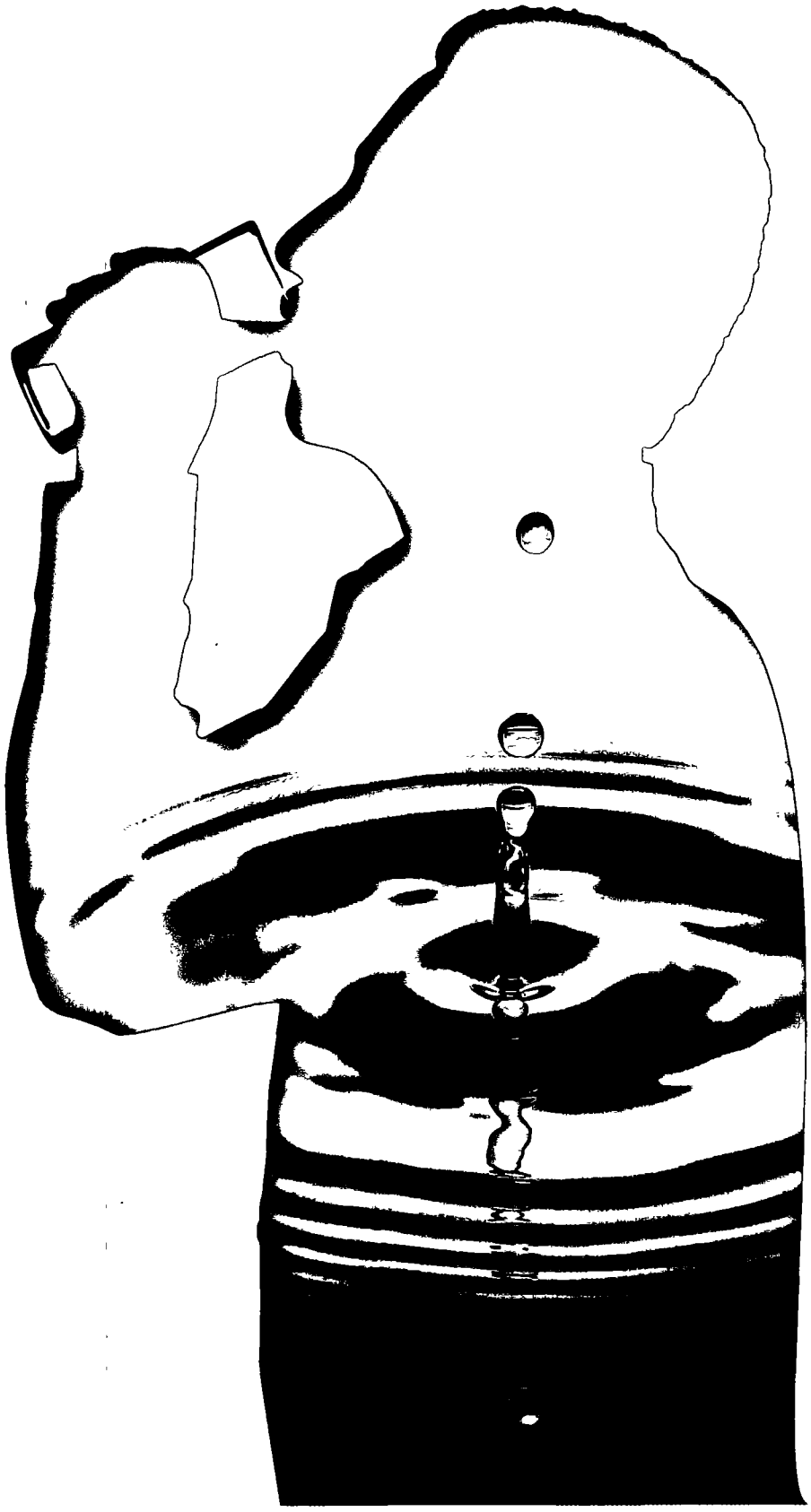

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groups were found, but the LDA group included patients who failed standard immunotherapy.[55] If these patients had continued with usual immunotherapy rather than switching to LDA, it could be assumed that the results in the LDA group would have been better than with the standard immunotherapy group.

Lastly, LDA offers the possibility of managing other conditions, including chemical sensitivity or autoimmune conditions.[51]

Summary

Highlights on diagnosis and management of allergies were presented. Immunotherapy is an excellent treatment modality able to induce a change in the dysfunctional immunological system, leading to a cure or at least long-lasting control of the allergic conditions. Different methods of administration have been succinctly described. The value of a safer approach such as SLIT has been underlined. SLIT can be considered for patients with asthma and sometimes in cases where SCIT is considered dangerous or its administration elicited problems. The potential role of LDA for the management of the allergic patient has also been stressed.

Practitioners interested in the management of allergic conditions should consider attending courses offered by mainstream academies (AAOA, AAAI) as well as smaller medical societies such as the Pan American Allergy Society and the American Academy of Environmental Medicine where management of inhalant and food-related allergic conditions, LDA, and other treatment modalities can be learned.

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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.

Fungus Allergy and Hypersensitivity in Mold-Related Illness

by Alan B. McDaniel, MD

Introduction

Some molds release toxins, as certain snakes are poisonous. These mold toxins are diverse[1,2]: They can activate or impair our innate immune system, may provoke disabling chronic inflammation, cause many hormonal disturbances, and more – even promote cancer.[3–8] This is quite distinct from the hay fever-allergic reaction that molds can produce.[9–11] There is a third way that fungi (mold, yeast, etc.) can make us sick. This is generally neglected because of scientific orthodoxy and institutional dogma.

Fungus Hypersensitivity Can Create Inflammation that Mimics Infection

Case 1: Doc's oldest son got fungal ringworm (tinea corporis).[12] Doc prescribed *Lotrimin* cream (clotrimazole 1%), applied 4 times daily by the boy's mother, a nurse. It was no better after 10 days and the boy was taken to a dermatologist, Dr. W. When he prescribed Lotrisone cream (clotrimazole and betamethasone dipropionate, 1%/0.05%), Doc protested: This was the same antifungal that already had failed *and* it had steroids, which promote fungus growth. Dr. W winked and said: "Try it!"

In three days, the ringworm was gone. Allergy skin tests confirmed that No.1 Son reacted to *Trichophyton*, not immediately but quite strongly 24 and 48 hours after the test was placed. The *Trichophyton* causing No.1's ringworm had been arrested by the antifungal in Lotrimin, but the fungal remains in his skin provoked immune inflammation – until that was quenched by the steroid in Lotrisone.

Inflammation from Fungal Hypersensitivity Responds to Immunotherapy

Case 2: Both of M. B.'s ear canals started itching and progressed to became painful and swollen for years. A sensible ENT surgeon had *performed* a right mastoidectomy but found no disease. On Doc's examination, both ears were red and chronically thickened with "peau d'orange," and neither canal could admit even a newborn speculum. She had skin tests for allergy and days later had big reactions to *Aspergillus, Candida*, and *Staph* phage lysate – normal flora of the external canals.[13–15]

Desensitization shots were started and she was put on a "candida program."[16,17] Several months later, Doc operated on her worst ear, removing a mass of scar tissue that obstructed the ear canal and placing "pinch" skin grafts. Six months later, the operation planned for her other ear was unnecessary: Both ears had returned to normal appearance and function.

To understand what happened to these people, we must examine the immune system.

The Role of the Immune System

The immune system has one great task: It protects us from dangerous invaders. These microterrorists include parasites, bacteria, viruses, toxins (such as tetanus and *Stachybotrys*), and cancer cells.[18]

To master this task, the immune system must first discriminate between the many, many things that make up our own body (properly called "self") and the vast amount of everything else that is not our body (called "non-self"). Certainly, the immune system should not attack "self"!

Secondly, it must sort through that vast array of *non*-self and differentiate between the harmless and the dangerous. It must leave "harmless" things alone and save its killing energy to attack and destroy the "dangerous" foreign matter. All things considered, that is an awesome task. To achieve it, the immune system has two main divisions.

Immunity 101: The Innate ('Nonspecific') Immune System

First, some immune protection is programmed right into our DNA. Virtually all living things, even plants and quite primitive creatures, are genetically – innately – directed to defend themselves by attacking a variety of biochemical molecules.[19]

In humans, this innate immune system has developed several "operational arms." First, white blood cells (WBCs) called macrophages – literally *big eaters* – using primitive amoebic action engulf annoying foreign material and "process" it chemically. This material is importantly used to direct acquired immunity.

Second, these white cells also release a variety of chemicals, by which the innate immune system recruits more WBCs (think "pus") and promotes inflammation, which *should* be defensive and "direct" wound healing, if not in excess or prolonged.[20]

Finally, a sequence of proteins collectively called the complement cascade is considered part of the innate immune system. When triggered by various immune responses – and by

toxins – these proteins activate each other in a chain reaction that amplifies the power of the immune response.[21]

Immunity 102: The Acquired (Adaptive) Immune System

We higher vertebrates are also equipped with more versatile defenses, the acquired immune system (also called adaptive). It fields a team of "programmable" WBCs, including T and B lymphocytes. These cells are at first called "naïve," and indeed they are harmless as puppies – but they won't stay that way. Here's how immune cells learn "what to attack":

These naïve cells become educated by hooking up with "big eaters" of the innate system.[22] From them, they receive their load of ingested foreign material. Having been processed by the macrophages, this is now unmistakably labeled as "bad." The T and B cells are thus galvanized to attack the foreign material – and so the immune response is acquired. It is also enduring.[23] These educated immune cells alter their DNA, passing sensitization to all their descendants – creating clones of protective cells.[24]

On receiving this molecular mug shot, T lymphocytes are programmed to fasten onto and destroy anything carrying that particular foreign "label." They become killer cells – certainly no longer naïve.[25]

B lymphocytes, having received the same information and similarly primed, begin to make protein antibodies called immunoglobulins (especially IgG, -M and -E).[26] These molecular equivalents of Predator drones are released into the blood and specifically target the foreign material presented by the macrophages. Some reactions provoke little incident, but others produce very much inflammation indeed.

Both T- and B-cell activity lead to the release of chemicals that promote inflammation and recruit many other cells to the sites of conflict.[27,28] Both these effects amplify the innate system and trigger the complement cascade. Please note that ultimately, the innate and acquired immune systems *both* stimulate the same final consequences. This is a key point.

Immunity 201: Immune Protection

Many of a pregnant woman's immunoglobulins-G cross the placenta to her child. Thus, babies at birth are endowed with a good measure of immune protection, received "passively" from mother.[29] This is temporary, lasting 12 months or more (hence, babies of HIV-positive women are tested for antibodies only after age 18 months).[30] So, the baby's *acquired* immune system quickly gets busy learning its "craft," a lifelong process.

History, 1796: Smallpox killed 1 of 5 people who contracted it, but survivors never got it again; their acquired immune system had become educated to kill the virus on sight and prevent a recurrence. When Dr. Edward Jenner noted that the mild infection called cowpox rendered milkmaids immune to smallpox, he *inoculated* his patients with cowpox. They were then protected from smallpox.[31] From this concept, he is popularly credited with saving more lives than anyone else in the history of the world.[32]

Vaccinations educate our immune systems. They present harmless proteins that will stimulate an immune response protecting us from dangerous ones. When the immune system attacks dangerous "invaders," it keeps us healthy. This is beneficial immunity.

Immunity 103: Unwanted Immunity

History, 1819: Tom was a gentleman farmer. Every year, he'd get sick when the harvest was brought in: Watery eyes, running nose, sneezing, and fullness and itching in his throat. He thought it was a cold, noting that the farm workers had it too – but it happened every year. In London, he saw Dr. John Bostock, who diagnosed "hay fever."[33]

When the immune system is confused between harmless and dangerous, it attacks harmless nonself substances. This unnecessary immunological "warfare" makes us sick. We call this illness *allergy*.

Case 3: Big Al was a surgeon with five kids and a stressed wife. He was really tired and needed to drink two pots of coffee daily to keep going. He repeatedly asked his GP to test his thyroid gland. Every time it was checked, thyroid-stimulating hormone was normal, though the level got worse and worse. The gland was failing. Fine-needle aspiration biopsy showed that Big Al had autoimmune thyroiditis (AIT), which was slowly destroying his thyroid gland.

When the immune system cannot recognize that "self" is harmless, trouble follows. It may attack some part of its own body and can destroy it, as though it were rejecting a mismatched transplanted-organ. Our thyroid gland is the most common target: 12.5% of Americans test positively for antithyroid autoantibodies, including 24% of allergic women.[34,35] We call this autoimmune disease.[36]

Graduate Immunology: Application to Patient Care

Medical science has several occupations. In the simplest form, we endeavor to:

- Observe what is happening.
- Understand what we have observed.
- Apply this knowledge to cure people or relieve their suffering.
- Improve our results by observing what is happening ... etc.

There are many types of immune reactions – as you might expect from having learned that there are two types of immune system, many types of white blood cells, and very many chemicals produced by their activities. Doctors have observed these reactions for generations. Unfortunately, they still argue about what they mean.

Case 4: When Henry's cat scratched him, his skin swelled all along the scratch.[37] The first deliberate skin test for allergy was done in 1869 by Charles Harrison Blakely, who himself had hay fever. He nicked his skin (having been unsuccessful in recruiting other volunteers), put some pollen onto the abrasion, and within 20 minutes saw his skin swell up and itch intensely around the application.[38]

Do skin tests actually identify trouble-making pollens? Yes: When pollens or other allergens identified by positive skin tests are spritzed into the person's eyes, nose, or airways,

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they provoke the person's "hay fever" symptoms and more.[39,40]

19th-Century Immunology

Case 5: Dr. Wright made a night call to a household with diphtheria. Arriving home, he stabled his horse and, to prevent contagion, changed his clothes in the barn. Before going to bed, he paused to look through the doorway at his only son, baby George. The baby sickened and died of diphtheria the following week.

Tetanus and diphtheria were dreaded killers in preantibiotic times. By the 1890s, physicians had learned how to protect people after they'd been exposed – by giving passive immunity, the kind that a baby gets from its mother. Horses were injected with the deadly toxins and those that survived became immune – with lots of protective immune globulins circulating in their blood. This immune horse serum was injected and it protected the recipient.[41,42] A century later, we have better methods, but we must honor the innovative scientists of the Gaslight Era![43]

They also knew that injections should not be contaminated with bacteria. To prove the horse serum sterile, they injected rabbits with some of each batch – and watched to see if an abscess would develop. These frugal scientists found they couldn't use the same rabbits repeatedly: Previously injected rabbits often died immediately after the shot.[44] Nicolas Arthus noted that the *surviving* rabbits developed slow-healing lumps or nasty ulcers at the test site over a few days.[45] Humans had similar problems after repeated injections of horse serum – not with the first but on *repeated* injections.[46]

20th-Century Immunology

The fledgling science of immunology couldn't explain all this, but it tried. In 1921, Otto Prausnitz and Heinz Küstner demonstrated quite clearly that the immediate hypersensitivity of severe food allergy – and of hay-fever and fatal horse serum injections – is caused by a reactive substance in the serum.[47] They called it *reagin*, but we now know it as immunoglobulin E (IgE).[48,49] The allergists of the world reportedly took heart at the demonstration of reagin in the "P-K reaction": Now their skin tests and allergy shots had a solid experimental basis, affording their treatments greater validity, if not gravitas.

What of the rabbits' ulcers, the astute critic might ask? Because they weren't fatal, they were largely ignored. Scientists later showed that these lesions were caused by rabbit immunoglobulin binding to horse proteins, causing inflammation of blood vessels – "vasculitis."[50]

Immunology Becomes Politicized

Following Prausnitz and Küstner's epochal report, leading immunologists – first in Europe and then in the US – agreed from thence forward that they would define *allergy* solely in conformity with the P-K reaction. Arthur Coca, who coined the term *atopy* and developed the solution still used to make allergy extracts, protested this decision.[51,52] He stated that many types of food reactions did not fit the P-K model (being "nonreagenic/nonatopic"), but he and his supporters were voted down.[53]

The argument was not resolved, though; it got worse. As the world's allergists embraced the creed and catechism of reagin (IgE), groups of members found (as did Coca) that it did not encompass their clinical experience. They left to form their own, less-dogmatic societies. First to go were the ear, nose, and throat specialists in 1941, then general practitioners in 1956, and finally dissenting internists and pediatricians in 1965.[54–56]

The dispute over defining *allergy* became so acrimonious that there could be no reconciliation even after 1963, when Gell and Coombs showed that there are at least 4 major types of acquired immune responses.[57] Their four "classical" pathways are:

- type 1 reactions, caused by IgE (hay fever); they occur within minutes and give us protection against parasites;
- type 2 reactions, caused when immunoglobulin types G (IgG) or M (IgM) attach themselves to a foreign protein and provoke the complement cascade; these develop over hours to a day and protect against bacteria and viruses;
- type 3 reactions (Arthus reactions), occurring when IgG binds to a dissolved foreign substance and precipitates as an irritating, inflammatory complex; they occur in hours to a day and offer protection against toxins;
- type 4 reactions, caused by sensitized T-cells; these reactions peak at 48–72 hours (e.g., Tb skin-tests) and protect against bacteria.

In the opening paragraph, it was stated: "There is a third way fungi (mold, yeast, etc.) can make us sick. This is generally neglected because of scientific orthodoxy and institutional dogma." The important fact that hay fever allergy, the IgE-mediated, type 1 pathway called "allergy" does not activate the complement cascade.[58]

Are the majority of allergists correct, those who believe that mold can stimulate the immune system only through type 1, IgE-mediated reactions? If so, Shoemaker's observations that mold activates complement must be explained only as a direct effect of mold toxins, without acquired immunity.[59]

But antigen-antibody complexes (types 2 and 3 reactions) trigger the complement cascade (and type 4 may also be involved with complement).[60] What if the *dissenting* allergists are right; what if molds do indeed stimulate these late and delayed immune reactions? That would mean that nontoxic molds can trigger complement – and that we are dealing with a broader problem than mold toxins alone. Treatments for these two conditions are very different.

Seeking the Truth

> Think for yourself and question authority.
>
> – Timothy Leary, PhD

Allergists in the US agree that type 2–4 immune reactions – call them "late and delayed" reactions (L/D) – can be clinically important, causing asthma and other stubborn problems. However, for most, orthodoxy requires them to believe that type 1 reactions must trigger significant L/D hypersensitivity.

So, when skin tests show no immediate reaction but only later develop large red bumps lasting days to weeks, these lesions are dismissed. An academy expert describes these as "a delayed, IgE dependent reaction, without sufficient IgE to result in an immediate reaction" (does this sound strained?). [61] In a personal communication, a past-president of an allergy academy said his opinion was that such mold test results are "meaningless Arthus reactions" and the patient's symptoms were called "nonallergic."

Delayed type hypersensitivity to fungi was identified and described long ago.[62] However, in keeping with the IgE-orthodoxy, delayed type reactions on skin tests were attributed to "pathogenic fungi" and the immediate type (IgE)-sensitivity was associated with *non*-pathogenic, or allergenic, fungi. In this author's experience of recording late and delayed reactions after intradermal tests, the distinction is questionable.[63,64] It is plausible that Arthus reactions are not "meaningless" – and that the type of sensitivity is what renders the fungus pathogenic, rather than the implied converse.

How would allergists learn any differently? Commonly, protocols for provocation challenges require first, determining which allergens should be tested by positive skin tests.[65] While sensible and efficient if IgE were indeed required to precede all significant hypersensitivity reactions, this protocol clearly excludes all of what Coca (in 1943) called "nonreagenic" reactions.

Fortunately, some researchers have used a different approach, challenging common allergens regardless of their skin test responses. This is far from inefficient: they've found that a significant number of allergens provoking airway reactions were negative on skin tests – up to 45% (and only 14% IgE-RAST-positive!).[66,67] Indeed, antigens can provoke late or delayed reactions with *no* preceding immediate response – the "isolated late type" in 35% and "isolated delayed type" in 10%.[68] This is "key" information: Antigens that do not provoke immediate hypersensitivity ("non-IgE") can cause clinically significant immunological reactions.

Human–Fungus Interfaces and Hypersensitivity

Before science described the fungus kingdom, humanity had given its members common names: mold,

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mildew, yeast, rusts, smuts, and blights – they are all fungi and are rather similar.[69] Fungi are always present in the human environment. They live in our homes and the great outdoors and we breathe them. They populate our food, often intentionally: With fungus, bread is raised and wine fermented.[70] Blue cheese is made with *Penicillium* and soy sauce uses *Aspergillus* (black mold!).[71,72]

Fungus also lives on and inside humans: *Aspergillus* and *Candida* normally live in the external ear canal.[73] Fungus can (and does) live in anyone's gut – the frequency and dominant species are related to diet; knowledge about these populations is advancing with new analytic methods.[74] The healthy human has up to 10,000 fungi per gram of stool; *Candida* species are most common.[75,76] Informal polling at medical meetings indicates that *Geotrichum* (Camembert cheese), *Rhodotorula*, and other fungi are also seen (less frequently) on stool cultures.[77]

Fungi Provoke the Immune System Differently than do Pollens

Why do molds and yeast occupy center stage today? Exposure leads to sensitization. To be sure, some fungi make toxins ... but they also provoke late and delayed-type hypersensitivity much more often – and more severely – than do pollens. It appears this difference is due to the types and locations of exposures and even the kinds of proteins involved.

Type 1 reactions to pollens seem related to the relatively brief seasonal exposure of large quantities of allergens that remain on the surface of our mucous membranes, where macrophages and IgE-laden mast cells "hang out." In contrast, molds and yeast are ubiquitous and perennial. Living in and on the human body, they may cross our mucosal barrier and enter our fluid compartments, where IgG and IgM rule.[78]

Fungal antigens are also biochemically different from those of pollen. All these characteristics lead molds to produce type 2–4 immune reactions. Fungi so commonly cause late and delayed reactions that *Candida* is among the antigens that doctors used to test a patient's immune competency.

Case 6: Doc's left hand developed dyshidrotic eczema when he was an undergraduate. The dermatology resident at Student Health said that it was caused by a fungus but couldn't say where the fungus was located. Other dermatologists scoffed at the fungus theory and recommended many peculiar treatments. The problem gradually disappeared after about 10 years.

That is, until 6 years later, when Doc heard Billy Crook lecture on the "yeast connection" and decided to find out what the nonabsorbed antifungal nystatin would do ... and he did! After taking 1/8 teaspoon at dinner and another at bedtime, Doc woke with his biggest-ever jock rash. Then 2 days later, he had his worst-ever outbreak of dyshidrotic eczema – on *both* hands! The derm resident had been right – and the fungus was in Doc's gut. Nystatin killed it and dead yeast proteins flooded Doc's bloodstream. Every part of his skin that had ever been sensitized to fungus reacted (it was *bad*, y'all!).

With near-preternatural timing, Doc's allergy nurse then came to him with an issue: Queen Bee wanted to take *Candida* ("yeast") off the testing menu. Every time a patient tested positive for *Candida*, they had treatment problems. They did not react to the shot right away but got big, red lumps after a day or two – which lasted a week or more. Obviously, *Candida* provoked type 2–4 reactions more strongly than it did the type 1. Doc had not known to check for L/D hypersensitivity before treating with fungus.

Diagnosing Late and Delayed-Type Hypersensitivity

When humans are tested, most doctors record only the type 1 IgE responses at 10 minutes. Years of interviewing patients has validated this statement: Most allergists truly ignore late and delayed reactions developing over the next few days, calling them "meaningless Arthus reactions." Yet, as we've seen, research shows that many provocative allergens have no immediate hypersensitivity responses.

Veterinary case: Sue loved her friend's horse Cappy. He was a big, gentle 12-year-old with impressive dressage skills and bad lungs. In fact, his asthma got so severe that his destruction was planned, to Sue's distress. Cappy's owner told Sue that she could have him – if she could help him. Sue got a trailer and drove Cappy 100 miles to the University of Pennsylvania Vet School. They promptly tested Cappy for allergies with skin tests – and measured his reactions every 6 hours for 2 days. He had terrible late and delayed reactions to molds: Can we call it "sick-stall syndrome?" His stable was thoroughly cleaned, giving him astonishing relief.

Case 7: Dr. G.'s patient had chronic sinus infections, asthma, and occasional eczema. Her symptoms worsened in cool, wet weather; in musty places; and just before a rainfall. He tested her for allergy to mold using blood tests measuring both IgE and IgG. All 14 of her *IgE* tests were *negative*; 12 of 14 *IgG* tests were *positive* – several exceeding the upper limit of reporting.

Integrated Approach to Treatment

Along with "usual" efforts to improve your patient's health with nutritional, endocrine, psychosocial, and other support, *avoidance* is the most obvious first step in dealing with immunological hypersensitivity to harmless substances. Common recommendations are to keep the cat out, don't drink milk if it makes mucus, and put allergen-proof covers on your mattress and pillows if you react to dust. But what about the ubiquitous fungi? Home remediation improves the parameters of environmental tests, but the hypersensitive patient finds that molds cannot long be avoided.[79]

Case 8: An ENT-allergist from New Mexico spoke with Doc at an allergy course. After their arrival in the Southwest, his wife *continued* to be ill with headaches and "sinus," respiratory, and skin problems. Skin tests had shown no allergies at all, and

he was baffled. Doc told him to repeat the tests and measure her reactions at 24 and 48 hours. There were lots of these reactions and he used them to formulate allergy shots for her. At the next annual meeting, he delightedly reported that his wife had improved dramatically.

Immunotherapy (IT) develops tolerance by inducing T-suppressor cells that "quench" reactions to the foreign substances to which they are directed, switching the response from one dominated by IgE to IgG.[80] If the allergic response calls out the Marines (Th2 regulatory T-cells), treatment with IT means that instead, social workers (Th1 cells) will answer the summons. Quantitative skin tests measuring immediate, late, and delayed-type reactions yield the best data to formulate effective immunotherapy.[81]

Immunotherapy, injected or sublingual, is seen to be effective treatment for hypersensitivity – both immediate and late/delayed. Environmental control works only as long as the environment is controlled – remember: sensitization is long enduring. Desensitization by shots or sublingually – and by standard or enzyme-potentiated desensitization (also called LDA and LDI) – can give lasting tolerance.[82,83]

Summary

Fungi (molds, yeasts, etc.) cause immunological inflammation three ways. They can stimulate IgE-mediated immediate hypersensitivity. They also provoke non-IgE late and delayed-type hypersensitivity. Some of them, such as *Stachybotrys,* will release toxins that directly activate the complement cascade.

Nearly every physician knows about the first of these, though tests usually show that IgE is rather insignificant. The latter is becoming more widely recognized and stimulates discussion of ingenious testing and treatment options. The second – *non*-IgE immune hypersensitivity – is the most commonly encountered but the least often recognized. Our challenge is learning how to distinguish between these problems.

Monitoring mold-sensitivity intradermal skin test responses at appropriately strong dilutions for 48 hours shows more late- and delayed-hypersensitivity responses than immediate.[63] It is no surprise to the author (himself an allergic Tulane medical graduate) that a study of post-Katrina New Orleans children found no correlation between multiprick tests for immediate, IgE-sensitivity to mold and their asthma.[84]

There is an impressive proliferation of studies validating the correlation of mold exposure and illness: A search of PubMed for "asthma mold home" yields 240 references; many are new; most validate the relationship.[85] An authoritative and objective review of medical literature shows that exposure to water-damaged buildings is harmful to health, with "sufficient evidence to convincingly associate": asthma, lower respiratory symptoms, and bronchitis; allergic rhinitis, upper respiratory symptoms and respiratory infections; and eczema.[86] These three groups are typical *not* of IgE-mediated hay fever but of *late and delayed* hypersensitivity.

Of course, patients can have several, overlapping problems. Some fungi *do* provoke immediate as well as late/delayed reactions. Surely some people poisoned with mold toxin will already be allergic to molds. There is a great need to study "mold-patients" for these and other related problems associated with an overstimulated immune system and increased cytokine production – including fibromyalgia, insulin resistance, adrenal fatigue, and autoimmune thyroiditis and "nonthyroidal illness," to name a few.

There is reason to hope that this can be accomplished. As the science of immunology becomes increasingly sophisticated, doctrines and dogma laid down in the 1920s are reappraised and revised. Ultimately, we shall embrace a more inclusive paradigm of fungus-related environmental illness. This can encompass the reports of patients suffering from such conditions, rather than invalidating their complaints and the observations of their physicians. Most importantly, it will allow these physicians to cure the patients.

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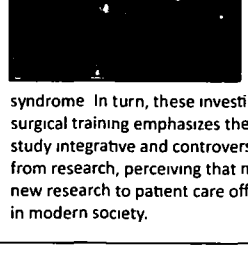

Alan McDaniel, MD, is a 1977 Tulane medical graduate. He trained in general surgery and emergency medicine before becoming board certified in otolaryngology with subspecialties in neurotology and allergy He practices privately since a two-year professorship at the University of Louisville Dr McDaniel has presented to various national meetings, including the American Neurotology Society and the American Academy of Otolaryngology – Head and Neck Surgery and to the World Congress of Otorhinolaryngology He has been a faculty member for American Academy of Otolaryngic Allergy Basic and Advanced Courses His two-day course, New Endocrinology, has been presented annually at the American Academy of Environmental Medicine since 2005, to physicians from five continents. Work with dizziness and allergy in the 1980s led him to seek solutions for chronic fatigue syndrome In turn, these investigations extended to the endocrine aspects of this and related conditions Since basic surgical training emphasizes the need to know several alternative approaches to an operation, it was logical for him to study integrative and controversial medical methods He has endeavored to understand these in the light of new facts from research, perceiving that medical history shows innovation begins as a minority opinion. He is excited that applying new research to patient care offers solutions to many of the chronic and worsening problems that are epidemic in modern society.

Prenatal Fluoride and Autism

by John D. MacArthur

> It is apparent that fluorides have the ability to interfere with the functions of the brain and the body by direct and indirect means.
>
> – National Research Council (2006)

Increasing evidence reveals that prenatal exposures to some widely used chemicals are implicated in the growing pandemic of developmental neurotoxicity.[1,2] Fluoride is the most controversial of these chemicals, because it is the only one intentionally added to the drinking water of more than 200 million men, women, and children in the US.

Topical fluoride in toothpaste has been used since the 1950s to reduce tooth decay. A primary mechanism of fluoride's ability to prevent dental caries is its strong antimicrobial effects. It is well established that fluoride can inhibit the growth of bacteria, says Robert Breaker, PhD, a National Academy of Sciences award-winning molecular biologist. He admits, however, "There has been little understanding of its precise effects on cells."[3]

Fluoride Weakens Bacterial Adhesion Forces

In 2013, a key antimicrobial mechanism of fluoride was identified by researchers in experimental physics at Saarland University in Germany. Using artificial tooth surfaces (hydroxyapatite pellets), they tested fluoride's effect on the adhesion forces of cariogenic bacteria (*Streptococcus mutans* and *Streptococcus oralis*) and a nonpathogenic bacterium (*Staphylococcus carnosus*).

After they were exposed to fluoride, atomic force microscopy revealed that all three bacteria species exhibited lower adhesion forces. Because fluoride makes bacteria less able to stick to teeth, decay-causing microorganisms are more easily washed away by saliva or brushing. The researchers said, "Fluoride appears to weaken bacterial adhesion forces in general."[4,5]

This raises the question, how do weakened bacterial adhesion forces affect the developing gastrointestinal tract, whose vast and complex ecosystem – collectively called the gut microbiota or microbiome – plays an essential role in neurological and immunological development and health?

Adhesion Forces and Bacterial Colonization of the GI Tract

The process of surface adhesion is a survival strategy employed by virtually all bacteria and refined over millions of years.[6] Adhesion of bacteria to intestinal mucosa is often recognized as a prerequisite for microbial colonization of the human gastrointestinal (GI) tract.[7] Emerging research shows that this colonization begins in the womb.[8,9]

Distinct microbial populations have recently been discovered at maternal sites that were previously thought to be sterile, including the amniotic cavity and meconium (first feces of a newborn infant). Our understanding of the impact of fetal microbial contact on health outcomes is still rudimentary.[10]

Of the many potential sources for a prenatal microbiome, amniotic fluid flora accounted for greater relative abundance of bacteria found in meconium than either the oral or vaginal cavities of pregnant women.[11,12] When pregnant women consumed specific probiotics, microbial DNA in their amniotic fluid was associated with changes in gene expression in the fetal intestine.[13]

Fluoridated Amniotic Fluid

Amniotic fluid is arguably our most precious bodily fluid. Early in the second trimester, a fetus begins swallowing amniotic fluid, which passes through its digestive system and kidneys, is excreted as urine, then swallowed again – recycling the full volume of amniotic fluid every few hours. By the time the child is born, they will consume up to 15 ounces of amniotic fluid per day.

Fetal swallowing contributes importantly to gastrointestinal development as a result of the large volume of ingested fluid. Nutrients, hormones, and growth factors in amniotic fluid bathing the fetal intestine during the third trimester are needed to produce a profound maturational effect on the intestine's ability to appropriately respond to colonizing bacteria.[14]

Fluoride concentrations in human amniotic fluid are about 50% of maternal serum levels and are considerably higher at term than earlier in pregnancy.[15,16] Women who consumed 1.25 mg of fluoride per day had a significantly higher fluoride concentration in their amniotic fluid than women who consumed 0.25 to 1.0 mg per day.[17] Note: the US Institute of Medicine says that the recommended "adequate intake" level of fluoride for pregnant women is 3 mg per day.[18]

Ron et al. (1986) found that the fluoride concentration in women's amniotic fluid was 0.017 mg/l, when their drinking water contained <0.5 mg/l of fluoride.[16] A similar fluoride concentration is secreted by salivary glands into the ductal saliva of children who drink fluoridated water.[19] This very low level of fluoride provides the "systemic" benefit, the primary rationale for swallowing fluoride in water.

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Fluoride and Autism

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A low concentration of fluoride – continually swallowed and recycled in amniotic fluid – must also be bioactive in the fetal GI tract. In fact, a primary reason why pregnant women are encouraged to consume fluoridated water is to help "delay colonization of the infant oral cavity by cariogenic bacteria."[20]

Gut Bacteria and Autism

Antimicrobials, including low-dose antimicrobials in food and water supplies, indiscriminately affect all members of the gut microbial ecosystem, especially decreasing the levels of beneficial bifidobacteria and increasing the levels of potentially harmful clostridia, as seen in the microbiota of autistic children.[21,22]

Autism is closely associated with a distinct gut microflora that can be characterized by reduced richness and diversity as well as by altered composition and structure of the microbial community; specifically, lower levels of important groups of carbohydrate-degrading or fermenting microbes.[22–26]

In a rodent model for autism spectrum disorder, autismlike behavior is associated with altered microbial colonization and activity.[27] These mice have abnormally low levels of *Bacteroides fragilis*, a bacterium that modulates levels of several metabolites and is one of the earliest-colonizing and most abundant microbes in a healthy human intestinal tract.[28] Feeding *B. fragilis* to these mice ameliorates defects in communicative, repetitive, and anxietylike behaviors.[29]

Gut Bacteria, Immune System, Autism, and Fluoride

Increasing evidence indicates that gut microbiota also influences the immune systems and vice versa.[30] The GI tract has 70% to 80% of the body's immune cells and is the primary site of interaction between the immune system and microorganisms, both symbiotic and pathogenic.[31] Proper microbial colonization and composition of the GI tract are essential for the maturation of the immune system.[8,21,32,33] Different bacteria have clearly defined adherence sites and immunological effects.[34]

Immune system dysregulation in autism spectrum disorders has been reported in several studies.[35]

During colonization of the gut with *B. fragilis*, the cellular and physical maturation of the developing immune system is directed by a bacterial polysaccharide.[28] Ochoa-Repáraz et al. (2010) found that a polysaccharide of *B. fragilis* can protect against central nervous system demyelinating disease.[36] Human and animal studies implicate impairments of myelination in autism spectrum disorder.[37,38]

Sodium fluoride has been shown to reduce bacterial polysaccharide production by inhibiting bacterial attachment.[39]

A mechanism of action for fluoride's ability to reduce bacterial adhesion forces is its inhibitory effect on the activity of glucan-binding proteins.[40] In the GI tract, glucans represent a significant potential in the suppression or treatment of several gastrointestinal problems.[41]

Adhesion Molecules, Autism, and Fluoride

In its comprehensive 2006 report *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*, the US National Research Council concluded, "It is apparent that fluorides have the ability to interfere with the functions of the brain and the body by direct and indirect means."[42]

Fluoride's indirect effects on neurodevelopment via the fetal microbiome have yet to be researched. There is, however, growing evidence of fluoride's direct effects on the fetal brain, which is exposed to the fluoride circulating in maternal blood.[43]

Autism involves early brain overgrowth and dysfunction, an excess of neurons in the prefrontal cortex caused by a prenatal disruption of developing brain architecture as early as the second trimester.[44] Research by Lahiri et al. (2013) suggests that brain enlargement in autism is likely due to cell adhesion dysfunction.[45]

Neural cell adhesion molecules (NCAM) are widely expressed in the nervous system, where they are involved in axon growth and guidance – fundamental processes that underlie formation of the synaptic connections and myelinated nerve structure crucial to brain development.

Significantly lower serum levels of several types of adhesion molecules, including NCAM, have been found in persons with autism.[46,47] Neural pathways involving synaptic cell adhesion are disrupted in some people with autism, including alterations in the structure and expression of NCAM.[48,49]

Fluoride exposure has been shown to cause a dose-dependent decrease in NCAM expression levels in rat hippocampal neurons. In particular, the NCAM-140 protein expression level was significantly lower in response to the lowest dose of fluoride used.[50,51] NCAM-140 is found in migrating growth cones that are crucial to the formation of synaptic connections.[52]

Fluoride Adversely Affects Synaptic Development

Diseases such as autism and Alzheimer's are increasingly linked to defects in the organization and number of synapses, the tens of trillions of tiny yet complex structures that link neurons so they can communicate with each other. A molecule that helps create and maintain the scaffolding around which a synapse is built is postsynaptic density protein-95 (PSD-95). Neuronal synapses with less PSD-95 are likely to be weakened or lost.[53]

PSD-95 is a membrane-associated kinase concentrated at glutamatergic synapses. It regulates adhesion and enhances maturation of the presynaptic terminal. Research demonstrates that PSD-95 orchestrates synaptic development and plays an important role in synapse stabilization and plasticity.[54]

In rats that drank water with added fluoride for several months, the fluidity of brain synaptic membranes and the expression level of PSD-95 decreased in a dose-dependent manner.[55,56]

Rats anesthetized for 4 hours with 2.5% sevoflurane, a fluoride-based

anesthetic, showed long-term deficits in hippocampal function and decreased hippocampal PSD-95 expression. Seven weeks after exposure, they had significant spatial learning and memory impairment.[54]

In humans, exposure to 2.4% sevoflurane significantly increases serum fluoride levels.[57] (Sevoflurane is the most prevalent volatile anesthetic in pediatric anesthesia.)

US Fetuses Overdosed with 'Developmental Neurotoxicant'

In 2009, researchers at the EPA's Neurotoxicology Division found "substantial evidence" that fluoride is "toxic to the developing mammalian nervous system."[58] Pregnant women already minimize or avoid other "developmental neurotoxicants" in the same category with fluoride: ethanol (alcohol), nicotine, diazepam (Valium), caffeine, lead, arsenic, amphetamine. They're also advised to avoid tetracycline, even though the EPA has only "minimal evidence" of its developmental neurotoxicity.

Fluoridation promoters say not to worry because "dose makes the poison, and the recommended level of fluoride in US drinking water is only 0.7 mg/l" (a concentration, not a dose). When it comes to neurodevelopment, however, a toxic substance's capacity to disrupt the developing brain does not simply depend upon dose. It also depends upon the "duration of exposure, and most important, on the timing during the developmental process," says the National Scientific Council on the Developing Child.[59]

In 1997, the Institute of Medicine (IOM) established 0.7 mg of fluoride per day as a tolerable upper intake level (UL) for infants 0 to 6 months old (based on US research from the 1930s and 1940s).[60] A UL is the maximum level of total chronic daily intake that is unlikely to pose risks of adverse effects to the most sensitive members of the healthy population.[61] A fetal UL was not determined but would be significantly lower, because in the unborn fetus, "sensitivity increases due to active placental transfer, accumulation of certain nutrients in the amniotic fluid, rapid development of the brain."[62]

Fetal blood levels of fluoride can vary widely, but they average about two-thirds of maternal levels. Therefore, when a pregnant woman consumes 3 mg of fluoride, her fetus is exposed to the equivalent of consuming about 2 mg of fluoride – an amount nearly three times the tolerable upper intake level of a 6-month-old infant.

"As intake increases above the UL," the IOM says "the risk of adverse effects increases."[63] Again, fluoridation promoters say not to worry, because the only adverse developmental effect from a chronic intake of fluoride above its UL is dental fluorosis, a cosmetic not a health issue. "Because the cosmetic effects of the milder forms of enamel fluorosis are not readily apparent," the IOM selected moderate enamel fluorosis as the critical adverse effect for infants and children.[64]

The IOM did not consider adverse neurological effects, only dental fluorosis. There is, however, a connection between tooth development and brain development.

Developmental Defects Increase with Fluoride Levels in Drinking Water

All enamel defects are indications of severe stress, because they result from systemic cellular disruption during prenatal and early postnatal life that can affect other ectodermally derived structures, including the brain. Chronologically distributed enamel defects are a valuable aid in neurologic diagnosis, since they occur commonly in brain-damaged children. Developmental enamel defects in primary teeth have been found at least twice as frequently in children with mental retardation as in control children.[65,66]

Some enamel defects are essentially birth defects resulting from a pregnant woman's consumption of fluoride. Similarly, a thin upper lip and flattened philtrum (the groove in the middle of the upper lip) are birth defects resulting from consumption of alcohol during pregnancy. They certainly signify more than a cosmetic effect, as does the gray-blue line on the gums of people with lead poisoning.

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Dental studies show that the prevalence and severity of developmental defects of enamel in children increase significantly as fluoride levels in drinking water increase from less than 0.2 mg/l to more than 0.7 mg/l.[67–70] Fluoride supplements (0.25 to 0.75 mg/day) are also associated with developmental defects of enamel.[71] Note: research shows that the use of fluoride supplements (1.5 mg/day) during pregnancy doubles fetal blood concentrations of fluoride.[72]

Fluoride levels in amniotic fluid have been positively correlated in a dose-response relationship with fluoride content and pathology of fetal bones – with significantly greater fluoride levels in fetuses born to mothers with dental fluorosis.[73]

British researchers estimate the prevalence of dental fluorosis of all levels of severity to be 15% in nonfluoridated areas and 48% in fluoridated areas.[74]

Choi et al. (2015) found that developmental neurotoxicity was associated with dental fluorosis. Children with fluoride-induced mottling of their teeth – even the mildest form that appears as whitish specks on the enamel – showed lower performance on some neuropsychological tests.[75,76]

Genetic Susceptibility to Fluoride's Adverse Effects

Fluorosis severity does not depend just on the amount of fluoride that one consumes. There are individual genetic and metabolic factors involved (as there are in autism spectrum disorders). Animal studies reveal a genetic component in the pathogenesis of dental fluorosis and in bone response to fluoride exposure.[77] In humans, severity of dental fluorosis varies individually at the same level of intake.[72]

Genetic sensitivity to fluoride's adverse neurological effects was confirmed by Zhang et al. (2015), who found that children with a variation of the COMT gene, which is associated with cognitive performance, had steeper cognitive decline from exposure to fluoride. Also, poor IQ scores were observed in the high fluoride exposure group (1.4 mg/l) compared with controls (0.63 mg/l).[78] Note: for generations, the recommended fluoride level in US public drinking water was allowed to range up to 1.7 mg/l.

SSRIs and Autism

In genetically susceptible individuals, autism may result from maternal exposure of a fetus to minute concentrations of pharmaceuticals, such as Prozac, a selective serotonin reuptake inhibitor (SSRI).[79] Because serotonin is critical to fetal brain development, concerns have arisen regarding prenatal exposure to SSRIs that manipulate serotonin levels [80] Serotonin elevation in the blood is one of the better-documented and consistent findings in autism and is probably gastrointestinal in origin[81] Note: 95% of the serotonin in the body is located in the gut.

Research shows that prenatal exposure to SSRIs is associated with an increased risk of autism.[82] A major study published in December 2015 looked at outcomes of 145,456 pregnancies over 12 years. The University of Montreal researchers found that taking SSRIs during the second or third trimester of pregnancy more than doubled the risk of the child's being diagnosed with autism by age 7.[83]

Two of the most commonly prescribed SSRIs, Prozac (fluoxetine) and Paxil, contain fluorinated compounds. According to Gary M. Whitford, PhD, DMD, an expert on fluoride metabolism, a 20 mg dose of fluoxetine can provide up to 3.3 mg of fluoride, "depending on how much fluoride ion is released during the drug's metabolism."[84] Note: Whitford was a key member of the Institute of Medicine panel that determined dietary reference intakes for fluoride.

Preeclampsia, Autism, and Fluoride

Taking SSRIs during pregnancy is also associated with preeclampsia, the dangerous pregnancy complication with immediate and lifelong consequences for mother and child. In a study involving 5731 pregnant women, the incidence of preeclampsia was 15.2% among those who continued SSRIs beyond the first trimester, compared with 2.4% among nonusers.[85]

Preeclampsia also increases the risk of having a child with autism spectrum disorder, and risk increases with greater preeclampsia severity.[86,87] Preeclampsia has the same key subcellular mechanism of pathogenesis as dental and skeletal fluorosis, endoplasmic reticulum (ER) stress. In fluorosis, fluoride causes the ER stress. In preeclampsia, the cause is still unknown (as discussed by the author).[88]

Fujita et al. found that autism spectrum disorder is related to ER stress induced by mutations in the genes encoding synaptic cell adhesion molecules, and that PSD-95 is involved.[89,90] As discussed above, fluoride decreases the expression level of PSD-95 in the brain.

Fluoride, Premature Birth, and Autism

Substantial laboratory and clinical evidence suggests that maternal fluoride consumption is a risk factor for premature birth, a leading cause of long-term neurological disabilities in children (as discussed by the author).[91] Premature birth is also significantly associated with autism. Large-scale population-based studies show that the prevalence of autism is 2 to 4 times higher in preterm children than in children born at full term.[92,93]

The preterm gut experiences abnormal bacterial colonization with a decreased rate of diversification and altered microbiome composition. It also has an increased number of pathogenic bacteria.[12] Placentas collected after preterm births have significantly lower levels of bacteria that act a bit like natural versions of medications used to stop preterm contractions.[94]

A December 2015 review concluded, "The maternal oral, vaginal, and gut microbiome influence the risk of pregnancy outcomes that have profound impacts upon the health of the neonate and infant, including preterm birth, preeclampsia, gestational diabetes, and excessive gestational weight gain."[95]

Hypothyroidism, Autism, ADHD, and Fluoridated Water

Fluoride effects on thyroid function are well documented. Thyroid hormones are essential for fetal and neonatal brain development, and even slight alterations during critical periods of development can have severe consequences on the development of the child.[96] Andersen et al. (2015) observed that children born to mothers with thyroid dysfunction had an increased risk of developing autism spectrum disorders, attention deficit/hyperactivity disorders (ADHD), and psychiatric disease in adolescence and young adulthood.[97] Klein et al. (2001) found an inverse correlation between severity of women's hypothyroidism and the IQ of their children.[98]

In 2015, a major population-level study that analyzed data from 99% of England's 8020 general medical practices showed a positive association between patients diagnosed with hypothyroidism and fluoride levels in their

drinking water. High hypothyroidism prevalence was 30% more likely in practices located in areas with fluoride levels in drinking water in excess of 0.3 mg/l. Practices located in the West Midlands (a wholly fluoridated area) were nearly twice as likely to report high hypothyroidism prevalence in comparison to Greater Manchester (nonfluoridated area).[99]

The study did not include undiagnosed subclinical hypothyroidism. The National Research Council (2006) said that in pregnant women, subclinical hypothyroidism is associated with "decreased IQ of their offspring."[100]

The most common neurodevelopmental disorder of childhood is ADHD. Another large-scale population-based study published in 2015 revealed that artificial water fluoridation prevalence was significantly positively associated with ADHD prevalence in the US. After controlling for socioeconomic status, each 1% increase in artificial fluoridation prevalence in 1992 was associated with approximately 67,000 to 131,000 additional ADHD diagnoses from 2003 to 2011.[101]

More Fluoride Absorbed from Artificially Fluoridated Water

Fluoridation promoters claim that because fluoride compounds have always been naturally present in drinking water, fluoride cannot be a factor in the increasing prevalence of developmental neurotoxicity. However, they overlook the fact that the degree of absorption of any fluoride compound after ingestion is correlated with its solubility. The readily water-soluble industrial fluorides (sodium fluoride, sodium silicofluoride, fluorosilicic acid) used to artificially fluoridate drinking water are rapidly and almost completely absorbed, in contrast to low-soluble natural compounds such as calcium fluoride.[72,102]

Industrial fluorides are added to nearly three-fourths of US public water supplies; therefore substantial amounts of fluoride are also ingested from foods and beverages processed in fluoridated cities. Note: women are advised to drink more water when pregnant.

Fluoride, Copper, and Autism

Water fluoridation chemicals have been shown to increase the leaching of lead and copper from brass plumbing fixtures into tap water (as discussed by the author).[103] Copper has an antagonistic relationship with zinc. Excess copper levels and zinc deficiency are common in children diagnosed with an autism spectrum disorder.[104]

Due to the multifaceted effect of zinc on gut development, it is likely that insufficient zinc supply will affect development of the fetal GI tract, contributing to many of the reported GI problems associated with autism.[105]

Prenatal Fluoride: All Risk and No Benefit

The US Food and Drug Administration (FDA) has classified fluoride as a Pregnancy Category C drug, which "may pose risks similar to a drug in Category X."[106] The risks of a Category X drug clearly outweigh potential benefits.

What are the potential benefits of ingesting fluoride during pregnancy? For the child, none. The FDA has long prohibited claims that prenatal fluoride supplements benefit the teeth of children.[107] For the mother: "No published studies confirm the effectiveness of fluoride supplements in controlling dental caries among persons ages >16 years."[108] A 2015 Cochrane Review could not identify any evidence determining the effectiveness of water fluoridation for preventing caries in adults.[109]

Lack of Fluoride-Pregnancy Research

As the National Scientific Council on the Developing Child points out, "There is no credible way to determine a safe level of exposure to a potentially toxic substance without explicit research that differentiates its impact on adults from the greater likelihood of its adverse influences on the developing brain during pregnancy and early childhood."[59]

"Overall, the available studies of fluoride effects on human development are few and have some significant shortcomings," concluded the National Research Council in 2006. "To determine the possible adverse effects of fluoride, additional data from both the experimental and the clinical sciences are needed."[110]

A decade later, explicit research into fluoride's ability to interfere with fetal brain development has yet to be done, despite the reality that US fetuses are routinely overexposed to the developmental neurotoxicant fluoride and that autism is becoming epidemic. A PubMed title search for autism shows that 2415 scientific papers were published in 2015. For fluoride, there were 641. A title search for autism and fluoride yields zero results, ever.

In the Saarland University study discussed above, when Loskill et al. (2013) exposed artificial teeth to a solution of 1000 mg/l fluoride ion (the concentration in toothpaste) for 5 minutes, all bacteria species tested exhibited lower adhesion forces by a factor of 2. Since then, no further research into fluoride and adhesion forces has been published, even though much attention has recently been given to the gut–brain connection. It is not known how lower concentrations and longer durations of fluoride exposure affect bacterial adhesion forces and health in the developing GI tract. Note: when pregnant women used a daily mouth rinse that contained 225 mg/l of fluoride ion, colonization of their infants by cariogenic bacteria was delayed by 4 months.[111]

Pregnancy and Fluoride Do Not Mix

Fluoride's role in the growing pandemic of developmental neurotoxicity requires urgent and thorough investigation. We cannot afford further delay, because it may turn out that, as with lead and alcohol, no amount of fluoride should be considered safe during pregnancy.

The good news is that on November 19, 2015, the US National Toxicology Program announced plans to conduct new laboratory studies to evaluate the effects of fluoridated water on "developmental neurobehavioral toxicity."[112] The bad news is that this could take many years.

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Fluoride and Autism

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In the meantime, based on the government's own research and recommendations discussed in this report, women who are pregnant (or intend to be) should avoid consumption of fluoride in tap water, bottled water, and supplements – especially if they have dental fluorosis, the visible evidence of their genetic susceptibility to fluoride's toxicity. Also avoid beverages made in fluoridated cities, as well as exposure to fluoride from dental products and procedures.

When a pregnant woman consumes fluoride, so does her baby. Why take the risk? Not ingesting fluoride has no downside for the fetus; however, its consumption may increase the risk of neurological deficits.

A worthy community endeavor would be to ensure that families and health organizations are aware of this pregnancy warning for fluoride.

> For centuries, humankind considered the womb environment sacred, free of violence and trespass. In that prenatal environment, with unbelievable precision, cells replicate, move about, and form buds and limbs and brains and sensory and reproductive organs, contributing to the most miraculous phenomenon on earth. ... Unfortunately, when development is violated in the womb ... the social and economic impacts are incalculable.
>
> – Theo Colborn,
> author of *Our Stolen Future*

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John D. MacArthur's previous contributions to the *Townsend Letter* include four reports: "Too Much Copper, Too Little Zinc, and Cognitive Deterioration in Alzheimer's Disease" (with George J. Brewer, MD), and "Fluoride and Preterm Birth" (October 2013); "Overdosed: Fluoride, Copper, and Alzheimer's Disease" (November 2013); and "Placental Fluorosis: Fluoride and Preeclampsia" (May 2015).

Curmudgeon's Corner

by Jacob Schor, ND, FABNO
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Saffron Floats

One could say that great minds think alike. It might be more accurate to say that eccentric minds sometimes get lost in similar parallel universes.

My colleague Mark Davis, the naturopath of dubious fame for being the fecal transplant expert, was our houseguest for a few days last November.

Over morning coffee, we realized that both of us had been engaged in a similar experiment, mixing dried saffron filaments with honey and adding the mixture to our morning coffee. We had both independently thought that this would be a great idea. If you stir 1 gram of saffron into half a cup of honey, each teaspoon will, in theory, provide about 30 mg of saffron. One could make a cup of saffron tea by simply adding a spoon of this saffronized honey to hot water and end up with a decent dose of saffron in it. We were both past drinking saffron tea; we were stirring our saffron-laced honey into our morning coffee.

It turned out that both of us had notice the saffron studies published over the past few years. The papers that initially grabbed our attention focused on psychological effects.

Agha-Hosseini reported back in 2008 that taking 30 mg/day of saffron improved premenstrual syndrome symptoms (PMS). Improvements were seen in the Total Premenstrual Daily Symptoms and Hamilton Depression Rating Scale. It did take 3 to 4 menstrual cycles to see results, though.[1]

Four earlier human clinical trials had shown that saffron significantly relieved depression. Two of these studies, one by Akhondzadeh and a second by Noorbala, both published in 2005, used 30 mg of saffron a day in 6-week trials. Akhondzadeh compared saffron against placebo, while Noobala compared saffron effect against the fluoxetine [Prozac]. Saffron worked better against depression than the placebo and better than the Prozac.[2,3]

These researchers reported similar results in 2006 and 2007 but used stigma and flower petals rather than just the stigma. In November 2006, Moshiri reported that petals (30 mg/day) were more effective than placebo.[4] In March 2007, Akondzadeh reported that in an 8-week trial, petals (30 mg/day) were as effective as fluoxetine (10 mg/day) in treating mild to moderate depression.[5]

A review by Kazdair et al. published in September 2015 lists a range of actions:

> Saffron has been suggested to be effective in the treatment of a wide range of disorders including coronary artery diseases, hypertension, stomach disorders, dysmenorrhea and learning and memory impairments. In addition, different studies have indicated that saffron has anti-inflammatory, anti-atherosclerotic, antigenotoxic and cytotoxic activities. Antitussive effects of stigmas and petals of C. sativus and its components, safranal and crocin have also been demonstrated. The anticonvulsant and anti-Alzheimer properties of saffron extract were shown in human and animal studies. The efficacy of C. sativus in the treatment of mild to moderate depression was also reported in clinical trial. Administration of C. sativus and its constituents increased glutamate and dopamine levels in the brain in a dose-dependent manner. It also interacts with the opioid system to reduce withdrawal syndrome.[6]

Another review, published a few months earlier in July 2015, combined data from 12 earlier clinical trials "examining the effectiveness of saffron (Crocus sativus L.) on psychological and behavioral outcomes." The conclusion: "Saffron may improve the symptoms and the effects of depression, premenstrual syndrome, sexual dysfunction and infertility, and excessive snacking behaviors."[7]

The idea that saffron has value in treating depression is certainly quite old. In Greek mythology, Crocus was a mortal youth who became overly enamored with the nymph Smilax. He was left forlorn when she grew bored with him. The gods turned him into the crocus flower that we obtain saffron from. Smilax was also turned into a flower, one that we call bindweed.[8]

In yet another meta-analysis, this one from September 2014, Lopresti and Drummund combined data from six randomized placebo-controlled trials and concluded, "Saffron had large treatment effects and, when compared with antidepressant medications, had similar antidepressant efficacy. Saffron's antidepressant effects potentially are due to its serotonergic, antioxidant, anti-inflammatory, neuroendocrine and neuroprotective effects."[9]

Obviously, using whole flowers would be more cost effective than stigmata. Fukui tested an even more cost-effective idea in 2011. Study participants were asked to simply smell a tincture of saffron several times a day. The saffron was dilute enough that the participants could not detect whether they had the tincture that contained saffron or the placebo. This no-cost intervention nevertheless significantly changed cortisol and other serum markers.[10] Fukui's study encouraged Dr. Davis and me to favor saffron tea over capsules, as it might act in part via an aromatherapy effect.

Saffron's effect on cancer is of great interest. Most if not all cancer patients will experience some degree of depression, and the idea that an effective antidepressant might also provide benefits against cancer is attractive. An October 2011 study reported that a molecular constituent of saffron called crocetin "significantly enhanced the cytotoxicity induced by vincristine" against cervical, NSCLC, ovarian, and breast cancer cell lines.[11] Another October article described using saffron in a liposomal form to increase cytotoxic action against HeLa and MCF-7 cells.[12] A May 2011 paper reported that "saffron exerts a significant chemopreventive effect against liver cancer through inhibition of cell proliferation and induction of apoptosis."[13] An April 2011 paper reported that crocetin "affects the growth of cancer cells by inhibiting nucleic acid synthesis, enhancing anti-oxidative system, inducing apoptosis and hindering growth factor signaling pathways."[14] Papers from both May 2011 and 2010 suggest a potential benefit against lung cancer, the more recent telling us, "Saffron could decrease the cell viability in the malignant cells as a concentration- and time-dependent manner ... [and could] be considered as a promising chemotherapeutic agent in lung cancer treatment in future."[15] An October 2010 paper had reached a similar conclusion: "The extract exerts pro-apoptotic effects in a lung cancer-derived cell line and could be considered as a potential chemotherapeutic agent in lung cancer."[16] A January 2011 paper reported that "Crocetin inhibits invasiveness of breast cancer cells through downregulation of matrix metalloproteinases."[17] Other papers have suggested possible utility in treating pancreatic cancer and lymphoma.[18–20]

Hosseni et al. reported in September 2015 the results of their small clinical trial in which 13 patients with cancer metastasized to the liver were divided into two groups. Both groups received standard chemotherapy treatment. Patients in one group received 50 mg of saffron in a capsule twice a day during chemotherapy, while the second group received placebo. Of the 13 patients who started, only 7 finished the study. Two of the 4 patients who took saffron showed a partial and complete response. No response was seen in the placebo group. Admittedly, the sample size is too small for this study to be convincing. On the other hand, most of us would probably volunteer to get the saffron if we were offered it and not the placebo.[21]

A September 2015 article published in *Oncotarget* by Rangarajan and fellow researchers at Kansas University describes an experiment in mice which suggests that saffron extracts strikingly inhibit pancreatic cancer cell growth in both cell cultures and in mice. "The mice who were given the crocetinic acid demonstrated a 75 percent reduction in their tumor growth, while the mice in the control group, which didn't receive the crocetinic acid, actually saw a 250 percent increase in tumor growth."[22]

Saffron continues to appear quite safe to use, even in high-risk patient populations. A September 2015 paper by Mousavi et al. reported on a double-blind, placebo-controlled study performed on patients with schizophrenia. A total of 66 male patients were divided into three groups. While receiving their normal treatment, they also received a 12-week treatment with an aqueous extract of saffron (15 mg twice daily), crocin (15 mg twice daily), or placebo. Sixty-one patients completed the trial; none of them reported a serious side effect. White blood cell counts increased significantly in patients receiving saffron aqua extract, but it was within the normal range and had no clinical significance. Other hematologic components, markers of thyroid, liver, and kidney, or inflammation markers had no statistically significant difference among the groups.[23]

Recent publications suggest that saffron has benefit for a range of other conditions. Human clinical trials have been published in the last year or two, suggesting a benefit in depression, Alzheimer's disease, glaucoma, macular degeneration, and erectile dysfunction.[24–29]

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Studies on depression have advanced, moving from treating patients with mild to moderate depression in 2014 to a study on treating major depressive disorders in 2015.[30,31]

I used to tell patients interested in taking saffron that they should make a water alcohol extraction, adding half an ounce of boiling water to a gram of saffron, letting it steep for a few days and then adding an equal volume of vodka and dosing it by the drop. While that method remains sound, both Mark Davis and I apparently simultaneously tried the same experiment; we both mixed a gram of saffron into half a cup of honey. Dr. Davis isn't the only colleague who shares my interest in saffron; I've been trading abstracts and full text articles on saffron with Dr. Davis Lamson, the other "Davis" in my world.

There is something emotionally touching to find both "Davis Senior" and "Davis Junior," the former being more than twice the age of the younger, fascinated by the same herb. It brings a sensation of confluence; we have all independently adopted the same therapy at the same time into our practices. To my amusement, *Davis Lamson's method of calculating the dose* of milligrams saffron per teaspoon of honey suspension was far more complicated and involved convoluted conversions of cups to milliliters then back to teaspoons, while Mark Davis and I took the simple route of simply dividing 1000 mg/gm by 24 tsp/ half-cup honey; we all ended up with about 42 mg saffron/ tsp honey.

In the end, this honey suspension experiment did not work as well as Dr. Davis and I had hoped. Saffron is so very light; despite how viscous honey is, the saffron floats to the top of the honey. Dr. Davis has already modified his approach and meticulously hand-grinds the saffron filaments with a mortar and pestle before mixing it in. I take a simpler approach; when the saffron floats to the top, I just stir it back in. It isn't a big deal.

I find myself feeling quite pleased with this saffron business. Perhaps it is all the saffron I've consumed of late. I think it is something else. The idea that Dr. Davis, Dr. Lamson, and I have wandered along our own paths to arrive at much the same place at the same time is pleasing. It is nice to find oneself in such fine company.

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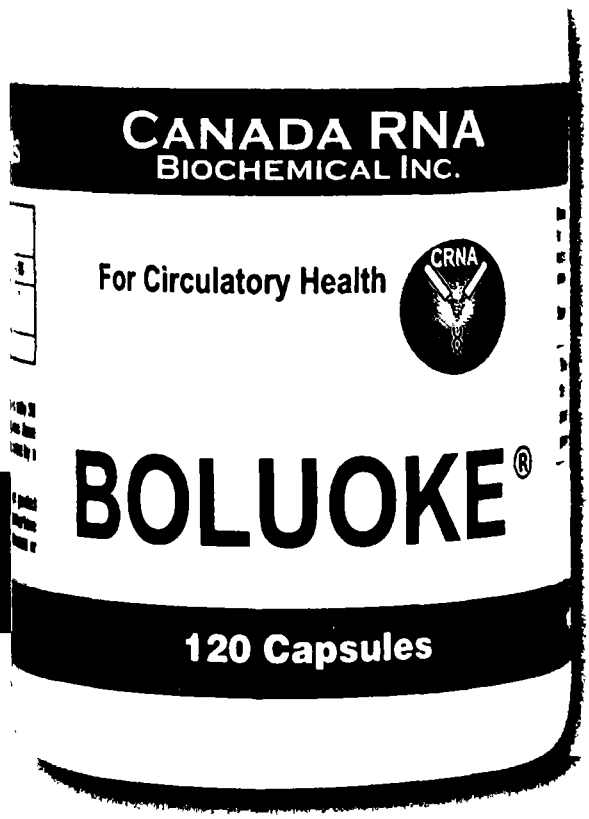

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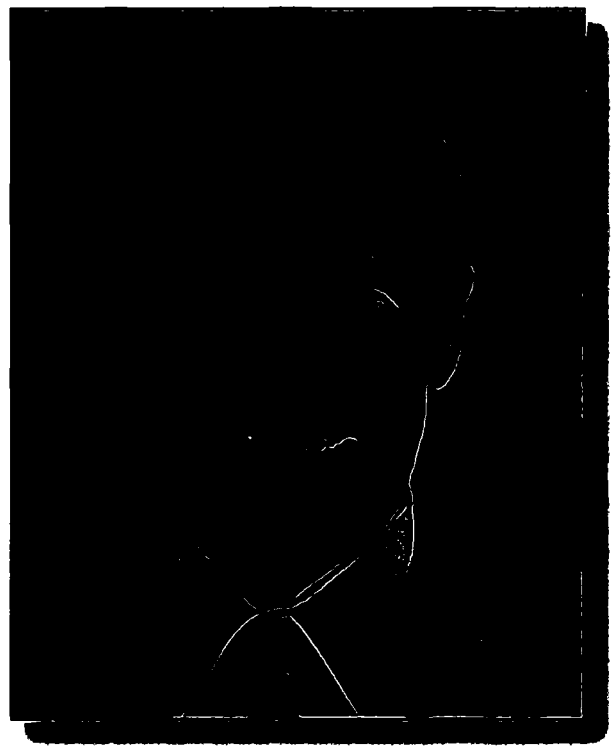

Spirit in Healing

Len Saputo, MD

with Nancy Faass, MSW, MPH

From Descartes to Quantum Physics

When Rene Descartes introduced science to the world, the scientific method quickly became the accepted way of thinking. It seemed that humanity had stumbled upon a rational, logical approach that promised to reveal the secrets of the universe. Spirituality on the other hand, was banished from the domain of science because there were no scientific tools or metrics with which it could be reduced and analyzed. Consequently, over the past 400 years scientists have simply *ignored spirituality.* With the advent of quantum physics, it appears that a deeper understanding of spirituality may be within the grasp of science.

At the time I completed my medical training, I was convinced that by dissecting matter into smaller and smaller elements, science would eventually crack the code on disease. After all, we had the electron microscope and could scrutinize matter at the level of the atom. We were reassured that it if we kept plugging along, medical science would discover the cause and cure for all diseases. It seemed to be just a matter of time.

My professors at Duke University Medical School taught us that physicians were in a high-stakes, life-and-death war against disease. Put simply, illness was the enemy and the medical profession, the savior. There was no accepted value or purpose for illness. My change in perspective occurred gradually over the next 20 years, practicing internal medicine full time, in private outpatient and inpatient medical centers. I became as comfortable in the ICU and the CCU as I was in my own office. I was adept at applying the life-saving benefits of hi-tech medicine and patient care. However, I also knew intuitively that something important was missing, an aspect of healing that went far beyond science.

Making Sense of Illness

As I became a more experienced and seasoned physician, I discovered that there were times when, despite the obvious associated physical and emotional disabilities, I could appreciate that illness was not necessarily random, nor did it only affect hapless, unlucky victims. I could see connections between symptoms and psychospiritual factors in some of my patients' stories. Was this mere coincidence?

I began to appreciate that it is sometimes possible to make sense of an illness from a perspective that science omits entirely. As I explored this with more and more of my patients, I began to see connections between their diseases and symptoms that were related to their psychological challenges. That is much of what modern psychiatry and psychology are about, so these are not new concepts in the practice of medicine. However, what I had not realized was that the "mind-body connection" was so consistently prevalent – nor did most of my professors and colleagues. As I observed and studied more deeply, it became apparent that although the mind-body connection is important, there is yet another dimension to illness that extends far beyond this perspective.

I have noted a great many instances in which my patient's illness has had a much deeper meaning than physical disability or psychological stress. This occurs so frequently that I have come to believe the spiritual dimension can play a central role in our health. When illness occurs to any of us, we must go back and learn about who we are and where our challenges lie in our lives. It is important in the process of getting well to pay attention to why illness developed in the first place. I now look for this deeper meaning whenever I am working with patients, and for that matter, in everything that happens in my own life.

Spirit Defined

While *spirit* can be defined in many ways, I believe it refers to an omnipresent, loving consciousness to which we – and everything in the cosmos – are inseparably connected. Our soul is the human counterpart of this same universal spirit that indwells within each one of us, guiding us forward and linking us back to this universal consciousness. Healing is often referred to as a return to universal "oneness." We are indeed *single* and whole human beings, and at the same time we are integral fractals of an infinite whole that we cannot fully comprehend. Any given aspect of our inner life or our exterior bodily existence can be analyzed separately from all other aspects, but we remain one unified entity. Our body is composed of trillions of cells that operate as one – and we also have an active *interior* life that evolves through levels of consciousness and more advanced stages of adult maturity as we progress toward the oneness of cosmic consciousness.

It has become apparent to me that the human body is a receptor for, and a reflection of, our spiritual health. All of our human challenges are perfectly manifested in our body as representations or extensions of spiritual dis-ease. I have repeatedly witnessed that my patients' headaches, back pain, heart conditions, and cancers, to name a few, are manifested at the physical, mental, and emotional levels by challenges originating and residing at the spiritual level. I have come to believe that these manifestations of illness are perfectly designed to simultaneously encourage and support possible next steps for spiritual growth.

Whole-Person Healing

As healers, I see our job as *curing* symptoms at the physical and emotional levels, and *healing* at the level of spirit. This is the process that many call whole-person healing. I believe that we are each here on this planet to learn certain lessons that make us more whole, and by whole I mean that as we live more in the moment, more conscious and connected with all that there is, we become more complete. If we can deal with issues that begin at the spiritual level and manifest in the body and mind and emotions, then we can address those issues at their source.

When I realized that this is how the universe works, the physically oriented "fix it" model could no longer be my primary modus operandi. Fixing symptoms is merely one merciful, but limited way of helping the sick recover from their physical disability and emotional distress. Compassion, of course, is important, but by itself is not sufficient for deep spiritual healing. The deeper, psychospiritual root causes of illness simply cannot be addressed at the biochemical or physiologic level alone, if *healing* is to be the goal. True healers understand the critical importance for patients, their families, and their doctors to go the extra mile, resolving the underlying psychospiritual roots of illness to heal at the level of the soul.

The Role of Spirit in Clinical Practice

For physicians who wish to integrate this dimension into their work, the question becomes a matter of how to incorporate spiritual awareness into clinical practice. How would they determine which patients desire or are receptive to this approach? Which interventions will be most acceptable and most effective, and what is the actual role of the clinician? An empathic response begins with our own lived experience. When we are stuck, we feel stuck – and frequently we are aware that this is occurring on multiple levels. Then we get sick, and it becomes obvious that we are stuck. How do we help people get unstuck?

- **Deep listening.** This work is all about listening and caring. First, I listen to my patients and second, I care about them. My connection with them is based on being truly present, to be in the moment, to be unassuming, to be willing to hear without judgment. I don't tell people what to do. I don't really give them advice. I am intuitively guided in this work, so my approach is to share ideas with them, and then ask them what they think. I see this work as directed by spirit, so it is a triad, a trilogy of patient, physician, and spirit.

- **Compassionate medicine**. Like all good clinical practice, the goal is to help our patients feel better by doing what we can, using the tools in our bag to help resolve their illness at the physical and emotional levels. I do that first, because that is why they have come to me, that is what they are paying for, and that is what they expect. I also feel obligated to at least offer a deeper way of looking at what has occurred from a spiritual perspective whenever possible. That may provide a glimpse of some of their deeper issues, where their spirit is damaged, and why they do not feel whole. Those conversations can begin the process of their return to wholeness.

- **Timeless resources**. There are many very different ways to deepen the journey that connects us with spirit. The secret is to be fully present with whichever approach you choose. The choice depends on what interests you, what you enjoy, and where your passion lies. For some, the greatest joy comes from simply being in nature. For others prayer, ritual, or spiritual practice is meaningful. Time spent listening to music or creating music can also have a profound spiritual dimension. We are all different, and there is no one way to connect with spirit.

I believe that our spirituality provides the mechanisms through which we can heal. There are any number of interesting and meaningful ways that people have used to enhance spiritual connection for millennia. Choose the style of connection that appeals to you, experience the process without judgment, and notice what happens with curiosity. These approaches are tools that can help us get into what is described as "the zone" in sports – a sacred space where we connect with spirit. The method we choose makes no difference.

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Communion with nature
Meditation
Community support
Intercessory Prayer
Imagery
Music and music therapy
Art and art therapy
Dance and movement
Massage, therapeutic touch, Reiki, energy medicine
Breathing exercises
Somatic Experiencing
Meditative exercise such as yoga, chi gong, tai chi
Chanting
Sweat lodge and vision quest
Laughter

Somatic Experiencing

One of the most effective strategies for personal evolution is Somatic Experiencing, a discipline that applies body work in conjunction with psychotherapy, enabling the patient to safely resolve old emotional issues. When I use this approach, we spend a substantial amount of time talking about what happened in my patient's life story that may be unresolved. At their core, most people are intact, in terms of their essence and who they are. However, frequently there is a great deal of emotional distress and suffering as a result of the way in which people were treated, and often this occurred in childhood. In many cases they were subjected to physical, sexual, or emotional abuse, frequent criticism, or neglect, and their attempts to cope often reflect the limited tools they had available at the time. When old issues are not successfully resolved, those painful memories may be pushed below the level of consciousness, but they remain in the unconscious and continue to haunt people for decades. The beauty of being able to work with someone 20, 30, 50, or 70 years later is that they usually have acquired the tools they need to resolve most of those earlier issues. Often, however, there is also a fear of the original trauma, forgotten long ago. Unconscious fears may still be pushing buttons, triggering reactivity, and distracting the patient from rational problem solving. Those old issues can be surprisingly powerful, resulting in anxiety, depression, panic attacks, or any number of other emotions, behaviors, or symptoms.

The body holds every memory that we have ever experienced, captured in patterns of muscle tension. The issues, and the memories that trigger them, can still be accessed, because they are manifested in the body at all times. Exploring those issues in adulthood with patience and compassion allows patients to reassess, to realize that they were not treated with respect. It becomes understandable that they reacted in ways that were not the most mature. Taking another look at old emotional wounds from an adult's perspective, they have clarity of vision and compassion for their former selves, "Ah, that was not me, that was not my fault. This was done *to* me. So my problem is not that I am defective as a human being. The problem is that I was treated badly, and what was done *to* me has led to my struggles." This kind of insight is at the heart of the philosophy of Somatic Experiencing.

The Human Condition

I believe that everyone has wounds. Everyone! There is no one that I have ever met who does not have wounds. This is the human condition...so few people have idyllic childhoods. The things that many people go through are truly daunting. Often parents are very young, were abused themselves, are busy with their own lives, overwhelmed by new responsibilities, and not necessarily appreciating the wonderful gift of a human life that has been entrusted to their care. They fall back on stereotypic childrearing. "Children are to be seen and not heard." "You'll never amount to anything." "Spare the rod and spoil the child." "This hurts me more than it hurts you." The pattern goes on and on, perpetuated in every generation, and the majority of people come through wounded.

That is what happens in life and what we are born into. Yet this suffering provides an opportunity for deep soul searching, to go beyond the suffering, to evolve to a better place, to a higher level of consciousness where we can achieve greater awareness and understanding to heal those wounds. This is essential because that trauma needs to be healed at the level of spirit.

Spiritual Practice

In terms of spiritual development, abundant research has shown that people with strong faith, religious belief, or consistent spiritual practice enjoy better physical, mental, and emotional health and in fact grow in their ability to self-heal. While mainstream medicine has not yet formally endorsed prayer or spirituality, increasingly, a subset of physicians is incorporating prayer into their armamentarium of tools to speed their patients' return to wellness.

One of the most compelling studies on the effects of intercessory prayer was performed at San Francisco General Hospital in 1988 by Randolph Byrd, MD. Researchers traced the progress of 393 patients in the coronary care unit, evaluated in two groups. Both groups received appropriate medical treatment, but in addition, one group received intercessory prayer. As an aspect of the double-blind design, neither the doctors nor the patients knew who was the recipient of prayer. Yet those prayed for experienced more favorable outcomes: fewer cases of cardiac arrest, less incidence of congestive heart failure, fewer cases of pneumonia, less need for additional medical procedures, and decreased use of antibiotics.

A similar study design applied to AIDS outpatients also focused on remote or distance healing. Patients who were prayed for experienced beneficial clinical progress including reductions in new complications of their AIDS, reductions in disease severity, fewer hospitalizations, and few visits from medical personnel. A third study of intercessory prayer, which focused on rheumatoid arthritis patients, found that over a 12-month period, recipients of prayer experienced reduced pain, less fatigue, improved joint function, and reduced joint swelling.

Shamanism

In the world's many wisdom traditions, spiritual guides and shamans served as healers and humanity has depended on such spiritual help for millennia. People worldwide continue to rely on prayer, worship, and meditation for healing, often guided by rituals, symbols, or scriptures. The medical profession may have forgotten the central role of these spiritual aids, which are found in all known cultures, but humanity has not, and I believe it never will. While we have no desire to return to the time before the life-saving miracles of modern medicine, often these rituals meet other human needs that are meaningful aspects of healing.

Spirituality in the Global Community

This is not where the story ends. The meaning and impact of illness extends far beyond its effects on us as individual human beings. It is also about the effects on families and communities, nations and the planet. These effects, however small, have the potential to change the whole in subtle, but meaningful ways. Everything that happens in every nanometer of space in every nanosecond affects everything else in the universe to some extent. We can look at the universe as a giant spider web. There is no separation of anything that happens in the universe (it is a "uni" or "one-verse") and everything inherently affects everything else, always. We live in a dynamic universe characterized by continuous change and constant evolution.

Advances in the integral theory of medicine have further expanded our concept of the whole, experiencing person. In addition to the interior (mind-heart-spirit) and exterior (bodily existence, including our brain and nervous system) of the individual, the physician-healer must consider the influence of both the interior and exterior of the *collective life of the society*. Our collective interior is constituted by the religious beliefs or spiritual insights that condition our individual choices; our ➤

Not long ago, I was honored to participate in an extraordinary Lakota/Sioux healing ceremony. These demanding Yuwipi ceremonies are extremely taxing to the shamans who specialize in conducting them; they willingly sacrifice some of their own life force every time the ceremony is performed. As a result, it is said that Yuwipi healers lead short, difficult lives that are consecrated to the healing needs of their communities.

This particular ceremony was conducted over a period of three days on behalf of two sick infants. One of the infants had *congenital pyloric stenosis*, a condition usually treated with surgery to widen the narrowed juncture between the stomach and the duodenum. The other infant had been born with *neutropenia*, a genetic disorder of the bone marrow characterized by a lack of production of white blood cells. This rare condition has no form of straightforward Western treatment.

The ceremony began as we entered a purification lodge. I had attended sweats before, but none anywhere near this scorching. I fell into a panic and hovered low to the ground in the thick darkness to avoid the boiling heat. My ears, nose, and face felt as though they would burst into flames, yet the sweat had only just begun. As I prepared to bolt for the door, the memory of why I was there flashed through my mind. Now the physical discomfort vanished; I dropped inward, where my only thought was to pray for the children. Two hours of darkness, timelessness, and full absorption passed. Then the doors of the lodge burst open and the trance was instantly broken. Once again, I felt that ruthless sensation of searing heat. We exited, now purified for the ceremony.

From the sweat we were led to a room where an altar was laden with sacred objects and flowers. Before it was an elder shaman who had traveled from South Dakota. He was crouching on his knees, praying at the altar. I noticed that each of his fingers was individually tied behind his back with rawhide rope. Next to him was an assistant holding a sacred pipe. Seated all around him were drummers, chanters, and people with rattles – about 20 Native Americans in all.

The lights were turned off and the pitch-black room felt eerie. Following the shaman's cues, the drummers drummed and the chanters chanted in unison, all against the backdrop of the rattles. As the energy rose, static electricity burst from the rattles around the darkened room. I once again became mesmerized, falling into trance, experiencing the sacred space, the "oneness" of the spiritual world, and prayed for the healing of the children. We followed this same approach for three successive nights. Within a few weeks, we learned that the children had fully recovered without any other form of treatment, which was confirmed by two physicians.

collective exterior is made up of the objective or external social, economic, political, and environmental systems of daily life.

All of these dimensions are crucial in the return to healing. Health practitioners of the future will view the patient through each of these lenses, providing more options for prevention, curing, and integral treatment. As we revise and update the meaning of holism, I believe that integrative medicine practitioners will look beyond physical ailments and psychological challenges to address the root causes of illness. This can be achieved by exploring the meaning of illness in the context of the patient's whole life story and how that relates to their family, their society, their culture, their environment, and the greater universe.

Closing Thoughts

Healing is a two-way street. We can *cure* illness at a physical level with supplements, drugs, and technologies, but I believe we can only truly *heal* at the spiritual level. Physical conditions are a gift from spirit to help us understand what is occurring spiritually that requires our attention. That is the beauty of illness. Although there is suffering involved, that is how we are built. Our physical, mental, emotional, and spiritual lives are ultimately an opportunity to return to wholeness.

This approach is not for everyone. If one only sees life as physicality on the material plane, then this may not make a great deal of sense. However, if someone is attuned to the spiritual dimension, then an openness to this approach provides food for thought.

Perhaps our most important and meaningful purpose on earth is to grow spiritually. We all have spiritual work to do, and we know it. Although there is a tendency to romanticize these efforts, spiritual growth is not usually easy. If we can truly understand and accept this, that may allow the inherent suffering associated with this growth to become more of an option, rather than a requirement. This makes it possible to find joy in the process of shifting our focus from our own narcissistic needs to sharing, giving, and loving unconditionally to make others happy. If the underlying energy of the universe is love, then it makes perfect sense that we are simply the consciousness of the universe reflected upon itself.

Len Saputo, MD

Len is a board-certified internist with 50 years of experience who has pioneered the development of an integrative, holistic, person-centered, preventive health care model termed "Health Medicine." He is the founder of the Health Medicine Forum, a non-profit educational foundation and of the Health Medicine Center, a clinical practice in Walnut Creek, California where this model is applied in patient care. Len is a practicing physician, motivational speaker, television and radio personality, and was formerly ranked number one in the world in men's senior tennis by the International Tennis Federation. He is the author of the Nautilus Gold Award winning book, *A Return to Healing: Radical Health Care Reform and the Future of Medicine.* Len's website, www.DoctorSaputo.com, has more than 2600 audio and video files organized to provide information at no cost on integrative approaches to more than 30 common health conditions. Len is also deeply involved in NIH-funded research at UCSF on the use of infrared light therapy to speed healing and for pain management.

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In Memory of Anne Beattie-Moss

Anne Beattie-Moss, cofounder of the Moss Reports and my business partner for almost 25 years, has passed away. Anne died on Monday, December 14, 2015, of metastatic peritoneal carcinomatosis (secondary to fallopian tube cancer). The disease was discovered in June 2015 in a very advanced stage. She underwent state-of-the-art treatment, with extensive surgery and heated chemotherapy (HIPEC), at the University of Pittsburgh Medical Center (UPMC) Shadyside. Despite this, and the heroic efforts of her doctors, her aggressive cancer recurred within a few months and proved incurable.

Luckily for us, Anne was able to meet with her closest relatives on Sunday morning, December 13, and give us some parting words of wisdom and advice. Anne has been such a huge part of my life – as best friend, business partner, daughter-in-law, adoptive mother of my grandchildren, and next-door neighbor – that we are simply devastated by this loss. But I promised Anne that I would keep the Moss Reports and cancerdecisions.com going. I will therefore continue to update our Moss Reports in the course of 2016 and continue doing phone consultations for cancer patients.

As the managing director of the Moss Reports, Anne herself helped thousands of people with cancer, whether or not they bought a report or scheduled a phone consultation. As you know, if you dealt with her, she had an incredibly upbeat and healing presence. I hope that presence will still adhere to our company, despite the tragic circumstances of her passing.

There were so many aspects to Anne's life and work.

At her memorial service, others spoke about her incredibly sweet personality and her intellectual, artistic, and spiritual qualities. But few people saw or knew the full picture of Anne as a presence in the running of the business that we founded together, Cancer Communications Inc. Anne was a very capable administrator, who kept our business (and family) alive and well for a quarter of a century. In this capacity, she counseled and consoled innumerable cancer patients. She also interacted with hundreds of medical professionals over the years and uniformly earned their respect and admiration.

No one will ever know the countless hours she spent talking to patients, who never intended to book a phone consultation. This was part of the business philosophy, but also a kind of spiritual calling.

At her death there was outpouring of grief and support from around the world. I will give a few examples:

"I wish to express my deepest sympathy at the time of the passing of Anne Beattie-Moss ... what a wonderful human being she was. Surely the world is a better place because she came this way."

– Harold Freeman, MD, Past National President
American Cancer Society, New York City

"I am very very sorry to hear this sad news. I PRAY for PEACE to her SOUL!"

– Bharat Aggerwal, PhD, Professor, M. D. Anderson Cancer Center
Houston, Texas

"I am saddened to hear of your partner's death to cancer. Your comments make me aware how important she was to you, your organization, and family and friends. A loss is always very painful and difficult. I know that you are overcome by the grieving process now and I want to extend to you my support and understanding of what you are going through."

– Jonathan Collin, MD, Port Townsend, Washington

So sorry to hear this, Ralph. My thoughts and prayers with you and your family during this difficult time."

– Wayne Jonas, MD, former director of the Office of Alternative Medicine (OAM), National Institutes of Health, President, Samueli Institute, Alexandria, Virginia

"My sincere condolences ... thank you for continuing your wonderful and amazing work in her honor. I am sure my father, if he were alive today, would also send you his heartfelt condolences and prayers."

– Phiya Kushi, son of Michio Kushi,
founder of Macrobiotics in America

"I am without words. ... If there is a meaning to all this we must not cease to find love in everything what is happening."

– Ralf Kleef, MD, Kleef Clinic, Vienna, Austria

"It is terribly sad to hear about the loss of a young life with promise and a lot more to do. ... Please accept sincere condolences and sympathies for the family and you."

– Prof. Jay Mehrishi, Cambridge, England

"The Moss Reports are a wonderful resource for cancer patients, so her life has indeed touched and helped many."

– West Lafayette, Indiana

"Our condolences on this great loss. Her work and the lives both you and she continue to touch will stand as her everlasting legacy."

– Burr Ridge, Illinois

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" ... a crushing tragedy painful for everybody, who knew her."
St. István University, Hungary

" ... a loss to all of us and to the healthcare community. We will miss her a lot!" – Columbus, Ohio

" ... She project[ed] an aura of love and service in all her communications." – Housatonic, Massachusetts

"Our deepest condolences goes out to you and your staff as well as your family." – Freeport, the Bahamas

"She for sure was an inspiration. ..." Quebec, Canada

"Many years have passed [since your visit of October 2000]. ... She talked a lot about dancing and I was absolutely fascinated by her." – Bad Mergentheim, Germany

"I'm stunned. I have tears in my eyes. Anne was so kind to my patients and really lovely. I'm sending love and prayers to you, your family and everyone who loved her." – Warren, Ohio

"My heart breaks for you and your family. The few contacts I had with Annie over the years demonstrated to me her compassion and efficiency – a rare combination."
– Cape Cod, Massachusetts

"Anne was such a great person when we were dealing with her, she was always promptly response and kind in any aspect. What a big lost in the family and business. Wish her no pain, no struggle and rest peacefully in the heaven."
– Guangzhou, People's Republic of China

"Sorry for the loss of a beloved family member and partner. I know what it means to lose a beloved one and this is why we are working so hard to ... kill cancer at an early stage of the disease." – Tel Aviv, Israel

"A great loss for everyone..." – London, England

"What tragic news. ... I send my deepest condolences and sympathy." – San Francisco, California

Thank you to all who wrote expressing sympathy and condolences. It is much appreciated in a time of need. I am sorry that I have not yet been able to write an individualized note of thanks to all those who wrote to us in this difficult and tragic moment.

Below is the obituary that appeared in the *Center Daily Times* of State College, Pennsylvania. It includes details of where to make donations in her name, should you wish.

Anne Beattie-Moss, 65, of State College, died Monday, December 14, 2015, at Mount Nittany Medical Center, State College. Born Anne Katherine Fogelsanger on April 6, 1950, in Bellefonte, she was the daughter of the late Arthur Beattie and Helen Pauline Shoemaker Fogelsanger ...

From childhood, Anne had a passion for dance, and for teaching and helping others. Her compassionate heart, joyful and adventurous spirit, and her radiant smile uplifted and inspired all who knew her, and will never be forgotten.

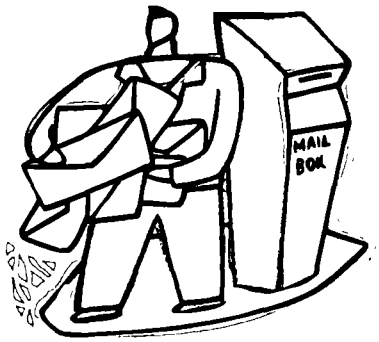
She was a 1968 graduate of State College Area High School and was Centre County's Junior Miss that same year. She also won the talent award in the statewide pageant for her dance performance and choreography.

She received a Bachelor of Fine Arts in Dance from Stephens College in 1971 where she studied with Harriette Ann Gray, a soloist with the Humphrey-Weidman Company Anne was a student of American modern dance history all her life; Doris Humphrey and Charles Weidman were her favorite choreographers, and her own dance style reflected their vibrant "fall and recovery" techniques.

While in college, Anne also attended the intensive summer dance program at the Perry-Mansfield Performing Arts School in Steamboat Springs, Colorado. She moved to New York City in the early 1970s where she performed with many modern dance companies ... before getting her Masters in Dance Education at New York University in 1977.

Anne explored her interests and helped others in many chapters of her life. She was a loving and devoted mother to her three children. She taught dance and exercise at the Borough of Manhattan Community College and elsewhere; she trained as a Lamaze Certified Childbirth Educator with the technique's founder, Elisabeth Bing; and she went on to run a successful pre-natal exercise studio in home in Park Slope, Brooklyn. She took great joy in understanding the science of anatomy, and graduated from the Swedish Institute College of Health Sciences as a certified massage therapist in 1990. For almost a decade, Anne was in private practice as a medical massage therapist with a devoted clientele. In 1991, she also started a career in the cancer field as the Managing Director for Cancer Communications, Inc., State College, and worked tirelessly to help cancer patients even when she herself was ill. ...

In lieu of flowers, the family has established an education fund for Anne's younger children for those who wish to make a memorial contribution. These may be made directly to The Beattie-Moss Children Education Fund, c/o Citizens Bank, 1248 S. Atherton St., State College, PA 16801.



Letter to the Editor

Follow-up: Potential Mechanisms of Autonomic Involvement in Subgroups of Chronic Fatigue Syndrome Patients

In November 2014, *Townsend Letter* ran my article which theorized that in a subgroup of CFS patients, autoantibodies to beta adrenergic receptors (BAR) and/or muscarinic cholinergic receptors (MCR) may play a role.[1] To paraphrase that article: viruses are thought to be capable of triggering the development of autoimmune diseases in those with a genetic predisposition. Some patients with CFS have evidence of Hashimoto's thyroiditis, autonomic dysfunction, and/or cardiac conditions in themselves and/or family members, and BAR and/or MR autoantibodies have been seen in some patients with autonomic dysfunction, cardiac conditions, and/or endocrine conditions with autonomic dysfunction.[2–4] In one orthostatic hypotension (OH) study, wherein autoantibodies to BAR and/or MR were found, researchers that also noted that 4/6 patients had other autoimmune diseases.[2–4]

In 2015, CFS researchers, in an incredibly well-designed study, found higher levels of one or more BAR and/or MR autoantibodies in 29.5% of patients with CFS.[5]

They also found that some of these autoantibodies may be more frequent in certain patients with CFS: "There was also an association between M1 and beta2 antibodies and elevated thyroid peroxidase/thyroglobulin (TPO/TG) and antinuclear antibodies."[5] After treatment, a decrease in these autoantibodies correlated with improvement of symptoms, "Elevated antibody levels were detected in pre-treatment samples against beta1, beta2, M1 and M4 receptors in a subset of patients. Remarkably, elevated antibody levels had normalized in the majority of clinical responder post-treatment," indicating that they may play a role in the illness CFS in a subset of patients.[5]

According to these authors, "Remarkably, we observed a significant correlation of levels of BAR and MCR antibodies with immunoglobulin levels, T cell activation, and elevated ANA and TPO antibodies. This fits well with findings in other autoimmune diseases. ... Although the function of these antibodies in CFS at present is unclear, the association of BAR and MR antibodies with immune activation markers and their decline in CFS patients responding to B-cell depletion may support a pathogenic role. ..."[5]

As other CFS researchers try to replicate these findings, they may potentially find the same or other BAR and/or MR autoantibodies, depending on patient selection: inclusion/exclusion criteria and the percentage of patients with an infectious trigger, autonomic dysfunction (OH or postural orthostatic tachycardia syndrome POTS), and/or other comorbid diseases. In this CFS cohort, they did use exclusionary criteria, and while 100% had postexertional malaise, only 38% had tender lymph nodes and 35% had sore throat.[5]

Meanwhile, these findings are very exciting because in some patients, CFS may turn out to be, in part, an autoimmune disease, and that could open up classification, diagnostic, and treatment options.

I wrote that *Townsend Letter* 2014 article because, ever since my mother developed dilated cardiomyopathy and especially after she had a dramatic response to a selective beta blocker, I believed that beta adrenergic and/or muscarinic cholinergic autoantibodies played a role in Mom's DCM, my CFS, and CFS in a subset of other patients (and that Mom's DCM was most likely due, in part, to beta 1 adrenergic autoantibodies.) I never stopped asking for myself and/or my family to be tested for these autoantibodies including contacting the teams who found these autoantibodies in OH and POTS cohorts. I am glad that CFS researchers have finally found them to be positive in a subgroup of patients with CFS, and I hope to finally be included in a study to find out if I am positive.

Laurie Dennison Busby, BEd

Notes

1 Busby LD Potential mechanisms of autonomic involvement in subgroups of chronic fatigue syndrome patients *Townsend Lett* November 2014 See also for additional references
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3 Li H, Kem DC, Reim S, et al Agonistic autoantibodies as vasodilators in orthostatic hypotension· a new mechanism *Hypertension* 2012;59(2) 402–408 doi 10.1161/HYPERTENSIONAHA 111 184937
4 Yu X, Stavrakis S, Hill MA, et al Autoantibody activation of beta-adrenergic and muscarinic receptors contributes to an "autoimmune" orthostatic hypotension: Receptor autoantibodies in orthostatic hypotension *J Am Soc Hypertens*. 2012,6(1)·40–47 doi:10 1016/j jash 2011 10 003
5 Loebel M, Grabowski P, Heidecke H, et al Antibodies to beta adrenergic and muscarinic cholinergic receptors in patients with chronic fatigue syndrome *Brain Behav Immun* 2015

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Saving Our Eyesight

review by Katherine Duff

Stop Vision Loss Now! Prevent and Heal Cataracts, Glaucoma, Macular Degeneration, and Other Common Eye Disorders
by Bruce Fife, ND
Piccadilly Books Ltd., P.O. Box 25293, Colorado Springs, Colorado 80936
© 2015; $16.95; 256 pp.

There are few things in this life more precious than our eyesight. Unfortunately, it is not until something goes wrong that we feel our true appreciation. This is when we learn that most eye diseases are diagnosed as age-related and there is not much that can be done. Bruce Fife, ND, has taken another approach in his book *Stop Vision Loss Now*, wherein he offers a plan to prevent, slow the progression, and heal some of the disorders of the eye.

He begins with a discussion of the anatomy of the eye and how it functions. As he describes the parts of the eye and their coordination required for us to see, he also includes the disorders that occur when those parts weaken or fail. Glaucoma, cataracts, and macular degeneration are just of few of the common conditions that can arise. And to truly understand the eye, he reminds us that it is actually an extension of the brain. The eye is formed in the fetus from the brain, and the optic nerve extends from the retina deep into the brain. Neurological research then is relevant to our understanding of eye health.

In his chapter "Vision Busters," we learn exactly what "age-related" really means. It is not chronological age but rather an accumulation of damaged cells through free radical damage, chronic inflammation, and advanced glycation end products (AGEs). The free radical damage occurs through any number of sources that we experience in daily life, including excess sunlight. The AGE is a result of glucose in the blood that has attached to proteins, and the end product accumulates in several parts of the body, including the retina, vitreous humor, lens, and cornea.

Fife provides a comprehensive list and discussion of antioxidants to address the free radical damage. Here we learn how the nutrients are essential to eye health, what their deficiency may cause, and how best to treat. Vitamin A is essential to many parts in the eye, and a deficiency may show up as night blindness or ulcers of the cornea. It must then be determined if the deficiency is a result of poor diet or malabsorption. If supplementation is called for, there are guidelines for appropriate dose or the recommendation to consume pro-vitamin A carotenoids found in the orange, red, yellow, and green fruits and vegetables. Another hint here is to consume the carotenoids with fats, which will increase conversion to vitamin A by a factor of 6.

An important part of this book rests in the author's examination of fats and eye health. Here his recommendations may run counter to some conventional wisdom, as he recommends the consumption of saturated fats and avoidance of polyunsaturated oils such as sunflower, safflower, corn, and soybean. He introduces the medium-chain triglyceride coconut oil, the basis for his dietary recommendations.

As founder and director of the Coconut Research Center, Fife has written several books on the benefits of coconut oil, one of them concerning Alzheimer's disease. He knew that eye health can take leads from neurological research, so the known benefits of coconut oil in the diet can also affect the eyes. Coconut oil increases absorption of nutrients such as antioxidants that protect the eyes from free-radical damage. Coconut oil is effective at controlling glucose and insulin levels, and has been shown to reverse insulin resistance all, of which contribute to the formation of AGE plaques. It is also an antioxidant and anti-inflammatory, and improves circulation.

"Most eye disorders come without warning. There is no way to pre-diagnose, no way to predict who will develop age-related macular degeneration or glaucoma as they get older. Everyone is at risk ... prevention is the best approach."

Reduced caloric intake in the form of the ketogenic diet is also part of the dietary recommendations. The author notes that calorie restriction has been considered the anti-aging diet for its ability to slow the aging process. It does this by reducing blood glucose levels and encouraging the formation of ketones from fat tissue. This has been shown to benefit those with conditions such as Alzheimer's and other brain diseases and injuries. We learn that the diet benefits eye health in many ways: it prevents blockage of the ocular drainage system, which can preserve the optic nerve; reduces age-related photoreceptor cell death; has reduced retina cell loss; and more.

The ketogenic diet calls for no sugar, low carbohydrates, moderate proteins, and high fats, including animal fats, which are important for the formation of ketones. Another way to increase ketones is to substitute coconut oil for other fats and add it to foods or even eat it by the spoonful. Sample meal plans are included.

Besides its use in diet, coconut oil can be applied to the eye with a dropper for cases of dry eye. It can also be used for mild eye infections due to its antimicrobial properties. Even coconut water drops have been found to improve cataracts.

This is a very thorough book – with one exception, and that is lack of consideration of exogenous chemical exposures. In our world that is rife with chemical products such as those found in air fresheners, pesticides, and newly built homes, we can assume that we can experience more free radical damage and must account for that. But there are also some chemicals in common use that can directly damage the eye, such as formaldehyde. And while Fife recommends consumption of animal fats, he does not make a distinction between animals raised organically or not. This can be problematic, since the fat-soluble chemicals, such as pesticides, that the animal is exposed to will be stored in their fat tissue for us to consume.

Those omissions aside, this book is a great antidote for anyone who has been diagnosed with an age-related eye condition and been told that there is nothing that can be done or surgery is the only answer. At 250 pages, it is densely written and supported by research. There are adequate instructions and explanations for every aspect that Fife discusses. But of course, the best use of this book would be for prevention of eye disorders. ◆

The Current State of Dementia Prevention and Treatment

Cognitive decline is a major concern for both American and international patients, with over 5.4 million Americans and 30 million individuals affected globally. Projections predict that 13 million Americans and 160 million worldwide will be afflicted in the near future. Half of the population over 85 is currently suffering from Alzheimer's, and given the shifting demographics of our population, the burden on society is simply unsustainable. Those over 85 are the fastest growing age group. Unless you want to be a burden to your family and exist without the full function of your brain, you need to start appropriate prevention strategies as early as possible, preferably by age 50.

Although Alzheimer's accounts for about 75% of dementia cases, other diseases such as traumatic encephalopathy, Pick's disease, frontotemporal dementia, vascular dementia, Lewy body dementia, and medication-related dementia should be considered when cognitive decline is noticed. The diagnosis of the various dementia types has been refined and perfected. Well-performed neuropsych exams are usually as effective as any currently available scan, if not better, for categorizing the patient. These cognitive tests have been highly developed over the last 20 years and are quite impressive, with high sensitivity and specificity. Imaging tests such as MRI, PET, and SPECT are essentially confirmatory in most cases. Symptoms such as word-finding difficulty, getting lost, reasoning or judgment lapses, lack of insight, affective disorders (especially if uncharacteristic of the patient's personality), and abnormal behavior patterns all contribute to earlier diagnosis. Early diagnosis however is not prevention, which is what we all look for. The burden of being a caretaker for a loved one with a disease that can last decades is devastating, costly, and stressful.

Currently, conventional medicine offers almost nothing in terms of prevention, and treatment is centered on patentable pharmaceuticals, which have shown almost no efficacy. The "benefits" of these targeted drugs are reported in terms of statistical significance, which should not be conflated with clinical significance. A clinically significant drug is reported with a low number needed to treat (NNT), whereas statistics such as relative risk can make a drug look better than it is clinically. In other words, these drugs do not work as often or as much as we are led to believe in real terms. Furthermore, the side effects are usually severe, and if they are tolerated at all, it may be the result of the patient's inability to communicate or lack of sensitivity.

The primary drugs used are the cholinesterase inhibitors such as Aricept and Exelon. In addition, glutamate blockers such as Namenda, SSRIs such as Paxil, and atypical antipsychotics such as Seroquel are frequently used. These drugs have draconian side effects and do nothing to address the cause(s) of dementia. Indeed, the pharmaceuticals are developed with studies that attempt to isolate a single pathway, pathology, or symptom in a double-blinded placebo controlled study (DBPC) which the FDA requires. This very paradigm is what needs to change. The assumption that a complex process such as dementia, which involves the most enigmatic structure known to humanity (the brain), can be reduced to a single or even a few targeted approaches is absurd and doomed to failure, as we all have observed.

The thinking goes something like this: We notice an abnormal protein (tau) in Alzheimer's-afflicted brains, so we develop a drug, study it with DBPC study, get it past the FDA, make a lot of money, and hope it works. Why is anyone surprised when it doesn't? Human biology is incomprehensibly complex (especially neurobiology), so however attractive a reductionist approach may seem in pursuit of the silver bullet, it is not consistent with reality. That reality is that this chronic disease, like others, requires a multimodal approach with many variables. We need silver buckshot, not a silver bullet. We need to plug the 30 to 40 holes in the leaky bucket of an Alzheimer's brain, not just one. Then, if done early enough, clinical results will be seen.

That is exactly what Dale Bredesen, MD, of UCLA and the Buck Institute is attempting to do. I was fortunate to meet Dr. Bredesen at a recent event in San Diego (the Scripps Integrative Supplements Course), during which he described his approach, as well as its results, in the first 100 patients it was tried on. This is a bold, comprehensive program which attacks a very complex problem in the manner that it deserves – via multiple avenues at the same time. We have no problem understanding that hypertension typically requires several therapies, drugs, lifestyle alterations, and close monitoring to control, but dementia treatment has thus far not been studied like this.

We have no problem talking about carcinogens as they contribute to cancer. development (chemicals, radiation, diet, environment, genetic predisposition, etc.), but thus far we have had little discussion about "dementegens" that should be avoided. Factors such as trauma, drugs (antihistamines, anticholinergics, anesthetics, anticonvulsants, antipsychotics, beta-blockers, benzodiazepines, chemotherapy, narcotics, sleep meds, tricyclics, stimulants), trans fats, animal products, heavy metals, volatile organic compounds, and so on all can cause dementia.

Although some progress and billions of dollars have been spent on identifying pathological proteins such as tau, APP, APOE, and their derivatives, this has led to nothing more than pathological correlates. Developing targeted drugs against these proteins is futile clinically. The drugs may change the scan, but are unlikely to reverse the cognitive decline. They may yield some interesting new pathophysiology findings, but approaching this disease from a reductionist point of view, looking for one or two targets, is not consistent with the complex biology we are dealing with.

Dr. Bredesen treated one patient who had a hippocampal volume in the 17th percentile on a NeuroQuant scan (an age-matched MRI scan of the HC), and the patient improved to the 75th percentile

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in less than 1 year on his comprehensive program. This was thought to be impossible by current thinking, but it proves that the hippocampus and brain in general are much more plastic than we ever imagined. This patient's clinical findings also completely reversed, which is extremely encouraging.

Cases such as these should be aggressively studied and used as a model for future treatment of others. Success stories such as this need to be celebrated and investigated. It has always puzzled me why conventional medicine studies disease expecting to learn about health. If you want to learn about health, study that. Study the people who do not get Alzheimer's if you want to know what it takes to avoid it. Study the rare cases that recover. The majority of the dollars going into research should be directed toward the study of healthy individuals, not sick ones.

How is this done? It's basically a functional medicine approach with some twists. Genetic testing is done to determine predispositions. A full toxic burden is assessed and remediated if necessary. Specific diets (usually modified ketogenic) are applied. A detailed and personalized exercise program centered around interval training is implemented, brain training with various methods scheduled, lifestyle analysis is done with the full cooperation of partners, and custom recommendations implemented. Micronutrient deficiencies are repleted, sleep deficiencies fixed, and comorbidities addressed. Specific nutraceuticals including CDP-choline, lithium, fish oil, D3, B12, and whatever else is needed according to testing are prescribed. Full hormone replacement therapy is utilized, with specific attention paid to testosterone, estrogen and thyroid, and anything else that the patient requires. This is neither cheap nor easy and requires continuous monitoring as well as adjustments. The effort, on both the part of the practitioner and the patient, is great but the payoff is even greater. At whatever the cost, the outcome costs far less than the disease itself. This is what is required to make a meaningful impact on this disease, both from the point of view of prevention and reversal.

I was informed that a course is in the works in association with David Jones, MD, of functional medicine fame. This will codify the approach and is the first sensible protocol to combat this dreaded disease. This protocol, however, has side benefits instead of side effects. It will go a long way toward preventing cancer and heart disease, as well as other chronic conditions. Patients have lost weight and felt better, not worse, like with many standard treatments. What a concept! Make the patient feel better. How unique.

We must transform our thinking about dementia from a brain-based disease to a metabolic-based disease with effects on the brain (our most metabolically active organ). Some people even refer to Alzheimer's as type 3 diabetes due to the insulin resistance in the brain, which can exist independently of peripheral insulin resistance. The brain uses much more oxygen than other organs and has the highest mitochondria concentration next to the heart. We must avoid dementegens like we avoid carcinogens. We must stop putting our children in harm's way with sports such as football and soccer. We must clean up our environment. What you do at age 40 to 50 will determine if your brain functions when you are 80 or older. Don't take your brain for granted. Your future is at stake.

Ira L. Goodman, MD, FACS,
ABIHM, FAARM

Tragedy of the Flint Michigan Contamination: Lead in the Water – Is It Time to Freak Out?

The simple answer is ... it's not so simple. But you must pay attention to what is happening to you and your family to be able to respond accordingly.

Over 27,000 innocent children in Flint, Michigan, have been exposed to startlingly high levels of lead in their city water supply – sometimes 13,000 times the concentration found in nearby localities – for many months, without any warning, even without early official acknowledgment when the problem was identified. The city emergency manager had changed its water supply but failed to comply with federal and state standards, with dire consequences. They switched back after 18 months to the earlier, safer water source, when Flint declared a state of emergency. Now city dwellers are left with corrosive toxics leaching from their pipes for who knows how long.

So how can you really know "what is happening"? That is the hard part. So let's make it easier for you to see it right now.

Recent reports suggest that the major "toxic exposure" is to lead. Quite honestly, it is impossible for just lead to be the only poison to which you're being exposed during this event. Over time, scientists will determine and share their additional discoveries with the public, so that even better treatments can be offered.

Is it true that younger children can suffer more serious damage from lead exposure? The answer "yes" is simple for you to see: brain and nerves and other organs are rapidly developing ... and lead strikes right in the middle of these. The results of such poisoning can be horrific.

Studies reported since the early 1980s have documented that higher lead levels in the body "led directly to" falling IQ. Kids sometimes "act dumb" when they're fooling around – but the tragedy of becoming a permanently "dumb adult" due to preventable brain damage is a life-destroying lifelong handicap.

How will you recognize more serious lead exposure problems? How about decreased bone and muscle growth and poor muscle coordination? Speech and language problems show up along with developmental delay, even seizures and damage to the nervous system and hearing, even to kidneys. Lower but still toxic levels can be seen as irritability or behavioral issues, difficulty concentrating, headaches, loss of appetite with sluggishness or fatigue; belly pains can show with nausea, vomiting, and constipation. Skin color can be pale due anemia. Some complain of muscle and joint weakness or pain, also a metallic taste.

Adults can show similar system problems, additionally developing as high blood pressure, heart disease,

leg circulation diseases and gangrene, declining mental function, memory loss, headaches, mood disorders, changes in sperm counts and even miscarriage or premature birth. Other heavy metals or chemical toxins (even from yeast/mold) can worsen symptoms such as this or create even other discomforting issues.

Sadly, there's no treatment available for this poisoning. Wait! – that's not true! But that is exactly what many worried patients (and parents) will hear from their local doctors in Michigan or around the country – "everyone knows that lead poisoning is irreversible." Commonly used blood testing is almost useless and rarely confirms toxic metal levels. Accurate diagnosis and precise treatment of heavy metal poisoning – such as with lead, mercury, arsenic, nickel, cadmium, even aluminum, and others – is a specialty in medical practice that has evolved over the past 60 years.

What are the two key factors that are critical to remove lead that is starting to damage body tissues?

First, you need management by a physician who understands and offers a treatment; called *chelation*. FDA-approved medications are available to remove toxic metals – and that is the only effective treatment, nothing else works, not drugs, not surgery, not anything else.

Second, you need chelation treatment that is started *early* enough and continued *long* enough. During this treatment program, your specialist will include nutritional supplements to replace "usual" minerals (such as magnesium, zinc, others) that are removed during the treatment for toxic metals, along with vitamins that help to reverse changes due to the poisoning.

The biggest problem that many patients and parents will face is that doctors and others who have no experience with, or any understanding of, lead poisoning and chelation therapy can discourage you from seeking such treatments. Delay in starting treatment of sudden exposures can result in permanent limitations of brain functions – thinking, intelligence, learning, memory, reasoning, then school performance and later career choices – for a child who depends on his parents to rely on physicians who can find out quickly what is going on and can fix it right.

How successful is chelation therapy at reducing lead deposited in children, even in adults? Medical studies for years have shown overall excellent results in children when proper treatment is continued as long as each particular patient needs. Each year, over 300,000 young children are found to have unsafe levels of lead in their blood; more definitive tests – urine "challenge" testing, hair analysis – would reveal even more. Adults have already had dozens more years to accumulate lead and other toxic heavy metals from so-called acceptable levels in the food, water, and air. Their program is longer because their body burden is much more than just from the recent exposure to poisoned water.

How critical is it for you to avoid further exposure right now? Absolutely required! So you must heed precautions offered by local public health officials. You might need to follow these preventive steps for quite a long time. Tainted water can seep into the underground water table, leading to long-term unexpected exposures such as well water, foods from gardens or even farms, public water such as swimming pools or local ponds, rivers, lakes, even city water supplies. What is worrisome is that poisons spread through the environment are much more difficult to remove and might linger for years, causing continuing health challenges long after any "cleanup" has been declared to be completed. The dangers are very real even though invisible.

Did you know that you can "see" and even "smell" lead-laden water, so you can easily avoid drinking it or using for cooking or bathing? That is a myth, pure bunk, a total lie. The *only* way to protect your children and yourself from continuing poisoning in Flint is to pay attention to recent local water testing that documents the level of toxic heavy metals found over time. Only in this way can you take needed steps to insure pure water and foods for your family – even if you need to make those changes for many months after the cleanup has been reported as concluded.

Is someone to blame for this serious event? Of course. Investigators will find someone who "did something wrong"; that's obvious. But your usual environment has already been a dangerous place for the last 60 years or more. Lead paints so common in the past (toddlers chewing on window sills or toys), lead gasoline (still used for small airplanes), lead pipes, and bootleg stills (lead solder) are easy examples, often explaining gradual toxic accumulations seen now in adults. The Flint water poisoning is a more acute event that suddenly changes everything for a large number of unsuspecting people – infants, children, and adults of all ages – adding further to their underlying body burden of lead and other toxic metals already accumulated over their lifetimes.

Is there a bright spot in this disastrous event? Only this: many thousands more people will learn now of the tremendous healing powers of chelation therapy. A few hundred physicians around the country have been trained to deliver chelation therapy, and various approved drugs are available. Beyond rescuing exposed children from a lifetime of lower potential and performance, the reduction of toxic heavy metals by chelation has been documented to improve a wide variety of conditions in virtually every organ. Reducing right now the lead levels in exposed children is essential to minimize or delay later crises as adults suffering heart attacks, high blood pressure, leg artery diseases and gangrene, loss of vision, and much, much more.

Who will really care about your family and your situation in the future? The "news cycle" will soon move on to other headlines, and you will be left stranded with the tattered remains of your life. Take advantage now of this opportunity to find a specialist who could help you with your poisoning problems. To consult with a specialist physician who has training in chelation therapy, contact the International College of Integrative Medicine (www.chelation.me) or the American College for Advancement in Medicine (www.acam.org). Be diligent in your search and review the doctor's credentials conscientiously. Remember: your toxic metal problem (from whatever source) is a serious health challenge and needs treating now ... it's urgent to get the lead out!

John Parks Trowbridge, MD, FACAM

John Parks Trowbridge, MD, FACAM, has been recognized as a specialist in chelation therapy since 1985. Recognized as an expert in various fields of integrative/"alternative" medicine, he has served as a leader of several professional organizations, has written books and published CDs and DVDs, and has lectured across the country and around the world.
281-540-2329
info@healthCHOICESnow.com. ◆

Guest Editorials

Calendar

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

FELLOWSHIP IN STEM CELL THERAPY – 5-Module Course online and weekends: May 19-21 (Hollywood, Florida), **September 22-24** (Dallas, Texas), **December 9-11** (Las Vegas, Nevada) CONTACT Metabolic Medical Institute, 561-910-4960, www mmimedicine com

MARCH 31-APRIL 3: ADVANCED TOPICS IN ENVIRONMENTAL MEDICINE in Irving, Texas (near Dallas) Includes Dr Alan McDaniel's 2-day Endocrinology course CONTACT American Academy of Environmental Medicine, 316-684-5500, www aaemconference com

APRIL 1-3: INTEGRATIVE MEDICINE CONFERENCE ON ENDOCRINOLOGY, AUTOIMMUNITY, AND CHRONIC INFECTIONS in Philadelphia, Pennsylvania CONTACT 954-540-1896, Sharon@iticonferences com, www itiphilly com

APRIL 2 APPLIED FUNCTIONAL NUTRITION 100 in Boca Raton, Florida CONTACT www facebook com/BioticsResearch

APRIL 2: COULD METHYLATION BE THE HOLY GRAIL OF AGING GRACEFULLY? in Bethesda, Maryland *CONTACT www facebook com/BioticsResearch*

APRIL 5-7 & 12-14: INCLINIC PRECEPTORSHIP BIOIDENTICAL HORMONES with Erika Schwartz, MD in New York City, New York. CONTACT dkingman@drerika com, drerika com/content/speaking-and-events

APRIL 8-10 SOUTHWEST CONFERENCE IN BOTANICAL MEDICINE in Tempe, Arizona Intensive with Donald Yance on new cancer drugs and synergistic natural medicines. CONTACT. 541-482-3016, www botanicalmedicine org

APRIL 8-10 11th ANNUAL JOINT AMERICAN HOMEOPATHIC CONFERENCE – Ascending to New Heights: Reaching the Summit with Homeopathy in Westminster, Colorado (near Denver). CONTACT. www homeopathycenter org/2016-joint-american-homeopathic-conference

APRIL 9: HORMONES & CARDIOMETABOLIC FUNCTION – GETTING TO THE HEART OF THE MATTER in Charlotte, North Carolina. CONTACT www facebook com/BioticsResearch

APRIL 9-10: MASTERING THE SCIENCES OF INTEGRATIVE BLOOD CHEMISTRY in Chicago, Illinois CONTACT www facebook com/BioticsResearch

APRIL 14-16: 14th ANNUAL INTEGRATIVE ONCOLOGY CONFERENCE @ Town & Country Resort in San Diego, California CONTACT www bestanswerforcancer org/annual-conference/2016-conference/

APRIL 14-17: 12th NATIONAL AYURVEDA MEDICAL ASSOCIATION CONFERENCE in Warwick, Rhode Island CONTACT www ayurvedanama org/?page=2016ConfOverview

APRIL 15-16. A4M SYMPOSIUM – The Power of Unwritten Prescriptions. Diet, Exercise, and Cardiometabolic Disease in Newport Beach, California CONTACT www a4m com/2016/newport-beach/a4m-symposium html

APRIL 15-17: 60th NORTHWEST NATUROPATHIC PHYSICIANS CONVENTION – FOOD AS MEDICINE in Portland, Oregon CONTACT nwnpc com

APRIL 15-17 SW COLLEGE OF NATUROPATHIC MEDICINE presents REGENERATIVE INJECTION THERAPY WORKSHOPS (Module 3) Lumbosacral Region & Pelvis in Tempe, Arizona CONTACT www scnm edu/RIT-WORKSHOPS

APRIL 29-MAY 1: 45th ANNUAL INTERNATIONAL ORTHOMOLECULAR MEDICINE TODAY CONFERENCE in Vancouver, British Columbia Current advances in orthomolecular psychiatry, paediatrics, oncology and general medicine CONTACT· 416-733-2117; www csom ca/omt/

APRIL 30-MAY 1: 6th ANNUAL INTEGRATIVE AND HOLISTIC NURSING CONFERENCE- Bringing Healing to You and Your Patients in San Diego, California CONTACT www scripps org/integrativenursingce

MAY 1-6: GERSON THERAPY PRACTITIONER TRAINING – MODULE I (of 2) in San Diego, California In-depth training in Dr Max Gerson's principles of dietary healing. *CONTACT 800-838-2256, gerson org/gerpress/practitioner-training; aonken@gerson org*

MAY 12-14: THE INSTITUTE FOR FUNCTIONAL MEDICINE'S 2016 ANNUAL INTERNATIONAL CONFERENCE - Creating Balance *Between* Motion and Rest in San Diego, California CONTACT. www. functionalmedicine.org/AIC

MAY 12-15· 20th CLINICAL APPLICATIONS FOR AGE MANAGEMENT MEDICINE in Championsgate/ Orlando, Florida CONTACT agemed org

MAY 17-20: INTERNATIONAL CONGRESS FOR INTEGRATIVE MEDICINE & HEALTH – Bridging Research, Clinical Care, Education, and Policy in Las Vegas, Nevada With IHPC, ACCAHC, AIHM and ISCMR. CONTACT· www icimh org/

***MAY 19-21: 24th ANNUAL WORLD* CONGRESS ON ANTI-AGING MEDICINE** in Hollywood, Florida **MAY 18-21:** ABAARM & ABAAHP exams. CONTACT. www a4m com/

MAY 19-21: METABOLIC MEDICAL INSTITUTE MODULES on Endocrinology, Clinical Practice Protocols, and Regenerative Medicine with Stem Cells in Hollywood, Florida CONTACT· www mmimedicine com/2016/hollywood/index html

MAY 20-22· PRECISION LYME TREATMENT WITHOUT ANTIBIOTICS in Kenmore, Washington Tools, Remedies, Techniques for Brain, Body, & Bugs CONTACT 908-899-1650, info@klinghardtacademy com, www klinghardtacademy com/Seminars-Workshops/Lyme-Conference-Biological-Medicine-2016 html

MAY 20-22: 2016 TRADITIONAL ROOTS HERBAL CONFERENCE in Portland, Oregon CONTACT· traditionalroots org/2016-traditional-roots-conference/

MAY 23-24· 18th INTERNATIONAL CONFERENCE ON COMPLEMENTARY, ALTERNATIVE, INTEGRATIVE MEDICINE & HEALTH in London, United Kingdom CONTACT waset org/conference/2016/05/london/ICCAIMH/

JUNE 3-6: MEDICINES FROM THE EARTH HERB SYMPOSIUM in Black Mountain, North Carolina CONTACT. 541-482-3016; www botanicalmedicine org

***JUNE 6-10: APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE* – 5 day foundational course** in Austin, Texas Also, **SEPTEMBER 19-23** in Baltimore, Maryland CONTACT www functionalmedicine org/AFMCP

JUNE 16-18: SOPMED (Society of Oxidative & Photonic Medicine) CONFERENCE near Salt Lake City, Utah. Oxidative, light, and energy medicine Limited to 300 participants CONTACT. 517-242-5813, info@sopmed.org,, www sopmed org

JUNE 23-25: A4M BHRT SYMPOSIUM in San Diego, California CONTACT: www a4m com/2016/june/san-diego/a4m-symposium html

JUNE 23-25 METABOLIC MEDICAL INSTITUTE MODULES on Weight Management and Compounded Prescriptions in San Diego, California CONTACT· www mmimedicine.com/metabolic-medicine-event-schedule.html

JULY 1-3: 3rd INTERNATIONAL CONGRESS ON NATUROPATHIC MEDICINE in Barcelona, Spain CONTACT icnmnaturopathy eu

JULY 15-17 HORMONE ADVANCED PRACTICE MODULE – RE-ESTABLISHING HORMONAL BALANCE in National Harbor, Maryland (DC) CONTACT www functionalmedicine.org/Hormone

JULY 15-17. ENERGY REGULATION ADVANCED PRACTICE MODULE – Illuminating the Energy Spectrum in National Harbor, Maryland (DC) CONTACT www.functionalmedicine org/Energy

JULY 22-24. 4th COLORADO INTEGRATIVE MEDICINE CONFERENCE – Focus on Mind-Body Medicine & Lifestyle Management in Estes Park, Colorado CONTACT: 970-310-3030, info@altermedresearch org, www altermedresearch org/cimc2016/

JULY 27-30: AMERICAN ASSOCIATION OF NATUROPATHIC PHYSICIANS' ANNUAL CONFERENCE & EXPOSITION in Salt Lake City, Utah *CONTACT www naturopathic org/aanp2016*

AUGUST 10-13: 25th ANNUAL IAACN SCIENTIFIC SYMPOSIUM – Renovation of the Structural Integrity of the Human Body Through Biomolecular Interventions Beyond the Collagen Connections in Jacksonville, Florida. CONTACT· www iaacn org/symposium/

AUGUST 11-13: METABOLIC MEDICAL INSTITUTE MODULES on Gastroenterology and Toxicology & Detoxification in Las Vegas, Nevada CONTACT www.mmimedicine com/metabolic-medicine-event-schedule html

SEPTEMBER 3-9: HEALTHY BIRTH, HEALTHY EARTH @ Findhorn Foundation, Scotland CONTACT www findhorn.org/programmes/healthy-birth-healthy-earth

SEPTEMBER 9-10: INTERNATIONAL ACADEMY OF ORAL MEDICINE AND TOXICOLOGY (IAOMT) *ANNUAL CONFERENCE & JOINT* MEETING WITH IABDM in Reno, Nevada CE credits CONTACT iaomt. org

SEPTEMBER 15-18: 2016 ACAM & AAPMD JOINT ANNUAL MEETING – An Interdisciplinary Approach to Advanced Prevention in Tucson, Arizona. CONTACT www acam org/ACAM2016

SEPTEMBER 19-23· APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE - 5 day foundational course in Baltimore, Maryland. CONTACT www functionalmedicine org/AFMCP

SEPTEMBER 21-24: A4M BHRT SYMPOSIUM in Dallas, Texas Also, ABAARM & ABAAHP exams CONTACT www a4m.com/conference-schedule html

SEPTEMBER 21-24: METABOLIC MEDICAL INSTITUTE MODULES on Neurology, Autoimmune Disease, Cardiovascular, & Stem Cells in Dallas, Texas CONTACT www mmimedicine com/metabolic-medicine-event-schedule html

SEPTEMBER 29-OCTOBER 2: 7th ANNUAL INTEGRATIVE MEDICINE FOR MENTAL HEALTH CONFERENCE in Reston, Virginia (near D C) CONTACT www.immh2016.com/

SEPTEMBER 30-OCTOBER 1: A4M SYMPOSIUM in Washington, DC CONTACT· www a4m com/2016/washington-dc/a4m-symposium html

SEPTEMBER 30-OCTOBER 2: KLINGHARDT EUROPEAN NEURAL THERAPY & INJECTION TECHNIQUES in Kenmore, Washington A transformative workshop basic to advanced skills CONTACT 908-899-1650, info@klinghardtacademy com, www klinghardtacademy.com/Seminars-Workshops/Injection-Techniques-and-Skills-2016 html

OCTOBER 6-9: AMERICAN ACADEMY OF ENVIRONMENTAL MEDICINE ANNUAL MEETING – The Role of Mitochondria in Health & Disease near San Diego, California. CONTACT AAEM, 316-684-5500, www aaemconference.com

OCTOBER 22-23 10th AUSTRALIAN HOMEOPATHIC MEDICINE CONFERENCE in Brisbane, Australia CONTACT www homeopathyconference com

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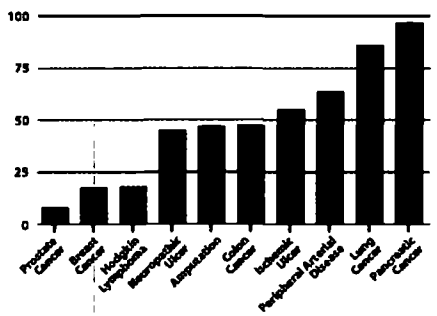
Chronic Wound/Diabetic Ulcer Healing/Surgical Healing: A New Plant-Based Treatment Clinically Effective in Just 30 Days

by Brian Scott Peskin, BSc; Amid Habib, MD; and Jeff Matheson, MD

Chronic, nonhealing wounds are a significant issue. Impaired healing of often-horrific chronic wounds and ulcers affects over 7 million patients and over 1.75 million diabetic patients a year in the US. Approximately 29.1 million Americans (9.3% of the population) had diabetes in 2012. Their numbers will continue to rise. *All diabetics suffer with impaired wound healing.*[1-3] Regardless of specialty, most physicians and practitioners will be faced with patients with wound-healing complications – often including diabetes – affecting the choice of modalities and protocols.

Figure 1: 5-Year Death Rate (%) – Diabetic Ulcers Have Worse Survival Rates Than Many Cancers[5]



Because there is no effective treatment, a limb-related diabetes amputation is performed every 8 minutes in the US and every 20 seconds worldwide. Diabetic foot ulcers can have higher mortality rates than many cancers, including prostate and breast cancer, Hodgkin lymphoma, and colon cancer (Figure 1).[4,5] *Neuropathy* and *ischemia* are the primary underlying risk factors for diabetic foot ulcers.[6] Because the diabetic patient isn't aware of skin irritations, lack of sensation from neuropathy will often further aggravate the condition. **Five-year mortality rates after new onset diabetic ulceration are between 43 and 55%** – up to 74% for patients with lower-extremity amputation. Even with adequate arterial inflow, diabetic foot ulcers have only a 24% closure rate at 12 weeks and only a 31% closure rate at 20 weeks.[7]

Approximately 15% to 25% of patients with diabetes develop a foot ulcer at some point in their lifetimes, and an estimated 12% of those patients (1.8% to 3% of all diabetics) will require lower extremity amputation.[8]

Nearly one-third of patients in hospital-based *outpatient* wound centers may not heal their wounds even though they are cared for over a long period of time.[9] Arterial ulcers are often extremely painful. Their healing is often more difficult because of the additional issues caused by a compromised cardiovascular system. Patients with an arterial ulcer show a higher rate of recurrence and nearly twice as many amputations.[6] ➤

Illustrations of Chronic Wounds and Diabetic Ulcers

Conservatively, according to 2007 data, costs for treatment and care of chronic nonhealing wounds of American patients exceeded $50 billion.[9] Thirty-eight billion was linked to the treatment of foot ulcers – approximately one-third of the $116 billion in direct costs generated by the treatment of diabetes and its complications.[6] As treatment duration lengthened, the cost of care significantly increased.[5] Prevalence of diabetic foot ulcers will only increase in the future. There are no effective ingestible drugs to speed wound healing – moist wound care, bioengineered skin, negative pressure therapy (NPWT), growth factor enhancers, aspirin, and hyperbaric oxygen treatment (HBOT) may all be used with differing degrees of results.

Plant-Based Oils: 30 Days to Successful Patient Healing

Three plant-derived components: Linoleic acid (LA), alpha-linolenic acid (ALA), and gamma-linolenic acid (GLA) – crucial compounds both directly utilized and metabolized to important eicosanoids – have been shown to be effective in treating complications of diabetes and, specifically, wound healing.[10] Because of the skin's EFA composition, maximum skin/epithelial tissue healing occurs with formulations containing more metabolically active LA than ALA.

First and foremost is "sealing the wound." Skin (epithelial tissue) is composed almost exclusively of the EFA linoleic acid (LA). For rapid manufacture of new skin to seal the wound, ensuring adequate, metabolically active LA is crucial.[10]

Next, inflammation must be minimized or the wound/ulcer's surface skin will not heal expediently, nor will its underlying tissue. Inflammation pathways promote thrombosis (clogged arteries), impeding blood flow and wound healing.[11] GLA supports maximization of PGE1 for decreasing thromboses impeding blood flow.

Increased cellular oxygenation/ increased cellular (mitochondria) energy: Increased cellular oxygen accelerates wound healing and protects wounds from infection, but because of high oxygen consumption requirements, the environment of early wounds is quite hypoxic (oxygen deficient). Always accompanied by hypoxia, chronic wounds can have as little as 10% of the oxygen content of normal tissue.[12] Via cardiolipin support, wound tissue can now obtain the required extra energy for repair, significantly accelerating healing.[13–15]

Accelerated underlying tissue repair: By optimizing cellular functionality with LA/ALA, all underlying tissue that is related to the wound/ulcer heals better because its cellular tissue membranes contains 25% to 33% LA/ALA.[16]

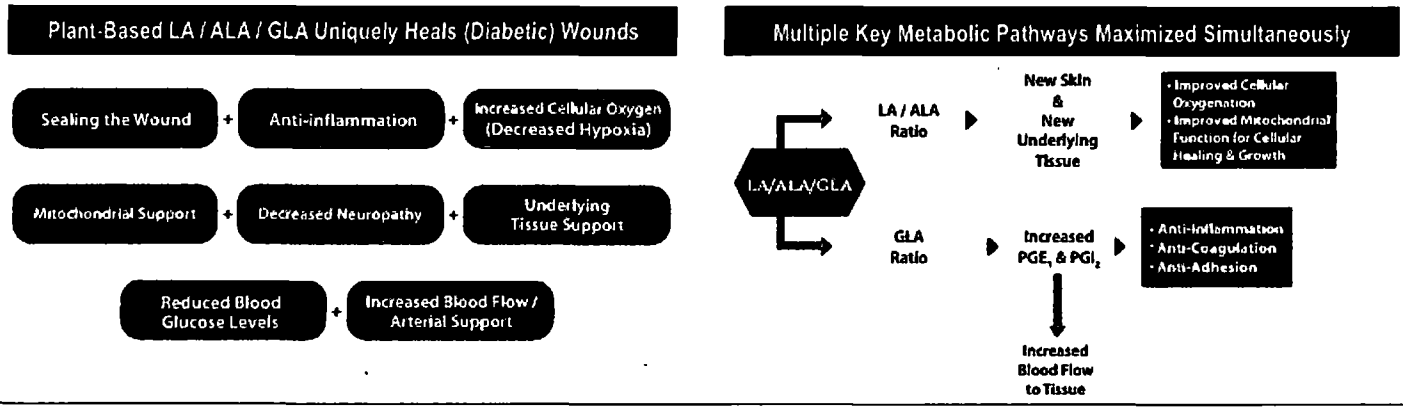
Reduced diabetic blood glucose levels: In part because of prolonged elevated blood glucose levels, *damage to nerve function (neuropathy) occurs in more than 90% of diabetics*. A calibrated LA/ALA formulation maximizes insulin-binding sensitivity, lowering elevated blood glucose levels. Patients taking LA lowered their blood sugars by an average of 15 points – very significant.[17] In 2013, LA's effect in reducing diabetic blood glucose level was reconfirmed.[18] A combination of LA and its metabolite GLA works synergistically in the cell membrane to reduce blood glucose and fortify the cellular fatty acids removed by elevated Lp-PLA2 in diabetics.[19]

Increased blood flow and arterial protection: Maximum blood flow is required for maximum wound healing. Decreased blood flow causes complications – from impaired oxygen transport (hypoxia) to impaired nutrient delivery required for expedient wound/ulcer healing. *Diabetics are at a significantly increased risk of cardiovascular obstruction*. Plant-based LA/ALA/GLA works synergistically to reverse existing cardiovascular disease (in particular, occlusions) in the diabetic patient.[20,21] Plant-based oils support "natural blood thinning" for maximum arterial blood flow and optimize multiple protective cardiovascular pathways simultaneously.[22,23] It is now known that metabolically active plant-based LA is effective in reversing heart disease, and that ALA is associated with less risk of a heart attack.[24,25]

Clinical Success – Physician Case Studies with Peskin Protocol EFAs: Just 30 Days to Clinical Effectiveness in Healing Diabetic Ulcers and Underlying Pathophysiologic Disorders, Increasing Blood Flow, and Improving Surgical Outcomes

October 22, 2015 – Case study: Nonhealing ulcer success – amputation prevented:

> I just received a text last night from a patient that I prescribed the Peskin Protocol EFAs last month. He had severe type 1 diabetes with all of the vascular complications. He underwent a pancreatic and kidney transplant. He had



a nonhealing ulcer on his right foot and was booked for amputation. He also has diabetic neuropathy. He texted me last night, after 5 weeks taking Peskin Protocol EFAs, stating: "There is a difference. I have less pain, walking better, and my foot is healing." Avoiding an amputation is a considerable feat! We have not only improved his life but saved the health system tens of thousands of dollars with just this one success.

March 27, 2015 – Case study: Improved blood flow (decreased occlusion) – amputation prevented:

I just saw an interesting patient who I've known for a while. She came to see me last month. The surgeons wanted to amputate her right leg due to arterial occlusion. She had a cardiac bypass and suffered daily angina attacks. I immediately prescribed the Peskin Protocol EFAs and saw her today. The angina is totally gone and the right leg is warm and pink! The Peskin Protocol EFAs will save her leg. Tremendous, in only 1 month!

Jeff Matheson, MD, pain specialist,
Toronto, Canada

March 10, 2010 – Case study: Neuropathic patient unable to walk; can now walk:

A 16-year-old boy, Diabetic (Type 1) for 8 years presented with retinopathy, nephropathy, and neuropathy, HbA1c over 14%, unable to walk or put weight on both feet due to severe pain. He was on Narcotics. Placed on specialized vitamin and mineral formula (Treolife VM) and Peskin Protocol EFAs. 10 weeks later, his HbA1c dropped to 7.3% and he is able to walk on his feet without pain and discontinued his narcotics.

On his specialized vitamins, minerals, and EFA supplement, his HbA1c dropped to 6.6% 8 months later and to 6% 11 months after its institution.

Amid Habib, MD, pediatric
endocrinologist specializing in diabetes
Altamonte Springs, Florida

February 25, 2008 – Case study: Major surgery (wound) healing – improved patient outcomes:

In my practice as a plastic surgeon, I have found myself understanding that to obtain good post-operative results according to the intensity that varies from minor to major operations (the majority are very intense operations), the repair phlogistic [inflammation] resolution, edema and the scar tissue are all key factors to success. I must point out a new major factor that improved greatly my patients' surgical results after introducing Peskin Protocol EFAs plant-based oils from 15 days prior to 30 days after surgery. The level of tissue repair is what I look for especially in my practice and having the trial opportunity of five patients using Peskin's recommendations; I found in all five patients an enormously improved result with better recovery.

The Peskin Protocol EFAs do not cause excessive bleeding. In fact, it makes surgery easier and improves patient recovery. This improved recovery included:

1. faster healing
2. less inflammation
3. less scar tissue and
4. less pain to the patient

Dr. Andrea Roncarati,
plastic/reconstructive surgeon
Ferrara, Italy

Notes

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Brian Scott Peskin, BSEE, is a consultant for numerous nutritional companies, including Your Essential Supplements (USA), BioAge Ltd. (UK), Pure Form Omega (Canada), Natural Bodz (Australia), and Succesboeken, (Netherlands). He holds multiple patents regarding plant-based lipid formulations. Peskin earned his bachelor of science degree in electrical engineering from the Massachusetts Institute of Technology, founded the field of Life-Systems Engineering Science in 1995, and was appointed adjunct professor at Texas Southern University in the Department of Pharmacy and Health Science from 1998 to 1999. He is chief research scientist at Peskin Pharmaceuticals (prof-peskin@peskinpharma.com).

Amid Habib, MD, has over 30 years of experience in the research and practice of pediatric endocrinology specializing in treating diabetes. He is past president of the Florida Endocrine Society, board certified in both pediatrics and pediatric endocrinology, and a fellow in the American Academy of Pediatrics and the American College of Endocrinology. He was one of the first 200 board-certified graduates in pediatric endocrinology. Dr. Habib stands at the forefront of the movement to blend the field of nutrition with the latest scientific advances in medicine.

Jeff Matheson, MDCM (Toronto), has worked in the following capacities· full-time emergency room physician for 15 years, medical director of Med-Emerg Inc. from 1998 to 2013, and founder of CPM Medical Clinics (pain management), which became the largest provider of pain management in Canada 2005 to present Additionally he has trained over 70 physicians in the practice of pain management.

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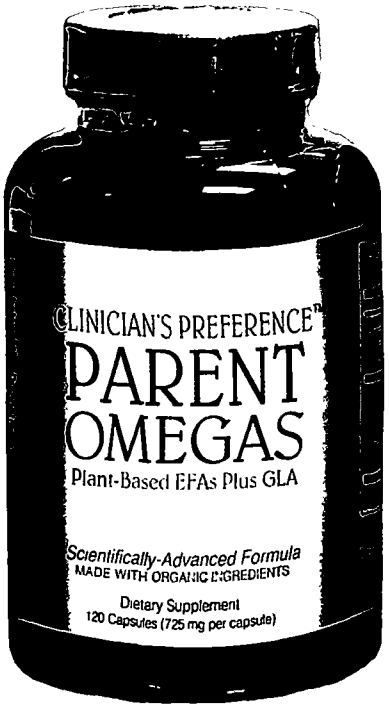

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Overcoming a Knowledge Gap to Develop Competent Nutrigenomics Practitioners

by Yael T. Joffe, PhD, RD, and Christine A. Houghton, BSc (Biochem.), GradDip, R Nutr, PhD Cand

Introduction

The last decade and a half has seen the global proliferation of nutrigenetic testing companies. Overall, the direct-to-consumer (DTC) model has been mostly unsuccessful and the growth has come primarily from companies' selling tests through practitioners. Many of the more reputable companies insist on their practitioners' completing an accreditation course before they are "certified" to sell the companies' tests. Although an admirable insistence, the integrity and depth of these courses vary. In addition, practitioners vary in their qualifications and experience. The result is that most practitioners are inadequately trained to interpret and effectively communicate nutrigenetic results and dietary recommendations.

Parallel to this growth in nutrigenetic tests, there has been a welcome increase in nutritional genomics academic programs, ranging from university short courses and elective modules in masters' programs, to postgraduate programs, masters', and doctoral degrees. A number of universities have begun to include a small amount of nutritional genomics teaching in their undergraduate curriculum. Understandably, these programs tend to be research based, and while they potentially offer academic integrity and research skills, they are not helpful in providing practitioners with the skills that they need to work with nutrigenetics in practice.

This article does not address whether or not the field of nutritional genomics is ready for practitioner use. (For this, we recommend "Nutrigenetics and Personalized Nutrition: Are We Ready for DNA-Based Dietary Advice?")[1] Rather, it addresses the practitioner "knowledge gap," describing what knowledge practitioners may be missing.

Defining the Knowledge Gap

The Nutrition Knowledge Gap

One of the greatest challenges is in bringing together the fields of nutrition and genetics. For doctors, medical specialists, dentists, homeopaths, and others, there is an acknowledged lack of nutrition education. For those with sufficient training in nutrition such as ➤

Figure 1: Nutrigenetics and Nutrigenomics: Know the Difference

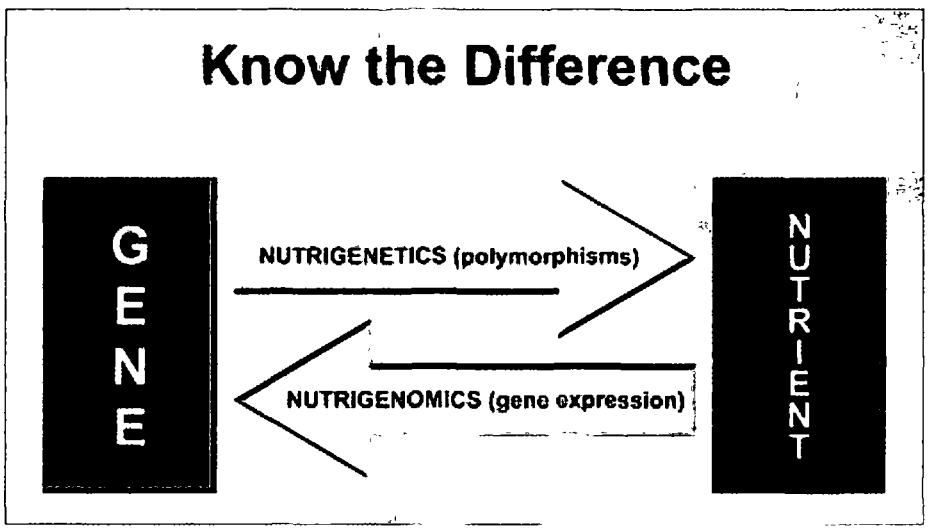

Figure 2: The Three-Pillar Approach

dietitians and nutritionists, the gap is the understanding of nutrition in a systems biology, functional, and political ecology context.

Nutritionism has become the ruling ideology of our current health care.[2] There is a great need for a new nutrition ideology, a new way of seeing and knowing about food, nutrition, health, and conditions such as obesity. Food needs to be taught, spoken about, and practiced not only in a biomedical model but also with due consideration of the social, environmental, political, and economic relations that govern how food is produced and consumed. This requires an understanding of nutrition that starts with genes and ends with the environment; no easy task.

The Nutritional Genomics Knowledge Gap

Many practitioners, and, surprisingly, academics as well, cannot differentiate between nutrigenetics and nutrigenomics (Figure 1). What is often referred to as *nutrigenomics* is in fact nutrigenetics. In this article we use the term *nutritional genomics* to mean both *nutrigenetics and nutrigenomics*. The tests that practitioners work with are more accurately nutrigenetics tests, and the training that they receive usually covers only nutrigenetic interactions (see sidebar: "Defining the Difference Between Nutrigenetics and Nutrigenomics"). This has resulted in an emphasis on SNPs (single nucleotide polymorphisms) and a "superficial" involvement with what the science of nutritional genomics has to offer. It is our contention that practitioners require an understanding of what we call the "three pillars of nutritional genomics" (Figure 2).

These include:

1. nutritional biochemistry
2. nutrigenetics
3. nutrigenomics

Biochemical processes are driven and understood through nutritional biochemistry. It is imperative to understand the biochemical pathways and the disruption thereof, which contribute to perturbations in health and potentially the development of disease. *Nutrigenetics* provides information on genetic sequence variants: SNPs as well as other variations such as copy number variants. These may (but not always) alter gene expression or enzyme function. By understanding nutrigenomics (nutrient impact on gene expression), a practitioner is able to identify and advise on nutrients and lifestyle changes that may alter gene expression. Put together, these three pillars of nutritional genomics will empower the practitioner to construct targeted and clinically useful dietary and lifestyle recommendations.

Defining the Difference Between Nutrigenetics and Nutrigenomics

Genetic variability (nucleotide sequence change) influences how we interact with our environment. *Nutrigenetics* describes the influence of gene variants on our ability to interact with bioactive molecules in the molecular environment surrounding our cells and the consequences of that interaction.

In contrast to nutrigenetic interactions wherein the gene variants act on the environment, with *nutrigenomic* interactions, the environment influences gene expression. Nutrigenomics is concerned with the influence of bioactive molecules interacting with a gene, potentially influencing gene expression. Either upregulating or downregulating (turning it up or down) or activating or silencing (on or off). *Nutrigenomic* interactions may be direct or indirect. In a *direct interaction*, the molecules are of small molecular weight, carrier mediated, and lipid soluble. In an *indirect interaction*, the molecules are larger and hydrophilic. These molecules interact at the cell surface.

Employing the Three-Pillar Approach in Practice

The Fundamental Strategy

A key consideration in the three-pillar approach is to focus initially on *upstream* biochemical events. Each gene codes for an enzyme, and that enzyme is involved in one or more biochemical pathways. If practitioners understand the nature of that pathway when it is functioning normally, they can better predict what may happen when a variant of the gene produces an enzyme operating at lower activity. Understanding the function of the key upstream biochemical pathways is at the core of this approach. Human cells utilize a number of core biochemical processes in maintaining their homeostasis; these include redox regulation, detoxification, inflammation modulation, energetics, and methylation. These five upstream processes form the foundation for the first pillar.

Redox dysregulation and associated inflammation as upstream factors are common elements of numerous chronic diseases.[3] Nutrigenetic test profiles typically include SNPs that affect the primary antioxidant enzymes and major inflammatory cytokines, whereas they are unlikely to include many of the disease-specific *downstream* gene variants.

The following example uses type 2 diabetes to examine the evolving identification of associated genes and their function. Genome-wide association studies (GWAS), linkage, and candidate gene association studies have identified a number of diabetes-related genes; however, these studies are inconsistent in their findings. A 2007 study identified the genes *PPARG, KCNJ11,* and *TCF7L2* as established genes associated with common forms of type 2 diabetes.[4] Eighteen months later, another study found that the number of gene loci robustly associated with type 2 diabetes had risen from 3 to 18 in the ensuing period.[5] Their findings included the obesity-related genes *FTO* and *MC4R,* and they concluded that 7 of these identified type 2 diabetes gene loci affect beta-cell function, but the function of 9 other genes was unknown. By 2010, largely through

GWAS, approximately 20 gene variants associated with type 2 diabetes had been identified, with some overlap of 10 with body mass index (BMI) and obesity, 4 with fasting glucose levels in the normoglycemic population, and over 30 with lipid levels.[6]

Clearly, this field is still evolving, and what is clinically significant is that there are no known interventions to modify the expression of some of these genes. In the three-pillar approach, these downstream genes may be considered only *after* the core upstream biochemical processes have been addressed.

As with many chronic diseases, redox dysregulation is accepted as a fundamental contributor to both the onset and the progression of type 2 diabetes. Examining the relevant gene variants from a nutrigenetic profile gives the practitioner a guide to the redox-regulating potential of that patient. Following such an analysis, the appropriate nutrigenomic interventions can be selected in order to modify the expression of one or more genes.

Case Study: A 46-year-old female presents with recently diagnosed type 2 diabetes. Her diet is poor and her BMI is 29. Nutrigenetic testing shows the following SNPs in her redox panel (Table 1). Space does not permit a full nutrigenetic analysis.

Pillar 1: The Nutrigenetic Profile

Table 1: Redox Panel

Gene	Variant	Genotype	Gene Codes for:	Nutrient Cofactor
SOD2 (MnSOD)	Val16Ala (C>T)	No variant impact	Superoxide dismutase (mitochondrial) MnSOD	Manganese
SOD3	760 C>G	CC	Superoxide dismutase (extracellular) CuZnSOD	Copper and Zinc
GPX1	*GPX1* Pro198Leu (C>T)	CT	Glutathione peroxidase (GPx)	Selenium

Pillar 2: The Biochemical Analysis

The superoxide radical is generated continuously by the mitochondria from inhaled oxygen. In certain circumstances such as during exercise, there is an increased flux of oxygen through the mitochondria. This increases the quantity of superoxide radical produced and this acts as the prooxidant signal needed to activate the cells' endogenous defense mechanisms. As a consequence, the expression of the *MnSOD* gene is upregulated so that more MnSOD enzyme is produced; the same applies to increased expression of the *GPX* gene. Just as exercise increases the flux of oxygen, glucose, and fatty acids through the mitochondria, so too does overeating. Several pathways in type 2 diabetes contribute further to this increased flux .[7]

These two primary upstream reactions constitute the first line of cellular defense against oxidative stress.[8] As shown in Figure 3, two superoxide radicals *dismute* to produce hydrogen peroxide, a nonradical reactive oxygen species (ROS) that can readily react with metal ions to produce highly toxic hydroxyl radicals (OH^-). If acted upon by GPx in the normal manner, hydrogen peroxide readily converts to unreactive water, thereby removing the oxidative risk.

Figure 3: Superoxide Redox Reaction
Reaction #1: 2O2- + 2h+ SOD H2O2 + O2
Reaction #2: 2 H2O2 GPx 2H2O

In our case study, the patient carries a "normal" *MnSOD* and so the mitochondria are likely to perform Reaction # 1 adequately, generating hydrogen peroxide. However, she carries a GPx SNP, thereby limiting the activity of the GPx enzyme. As a result, hydrogen peroxide will tend to accumulate at a rate faster than can be handled by the dysfunctional GPx enzyme. Consequently, hydrogen peroxide is more likely to react with available heavy metal ions to produce the hydroxyl radical, which can oxidatively damage a range of proteins, lipids, DNA and RNA, and other biomolecules. What this tells us is that although the patient carries a "normal" *MnSOD* gene, the potential for oxidative damage is still increased. *GPX1* has been implicated in the development and prevention of many common and complex diseases, including cancer and cardiovascular disease.[9]

Pillar 3: Nutrigenomic Interventions

The goal of a nutrigenomic intervention is to provide one or more food-derived compounds known to induce the expression of a specific gene for which increased enzyme activity is desirable. There are two fundamental aspects to consider: (a) is there an essential cofactor for the enzyme? and (b) are there food-derived bioactive compounds that can induce the expression of the gene itself?

In our case study, the *GPX1* variant produces the glutathione peroxidase enzyme that is suboptimal in its activity. The trace element selenium is an essential cofactor in GPx enzyme activity, and so the first approach is to evaluate the nutritional status of this nutrient in the patient and either increase dietary sources of selenium or supplement appropriately if necessary.

The second important strategy is to provide an appropriate bioactive where known; one reported nutrigenomically active food element is a melon/gliadin extract that has been shown to increase activity of GPx, SOD, and CAT enzymes.[10] It is important to note that direct-acting antioxidant vitamins (A, C, E, beta-carotene) have no place as nutrigenomic interventions unless there is demonstrable deficiency; altering the cellular redox milieu in this way is likely to mask the subtle signals that cells rely on to activate endogenous defenses.[11]

Further Implications

The role of redox regulation cannot be underestimated as a primary upstream event in disease etiology. ➤

Redox imbalance and inflammation function in a self-perpetuating loop, so that to satisfactorily address inflammation, redox balance must also be considered.[12] Similarly, elevated superoxide levels can inhibit the enzyme aconitase, the rate-limiting step in generation of ATP via the Krebs cycle. In detoxification reactions, phase I generates superoxide, and if phase II is not sufficiently active to prevent accumulation of toxic intermediates, key biomolecules and delicate organelles can be severely compromised. Similar arguments can be mounted to show how methylation and redox imbalance are closely interrelated.[13]

Case Summary

The approach described very briefly here addresses just a few of the upstream factors contributing to type 2 diabetes and its progression in this patient. In the clinical environment, the nutrigenetic report would identify SNPs from other genes associated with upstream factors such as those coding for inflammatory cytokines, other key protective enzymes such as antioxidant and detoxification enzymes, and the nonenzyme antioxidant glutathione.

In the three-pillar approach, the practitioner would consider the possible effects of these SNPs in the relevant biochemical pathways, ordering pathology (functional) tests where indicated. Appropriate pathology tests are useful in assessing whether the particular SNP is compromising biochemical function. These tests can be useful because not all SNPs result in compromised biochemical function for two reasons: (a) there may be other genes which effectively "substitute" for the defective gene – for example, quinone reductase (NQO1), a phase II detoxification enzyme, can quench superoxide radicals if SOD function is less than optimal; and (b) the patient's diet and/or lifestyle may be such that the expression of that gene has been modified nutrigenomically. Where a patient carries a SNP, and pathology testing confirms compromised function, the practitioner may then provide dietary and supplement recommendations known to modify the expression of the aberrant gene(s).

A recent study highlighted the Mediterranean diet as an effective intervention. In a randomized controlled trial, the researchers examined the effects of the Mediterranean diet in type 2 diabetics, investigating the upstream markers, plasma antioxidant capacity, endothelial function, nitrotyrosine, 8-iso-PGF2a, IL-6, and ICAM-1 levels.[14] They found that this intervention prevented the effect of acute hyperglycemia on endothelial function, inflammation, and oxidative stress.

As in the type 2 diabetes example we described earlier, addressing the upstream factors as shown in the Ceriello study is a strategy that may deliver significant benefit to the patient with or without considering the

downstream gene variants for which nutrigenomic interventions are not well understood.

Conclusion

What we have endeavored to identify is the knowledge gap experienced by most practitioners who wish to include the field of nutritional genomics in their practices. We have described why the current educational offerings are inadequate, but we have also shared what we believe to be the knowledge required to integrate nutritional genomics into clinical practice.

It is not enough to be told or even to know what impact a SNP may or may not have on enzyme function and what disease associations have been reported in the scientific literature. Nutrigenetics must exist in the context of nutritional biochemistry to provide a deeper understanding of the biochemical pathways that have been affected, and an understanding of nutrigenomics is the key to developing effective and meaningful dietary and lifestyle interventions. This three-pillar approach demands that practitioners undertake more in-depth, expansive training, but it will also ensure that they will then be in a position to understand the biochemical environment of gene variants and have the skills and knowledge to independently construct dietary recommendations that surpass the recommendations offered by commercial nutrigenetic tests.

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In the rapidly-evolving disciplines of nutrigenomics and nutrigenetics, Dr. Yael Joffe is acknowledged globally as an expert in the field. From her background as a dietician, she obtained her PhD from the University of Cape Town, exploring the genetics and nutrition of obesity in South African women. She is a regular speaker at conferences and workshops, tailoring her presentations to the needs of clinicians. She has coauthored *It's Not Just Your Genes*, has published on nutrigenomics in peer-reviewed journals, and has been involved in the development and supervision of nutrigenomics courses around the world. Dr Joffe is currently an adjunct professor, teaching nutrigenomics at Rutgers University, and has developed and teaches the Manuka Translational Nutrigenomics online course.

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Following 30 years in private practice as a nutritional biochemist, Christine is currently engaged in doctoral research at the University of Queensland, investigating bioactive nutrigenomic phytochemicals with significant clinical potential. Christine's forte lies in taking complex biochemical concepts and translating their essence into concepts relevant to the needs of practicing clinicians. She is a regular presenter at medical and nutrition conferences, where her knowledge of and enthusiasm for the roles of nutritional medicine and nutrigenomics in human health are very evident. She is the author of *Switched On – Harnessing the Power of Nutrigenomics to Optimise Health*. Her peer-reviewed publications include the Special Article published in 2013 in *Nutrition Reviews*: "Sulforaphane: Translational Medicine from Lab Bench to Clinic."

Anti-Aging Medicine

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

There Can Be No Anti-Aging Without Detoxification

Dr. Ronald Klatz, president and cofounder of the academy, presented the following at the proceedings of the A4M 23rd Annual Medical Congress on Anti-Aging Medicine on December 9, 2015, at which over 5100 physicians and scientists gathered from 60 countries worldwide to participate in this year's postgraduate and educational event.

Despite sustained growth of almost 9% each year since 1991 with the inception of A4M, the anti-aging marketplace now stands at $380 billion per year. This growth is projected to continue and reach $1 trillion before 2025. In the US, a subset of women known as the Bergen County of New Jersey Ladies have reached 91.5 years, thanks to their adoption of the anti-aging medicine philosophy.[1] This is a 23.5-year difference vs. its shortest-lived cohort of women in America. Therefore, the anti-aging dividend now stands at 23.5 years. Unfortunately, this laudable perk of longevity is now being threatened by a deliberate expansion of toxins into our environment.

There is a new threat, a silent menace, quietly undermining our best efforts to achieve a better quality of life, via alternative and natural health practices of anti-aging and functional medicine. Ever-increasing stealth toxicity in our environment can put a halt to all that has been established in anti-aging medicine if we do not address these issues now.

According to a global study released on June 23, 2015, by the organization Getting to Know Cancer, there are 50 chemicals the public is exposed to on a daily basis, which may trigger cancer when combined. These chemicals, commonly found nowadays in food, air, and water, are accumulating in our bodies and can trigger cancer development.[2]

Thirty years ago, air pollution and respiratory diseases were the 7th leading cause of death. Today, they are the primary cause in many nations, and in the US the 3rd leading cause of death. We are inhaling on a daily basis about 5000 different airborne toxins such as aluminum, lead, barium, thorium, coal ash, fungus, and microbes that come from our skies every day. Nitrogen dioxide (NO2) is one of a group of highly reactive gases. It forms quickly from emissions from cars, trucks and buses, power plants, and off-road equipment. NO2 not only has a damaging effect on the ozone but also is linked to adverse effects on the respiratory system.

SO2 is another example of a toxin that damages our lungs. The largest source of this gas comes from fossil fuel combustion at power plants and other industrial facilities. Smaller sources of SO2 gas include the burning of high sulfur containing fuels by locomotive, large ships, and non-road equipment. These toxins have a cumulative negative effect in the brain, heart, kidney, and liver. Robert Storey and colleagues from the University of Sheffield, UK, warn that airborne particulate matter (PM2.5) is the biggest modifiable contributor to cardiovascular disease, causing inflammation of the lungs and entering the circulation, thereby inflaming blood vessels, provoking clots, and causing heart rhythm disturbances.[3]

Not only are respiratory diseases increasing in the world, but contaminated waters and radiofrequency pollution, among other types of toxins, are also affecting people's health. The Safe Drinking Water Act defines the term *contaminant* as meaning any physical, chemical, biological, or radiological substance or matter in water. Some of these contaminants may be harmful if consumed at certain levels in drinking water.

These contaminants are listed on the Contaminant Candidate List (CCL) and are evaluated further for potential health effects and the levels at which they are found in drinking water. This step however, is ineffective, as the EPA does not

have enough resources to oversee and enforce companies that use lakes and rivers as dumping grounds. For example, 41 million Americans are living with toxic amounts of pharmaceuticals such as antibiotics, antiepileptics, mood stabilizers, hormones, pesticides, and other chemicals in their drinking water. These have a negative effect in human cells and wildlife.[4] Other samples of toxins in drinking water are chlorine, which causes bladder and rectal cancer, recently breast cancer; lead, which causes learning disorders and severe developmental delays; and *Giardia* and *Cryptosporidium*, which cause gastrointestinal diseases.

On December 20, 2010, the Environmental Working Group (EWG) released the results of a test that found the carcinogenic chemical chromium-6 in the drinking water of 31 of 35 US cities. Chromum-6 is highly toxic and has been found to cause allergic dermatitis, and gastrointestinal cancer in animals and humans. It gets into the drinking water system through industrial pollution from manufactures of textile, steel, and leather tanning. It is recommended to filter this toxin from our tap water via reverse osmosis, combined with newly developed superior solid carbon block filter purification.[5]

Most recently, we have a glaring example in Flint, Michigan, where we could witness the damaging effects on people's health from elevated levels of lead in the drinking water. People are exhibiting skin lesions, hair loss, high levels of lead in their blood, memory loss, vision loss, depression, and anxiety. People should not turn a blind eye to this catastrophic event until it is irreversibly late. We must not think that the problem in Flint, Michigan is an isolated example. This mass poisoning is happening to us all.[6]

Radiofrequency toxicity is now wildly recognized as a cause or contributing force for chronic fatigue, cardiac arrhythmia, high blood pressure, visual disturbances, altered sugar metabolism, EEG changes, immune abnormalities, joint pain, insomnia, and tinnitus. A 5-minute cell phone conversation with the handset held close to the ear can alter blood–brain permeability for up to 50 days. WHO/International Agency for Research on Cancer (IARC), reported on May 31, 2011, on radiofrequency electromagnetic fields as possibly being carcinogenic to humans, based on an increased risk for glioma, a malignant type of brain cancer, associated with the use of cell phones.[7]

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To stay updated on the latest advances in anti-aging diagnostic medical technologies, visit the World Health Network (www.worldhealth.net), the official educational website of the A4M and your one-stop resource for authoritative anti-aging information. Do not forget to view our recent "Immortality Now" videos, dedicated to up-to-the-moment health issues. Furthermore, be sure to sign up for the free Longevity Magazine e-journal, your weekly health newsletter featuring wellness, prevention, and biotech advancements in longevity. For any questions, please contact the A4M at 773-528-1000.

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Ask Dr. J

by Jim Cross, ND, LAc
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As doctors, we always like to think that we will be totally successful with each and every patient, if not at first then somewhere down the line. Sometimes our egos can interfere and prevent this from actually happening. We need to be extra careful to remain humble and secure in the realization that we know a lot but not everything and that hopefully every day we learn something new which enables us to become better doctors and better people. I had the great fortune of meeting Dr. John Bastyr when I was a naturopathic student. To me, he modeled the perfect behavior of a doctor, extremely knowledgeable yet even more humble. No one walking into the dining room of this hotel would have ever thought that the older gentleman sitting at this table of young, energetic future whiz kids was actually the leader of their pack.

Vicki was one patient who fit this model of not being helped initially, but way down the road, while I thought I knew all the answers. A divorced 48-year-old woman with a 16-year-old daughter, Vicki had a total body rash so severe that she was contemplating suicide. She had just watched an episode of my favorite TV show of all time, *Northern Exposure*, in which one of the characters had moved to Alaska to live in an artificially created, environmentally safe bubble that was built specifically for him because he had started to react to almost everything in his home and work environment. She reported that she felt just like Mike, played by the actor Anthony Edwards. Her rash actually worsened slightly when she was at home, but was still severely present when she was out and about.

Looking at her, I saw a rash that contained very red papules, some of them oozing and others crusted over with scales. The rash was all over her body except for her palms, soles, and face. She reported that it was extremely pruritic, which caused her to vehemently attempt to scratch it. She also said that the lesions tended to have a burning feeling. She had become extremely self-conscious about it and was happy as a clam that she worked for an Internet start-up where the majority of her work was done from home. She was also sending her now-driving daughter out to do the bulk of the shopping.

The rash had begun several months ago after an antagonistic break-up with her ex-husband and the subsequent move into a house with her daughter. It started around both ankles and slowly over time spread up her legs to her abdomen, back, and upper extremities. Oral and topical prednisone helped to just keep it at bay and allow her to not kill herself. She had seen several doctors who had tried various meds with no results. A friend had suggested a "Paleo diet," which she had scrupulously followed for a month with no improvement

Allergy scratch testing suggested that she had multiple allergies to cats, dogs, various chemicals, and most trees and flowers. Her personal medical history wasn't remarkable except for seasonal hay fever and multiple ear infections during the first 5 years of her life. She had to have tubes placed into her tympanic membrane when she was 4. Even her TSH was low, 1.4. I thought that there might be a connection with her emotional state and the stress increasing her reverse T3, leading to the skin issues. She didn't really have any other solid hypothyroid signs or symptoms, but then the perfectly simple patient rarely walks into your office!

My understanding of the reason why NAET (Nambudripad's Allergy Elimination Techniques) or emotional NAET works is based on quantum physics and the minute electromagnetic energy created when an electron moves. Since everything is made of electrons as well as protons and neutrons, then everything has an electromagnetic field. Fields are harmonic with each other or dissonant. When two fields are dissonant there are consequences, such as muscle weakness which can be tested by applied kinesiology as discovered by George Goodheart, DC. Needling 4 Gates for a simple food allergy (or 4 Gates + both Heart 7s in an emotional NAET treatment) resets the body's biocomputer to allow the correct message to enter and reset the body's homeostatic processes. The treatment is telling the body that this food or food + emotion isn't really dangerous and that the body doesn't need to be reactive to it. It is similar to tuning an instrument.

I started where I always do with a new patient: food intolerance testing. Also, because of her recent emotional breakup, I was thinking of an emotional tie-in to the food allergy. (Further below I will describe how I do this NAET/emotional testing, in another patient.) She tested positive for wheat and soy. Both also had emotional components that appeared to be related to her recent marriage dissolution. I had her stay away from those foods and also used EFT (Emotional Freedom Technique) to work on her emotional well-being. In addition I gave her handouts and advised her where to look for hidden sources of wheat and soy.

I expected to see immediately positive results given the success that I have had in prior skin cases utilizing NAET (Nambudripad's Allergy Elimination Techniques) and emotional tie-ins. She came back 2 weeks later, and her rash was exactly the same, maybe even a little worse. I questioned her about the rigidity of her food avoidance. She impressed me with what she ate, more importantly with what she didn't eat, where she bought her food, and how she prepared it. Also, she had even begun to talk to her ex-husband and was trying to stop blaming him for everything that happened. She felt as if she was making substantial emotional and dietary progress but had very little to show for it in terms of her skin condition.

My recommendation was to stay the course for 2 more weeks because sometimes dietary interventions don't give immediate results. She agreed to my recommendations. What I didn't know was that her best friend told her about vitamin D. Now, I should have seen this coming. She was very pale, sunburned easily as a child and adult, and hadn't been outside for months because of her skin condition.

She had started taking 5000 IU/day of vitamin D3, 2 days before our visit. She came back 2 weeks later and her skin was 25% better. I was amazed and felt great until she told me about the vitamin D. I still felt great for her but was wondering whether the food intolerances also played a part. I had her come back in another 2 weeks to see if continuing the D would continue the improvement.

Two weeks later, she came back severely depressed because the improvement had plateaued. Fortunately, I must have put on my thinking cap that day or my guardian angel told me to ask her more about her new house, I can't be sure which. She told me she had found the house very quickly because of her need to quickly leave her husband. The house sits in a gully on the north side of a hill in the middle of a watershed. It is an older home that does not have wood heat but propane. She didn't want to spend a ton of money so hadn't been heating it as well as she could have. I asked her about mold in the house. She reported that she always had to clean mold off of the ceilings in the bathroom and her room, which was on the south-facing side of the house. This was February, and she said she hadn't seen the sun for

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what seemed like months. Also she had a basement, but her landlord kept it locked because he stored some of his old stuff there. He had given her a break on the rent for this.

Now, that fate factor came into play again. Three months prior, I had attended Gordon Medical's seminar with Dr. Ritchie Shoemaker, who is "Dr. Mold." He claims that 25% of Americans can't process mycotoxins from mold and that exposure to mold can make these people extremely sick due to their inability to remove the mycotoxins from their bodies.

Her landlord let her look into the basement. She basically found what she termed "mold central," all kinds of weird-looking mold. She moved out that day, found another home that wasn't in the shade, and almost immediately started to notice changes. A great line of Jeff Goldblum's in the movie *The Big Chill* is, "Ever gone a week without a rationalization?" Not only did her rash begin to improve, but she noticed that her severe brain fog was also now improving. Her supposedly good appetite doubled, as did the size of her stools. Basically, she had found the source of her problems! She was also effusive with her praise, as I had encouraged her to pursue the mold option. In reality, I did very little except continue to advance my medical training, which allowed me to think of mold. May I always be this fortunate!

Another patient I had was a 46-year-old male lawyer who came in with chronic grass and tree allergies. They had started as a young adult and had progressed to the point where his cough was so consistent that he was beginning to cough every time he attempted to speak. Nothing he was being given worked even a little bit – over-the-counter antihistamines, oral steroids, cough syrups, and so on. He had heard about NAET, which I happen to also use. He came to me to see what I could do. NAET is a method that utilizes muscle testing to identify the food/allergen intolerance and then acupuncture or acupressure massage to remove the intolerance to the food.

Now, I'm lucky I had heard about NAET from Carolyn Reuben, LAc, who works in Sacramento, California, using EFT and NAET. She originally turned me onto the NAET training in Los Angeles. Fortunately, I also learned about emotional NAET from her. In this case, you are not identifying just the food intolerance the person has but also the emotional event in their life that triggered the intolerance or is presently contributing to it. I tested this patient and found nuts to be the main allergen, with an emotional component of guilt. We talked further about his guilt and came up with an interesting set of circumstances. He was a high-powered Internet executive who was working 12- to 16-hour days. He also had two kids, 6 and 8, plus his wife was a grade school teacher. His guilt was wrapped up in the fact that his wife worked full time and that she was the one who was actually raising their children. I didn't have time to perform the allergy elimination technique at this visit, but I recommended that he attempt to assuage his guilt. I asked him if he could leave work two days/week for a few hours and pick up his kids, thus allowing them time with their dad and his wife some free time for herself. Of course he said yes, and of course that was the last time I saw him.

When we don't get lost in our egos, we can learn a lot from our mistakes. Hopefully we don't make too many of them and do not repeat them. I had originally felt like Barry Bonds after he hit one of his steroid-induced homers into McCovey Cove! I had definitely hit the nail square on the head with this patient. What I hadn't anticipated was the emotional reaction that I had extracted from his deep subconscious. From this experience, I learned to never, no matter how clear the indication, delve into deep emotional treatments in the first few visits. I need to begin to establish a bond with the patient and then make emotional inroads with them if that is the path that presents itself.

I fared much better with another patient who presented with what she had been told was seasonal asthma. She was a 58-year-old female who had begun to notice a tightening in her chest during the height of pollen season in Sacramento 5 years prior. Each year the tightening was becoming more severe to the point now where she had been given a bronchodilator and a steroid inhaler to ameliorate her symptoms. They helped about 50%, and she was becoming nervous and extremely fearful of having a full-blown attack that she couldn't control. One of her first statements was that stress seemed to make the attacks worse. Upon further questioning, her life seemed to always have some sort of stressful component to it, going all the way back to her childhood.

Comments like that turn a certain type of light bulb on in my head. I was taught in NAET training to always diagnose and treat the food intolerances before the environmental ones. So I tested her. Amazingly enough she was positive for only one food, eggs. Given her oral history of stress, I tested for an emotional component, and of course there was one, which turned out to be helplessness. Unfortunately abuse, whether it is emotional, physical, verbal, or any combination thereof, is rampant in our society. Growing up, she only saw her father at dinner, as he worked long hours seven days a week. She had always been slightly overweight her whole life. He basically made fun of her at dinner every night. Of course, his favorite food was eggs, which were present at the meal in some form most every evening.

I treated her egg intolerance with the helplessness at its core. Her response was little short of amazing. Her bronchoconstriction completely cleared up, even though it was the middle of pollen season. She also related to me that she had been consistently having nightmares related to her childhood and that these had also stopped. I know we pay far too little attention to the emotional aspects of our patients' lives. This is the source of a large amount of their physical ailments. To really complete their cycle of healing requires us to look below the surface of their actual physical complaint and see what is lurking in the shadows. It isn't always pretty or easy, but the lasting results will usually pay dividends way past anything that Wall Street has to offer!

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Monthly Miracles

by Michael Gerber, MD, HMD
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The Many Faces of *Helicobacter Pylori*

Beyond Rosacea

Several years ago I read that *H. pylori* can cause acne, rosacea, and a host of other diseases as well as stomach and duodenal ulcers.

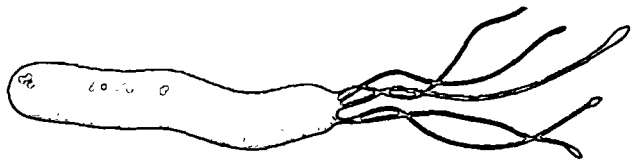
A spiral-shaped bacterium in the human stomach was first described over 100 years ago by Prof. W. Jaworski in Poland. It wasn't taken seriously as a pathogenic agent until 1984, when two Australian researchers, Barry Marshall and J. Robin Warren, identified it from intestinal biopsies from peptic ulcer disease patients.[1] They noted its pleomorphic aspects, which differed from patient to patient, and its ability to tolerate stomach acid by secreting urease and burying into the gastric and duodenal mucosa. They received the Nobel Prize in Physiology or Medicine in 2005.

Their work changed the treatment parameters from antacid therapy, which frequently caused relapse of the disease, to antibiotic therapy, which addressed the underlying cause of the illness. To this day, the standard allopathic treatment is the triple therapy of a proton pump inhibitor, frequently omeprazole 40 mg per day, with clarithromycin 500 mg twice per day and amoxicillin 1 g twice per day for 7 to 14 days. Diagnosis is made by carbon urea breath testing, stool antigen testing, blood antibody testing, and biopsy during endoscopic examination with a rapid urease test, histological examination, and microbial culture.

H. pylori is a widely prevalent microbe with nearly 50% of the Western world and over 80% of those living in developing countries infected (Figure 1). Only 15% to 20% of infected people have symptoms of peptic ulcer disease. Its prevalence is associated with socioeconomic status, water contamination, sharing of eating utensils, and food quality. The bacteria has an amazing ability to persist in infected individuals for decades and have coexisted with humans since they migrated out of Africa 60,000 years ago.[2]

Autoimmune Disease Associated with *H. Pylori*

H. pylori infection has been implicated in a variety of diseases not related to the GI tract. Skin disease association includes the following[3,4]:



Helicobacter Pylori

- Rosacea: *H. pylori* can increase the level of nitrous oxide in the blood or tissue contributing to the flushing and erythema of rosacea.
- Chronic urticaria: Several studies have found a link between *H. pylori* and chronic urticaria. It is thought that the infection increases the permeability of the intestinal lining and exposure to allergens and also produces antibodies that may increase the release of histamine in the skin.
- Psoriasis: *H. pylori* may be one of the organisms capable of triggering the inflammatory response in psoriasis.
- Sjögren's syndrome: *H. pylori* may induce an autoimmune reaction to the skin and glands, causing Sjögren's syndrome.
- Henoch-Schonlein purpura
- Alopecia areata
- Sweet disease
- Systemic sclerosis
- Atopic dermatitis
- Behçet's disease
- Generalized pruritus
- Nodular prurigo
- Immune thrombocytopenic purpura
- Lichen planus
- Aphthous ulceration

It has been speculated that *H. pylori* infection may be responsible for various endocrine disorders, such as autoimmune thyroid diseases, diabetes mellitus, dyslipidemia, obesity, osteoporosis, and primary hyperparathyroidism.[5]

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H. Pylori, Cognition, and Neurological Syndromes

Not only do *H. pylori* work on disrupting autoimmune regulation via cytokines, interleukins, humoral, and cell mediated reactions, they also play a powerful role in the modulation of hormones, neurotransmitters, demyelination, and blood–brain barrier disruption.[6] This infection has been well documented to be associated with depression, schizophrenia, epilepsy, multiple sclerosis, cognitive decline, other neurological diseases, gastrointestinal motility disorders, lymphoma, and vitamin and nutrient malabsorption.

Integrative Approaches to *H. Pylori* Treatment

My first interest in *H. pylori* aside from GI issues was rosacea. With our advantage of rapid diagnosis via EAV (electroacupuncture according to Voll) and the BioMeridian computer, it made assessment and treatment response immediately available. My favorite treatment has been with Pyloricil (Orthomolecular Products) containing mastic gum (guar gum) extract 250 mg, berberine sulfate hydrate 150 mg, bismuth citrate 125 mg, and zinc carnosine 37.5 mg per capsule. Dose is 1 capsule twice per day. If it did not test well or if the *H. pylori* seemed to no longer be responsive, I use mastic gum/DGL from Complementary Prescriptions with deglycyrrhizinated licorice (*Glycyrrhiza glabra* root and rhizome extract 300 mg) with gum mastic (*Pistacia lentiscus* resin extract). Chew 1 to 2 wafers as needed. I usually suggest twice per day and typically see resolution or good improvement in about 1 month. There are many other herbal and alternative treatments for *H. pylori* from around the world.[7]

The depth of research in this infection is truly overwhelming, and I hope that the reader will have a higher index of suspicion in seeking and treating this universal hidden plague.

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Dr. Ohhira's Essential Living Oils Honored with Second 'Clean Choice Award'

For a second time, *Clean Eating Magazine* announced Dr. Ohhira's Essential Living Oils as a "Clean Choice Award" winner.

"With more and more companies working to create clean and healthy packaged products and supplements, we feel it's important to reward their innovation and service to healthy eaters living a clean lifestyle," said Alicia Rewega, editor in chief of *Clean Eating Magazine.* "In every way, clean eating is all about consuming whole food and supplements in its most natural state, or as close to it as possible."

Dr. Ohhira's Essential Living Oils offers a certified vegan option providing balanced omega-3, -6, and -9 ratios that serve as a complete and balanced source of essential fatty acids. In response to the common omega-6 imbalance, the American Heart Association recommends regularly consuming fatty fish to promote a healthier omega-3 intake. However, an increasing number of consumers are looking for alternative sources of EFAs, due to issues of personal taste preference or vegan lifestyles.

The conditions and stipulations that made up the selection process for the Clean Choice Award winners included planet-friendly packaging; life-simplifying power; being current and cutting-edge; simple, real food ingredients; high score by the Environmental Working Group's (EWG.org) screener; availability and accessibility; being organic; sustainability; and being GMO free.

"Eight natural plant and seed oils are carefully extracted and prepared to provide a pure, undamaged form of plant-based 'good fats' for optimum health. The product is a scientifically designed blend of linolenic acid (omega-3), linoleic acid (omega-6), and oleic acid (omega-9) delivered in the preferred ratio of 4:1:1 – a great start for balancing the daily intake of healthy fats," said Muneaki Takahata, PhD, scientific researcher at Biobank Co. Ltd. and science advisory board member for Dr. Ohhira's Probiotic Formulations. ◆

Healing with Homeopathy

by Judyth Reichenberg-Ullman, ND, DHANP, LCSW, and Robert Ullman, ND

www.healthyhomeopathy.com

Asperger Syndrome and ADHD

Homeopathy: By Far The Safest Alternative to Treat Autism Spectrum Children

An article posted on the autism website Thinking Mom's Revolution, titled "The Thompson Transcripts," has revealed that a senior epidemiologist and whistleblower from the CDC (Centers for Disease Control), Dr. William Thompson, had admitted omitting "statistically significant information" from a 2004 study in the journal *Pediatrics* that looked at the timing of the MMR vaccine and autism. The study showed that African American boys, if they had received the MMR vaccine before 36 months of age, had an increased risk of autism.[1] This alarming information was reputedly suppressed by the CDC. A media campaign that discredited Thompson and his revelations ensued. We recommend reading the post.

We have recognized a link in our autism spectrum patients between the MMR vaccine and autism for more than 15 years. It's not true for every autistic patient, for sure, but there is a link that would be hard to ignore after hearing so many reports from parents of the temporal relationship between their child having a febrile reaction and brain cry after the vaccine and a rapid descent into the hell of a life dealing with autism for both the child and the parents. Fortunately, we have been able many of these children with homeopathic treatment continued consistently over months and sometimes years. (Also see Robert F. Kennedy Jr.'s book *Thimerosal: Let the Science Speak.*)[2]

Another disturbing article appeared in the *New York Times* on December 11, 2015. "Still in a Crib, Yet Being Given Antipsychotics" focuses on the off-label prescribing of powerful antipsychotic drugs to babies and toddlers who exhibit violent or withdrawn behavior, despite no published research into their effectiveness or potential risks to young children.[3] According to the article, nearly 20,000 prescriptions for Risperidone (Risperdal), quetiapine (Seroquel), and other antipsychotic medications were written for children age 2 or under, a nearly 50% increase from the previous year. For the same age group, fluoxetine (Prozac) was prescribed nearly 83,000 times to small children, a 23% increase over the previous year. Some experts in child psychiatry and neurology had never heard of children younger than 3 years old receiving such medication. Such an increase in off-label prescribing is troubling and demands investigation. After more than 30 years' experience treating children, we recommend homeopathy instead as a safe and effective alternative to drugging small children with off-label and potentially toxic drugs.

A third noteworthy article that we read recently was about elderly individuals who were actually autistic, but were misdiagnosed with other psychiatric conditions at a time in the 1950s and 1960s when autism was virtually unknown in the psychiatric community. "Autism's Lost Generation," which appeared in the *Atlantic*, chronicles the work of a University of Pennsylvania professor of psychiatry and pediatrics, David Mandell, and his attempt to unearth the records of patients who were misdiagnosed, and so mistreated for other psychiatric conditions rather than autism.[4] This research allowed a number of patients who were still alive to get off inappropriate psychiatric medications, and receive appropriate help for their actual condition.

Prior to and since our publication of *A Drug-Free Approach to Asperger Syndrome and Autism* in 2006, we have had the privilege to treat many cases of children with autism and Asperger syndrome using homeopathy. We recommend homeopathic medicine to parents seeking an alternative to pharmaceutical drugs. It has been immensely rewarding to assist in and witness the transformation of these children on the autism spectrum using safe and natural homeopathic medicines. Here we present a case of a child diagnosed with Asperger and ADHD to demonstrate the effectiveness of the homeopathic approach to improving the lives of these patients, old and young.

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Eli: Bright, Distractible, Yet Hyperfocused

Eli, aged 8, was an active, distractible child, with difficulty accomplishing his work at school. He could not finish anything or stay on task. It was hard for him to focus his attention because he found everything to be equally interesting. It was difficult for Eli to figure out when other children were listening to him and when they were bored, since he was challenged to read social cues. This difficulty, a common trait in Asperger syndrome, was a distinct liability for Eli socially. The child had only a few friends and insisted on playing by his own rules, ignoring the rules generally accepted by other children.

Eli would talk on and on about his favorite interests, such as science facts, space exploration, and cars, oblivious to the glazed looks on the faces of those around him. He could not fathom why others became upset with him. When it came time to make a decision, he would hem and haw as an avoidance tactic.

Despite these social liabilities, his teachers loved Eli. He was sweet natured, quite bright, and creative. The child was a joy to teach if the subject interested him, but otherwise he was bored at school. When he was engaged in the subject, Eli easily grasped complex information. When not interested, his lack of focus drove the teachers crazy.

On a bad day, Eli was totally unable to focus or to answer questions. It was even worse if he had stayed up late the previous night. If Eli's mind was set on a particular event, such as a school concert, and it failed to happen, the rest of the day did not go well. Even a small disappointment could ruin the rest of his day, such as when his mother accidentally sucked up his favorite feather with the vacuum.

Physically uncoordinated and unaware of his body in space, the youngster could step on those next to him or jab them in the ribs while sitting on their laps. However, he was able to ride a bicycle.

Eli shared with us that his favorite subject was computer math games. He was also fascinated by Legos. Unusually curious during our interaction, Eli bombarded us with questions. "I'm doing rocket science in my brain," the boy explained. Eli was eager to show us the exoskeleton wing covers of his ladybug key ring. He mentioned his love for sweets (sugar-free was what his parents allowed) and rotisserie chicken with the skin. Eli showed us one place on his skin that itched.

A Common Remedy for a Quirky Kid

We prescribed probably *the* most common homeopathic remedy for Eli: *Sulphur* (made from the element sulfur). We gave him a single dose in a 1M potency. It is very helpful for children who are intellectual, egotistical, and somewhat pedantic, especially in Asperger cases. The youngsters love to acquire knowledge and share their newly found wisdom freely with those around them. They're smart, learn easily and quickly, and are naturals at performing mechanical tasks. Like Eli, they are fascinated by science and by how things work in general. These individuals have a lazy, messy streak, can be know-it-alls and bossy, and their attention tends to wander. *Sulphur* patients often crave sweets and spicy foods, tend to be warm blooded, and can be prone to skin or digestive complaints.

When in Sweden, Do as The Swedes

This is a very typical case of Asperger syndrome with aspects of ADHD that most homeopaths should be able to solve easily and successfully. Our readers may be surprised because we often write about highly unusual cases and remedies. There is a reason.

We recently presented this case, along with three others, near Stockholm, Sweden, as part of a seminar honoring the 100th anniversary of the Swedish homeopathic medical society. As we wrote in our last column, homeopathic practice in Sweden has been limited since 1961. It is illegal for homeopaths to treat children below age 8 years, pregnant women, cancer, diabetes, epilepsy, HIV, and infectious diseases. Pregnant women are prohibited from using any natural therapies. Physician homeopaths have been able to recommend homeopathic medicines since 2011, but a 2013 ruling limited licensed medical professionals to patient-initiated, last-resort treatments.

There is limited availability of legal homeopathic medicines, which include only the most commonly used, or polychrest (45 or so most commonly prescribed remedies according to the old homeopathic literature). In Sweden, *Sulphur* is one of 109 permitted homeopathic medicines, as compared with modern full-scope homeopathic practice, which includes an ever-expanding pharmacopeia of more than 3500 homeopathic medicines. Because of these limitations, Bob chose to present two cases that fell within those limits, of *Sulphur* and *Nux vomica*. Judyth, one the other hand, opted to challenge those attending with two captivating cases of *Lac Leoninum* (lion's milk) and *Falco peregrinus* (peregrine falcon). We sincerely hope that the regulations regarding homeopathy in Sweden and other EU countries will soon be relaxed, to the benefit of patients and practitioners.

Six Weeks After Beginning Homeopathy

Both Eli's teacher and school bus driver reported a behavioral improvement. The child was accomplishing more done at school and seemed less distractible. He easily learned to ride his bike on sand bags without the kind of frustration or anger that he had exhibited previously. The teacher was

impressed that Eli could finish assignments and remain on task. Perhaps the biggest change was that the child spent much less time elaborating on his special interests.

During our conversation, Eli answered questions appropriately, without interrupting, and we enjoyed some normal conversational interchanges. He also responded well without interrupting others. Social interactions had improved markedly, Eli was getting along better with other children, and was even taking into account their needs. There were fewer screaming meltdowns, to the great relief of his mom. We gave Eli a second dose of *Sulphur* 1M.

Twelve-Week Follow-Up

Concentration and focus had further improved. Eli was more aware of other people, better at meeting and greeting, and considerably less self-absorbed. Eye contact and expressions of tenderness were far better. Eli's mother commented that he was much more independent. The youngster was more agile and sure on his feet, even to the point of learning basic rock climbing.

Eli's behavior relapsed after an exposure to Lysol at a neighbor's. Homeopaths see this phenomenon with some frequency in patients given single, high-potency doses of remedies after exposure to camphor, menthol, tea tree, or eucalyptus. Meltdowns returned and Eli wasn't sleeping well. We prescribed two doses of *Sulphur* 1M, one to take and the other to hold for the future.

Four Months

Reading and math skills improved steadily, as did eye contact. Now in third grade, Eli had his best start to a school year he had ever had. He could stay all day in the normal classroom for the first time. His eye contact was improved. Eli's mother marveled at his thoughtfulness. Eli shared with us: "Sometimes I think like a computer. I get a question in my brain, then I forget what I was thinking. The only thing I don't understand is subtraction." We prescribed a dose of *Sulphur* 10M to hold in case he needed it later.

Seven Months

Eli's mother had given him the *Sulphur* 10M 1 month earlier. He was now crying and blaming others quite a bit less. If he had a meltdown, it was milder, half as frequent, and much briefer. Eli related better socially, and even asked to invite other children to come over and play. Reaching out to build a friendship was a remarkable stride. When Eli went to another Asperger boy's house, the other mother noticed a huge difference. Another milestone was Eli's having attended a Christmas party of 100 people without becoming upset, something he never could have handled before. His mother commented again about Eli's increased expressions of tenderness as well, evidenced by his sweetly kissing the end of her thumb.

Fourteen Months

Eli could now tell his mom when he needed another dose of the *Sulphur* 10M. This had happened twice in the previous 6 months. He experienced brief flu-like symptoms whenever he needed a dose. Eli now had four friends. He was able to work independently and follow multistep directions at school. He had even stood up to an aide who limited his free time unjustly, and kicked a boy who bullied him at school. Overall, he was far less self-absorbed, exhibited much more kindness and generosity to others, and frequently commented, "I love you."

Eli told us quite clearly, "I'm like an active volcano. When something happens I don't really like, I erupt. I erupt, then stop, quick fast little eruptions. The most dangerous is the high-powered explosion when people are threatening me. Kapow! Choo!" How fascinating it is that volcanoes are one of the major sources of sulfur in the world! (We were able to witness this firsthand in Iceland on the way to the Swedish conference.)

Five Years

Eli has continued to do remarkably well on *Sulphur* in ascending potencies, needing a dose every 2 to 6 months. Eye contact and social interaction have drastically improved, as have his conversational skills. He has been homeschooled, can get up early in the morning to concentrate on his homework, and continues to progress in all areas. In 1 calendar year he has been able to catch up and do the work of three grades in order to bring him to his age-appropriate level.

Eli last told us, "I'm doing great. I've been reading. I've got math down, really down. Now I'm working on verbs." What a dramatic change in this young man, thanks to the gentle yet powerful effects of homeopathy!

Notes

1. The Thompson transcripts: shocking revelations by the CDC whistleblower [blog post]. Thinking Mom's Revolution. August 4, 2015. http://thinkingmomsrevolution.com/the-thompson-transcripts-shocking-revelations-by-the-cdc-whistleblower.
2. Kennedy RF Jr, ed *Thimerosal: Let the Science Speak*. Skyhorse Publishing; 2014.
3. Schwartz A. Still in a crib, yet being given antipsychotics. *New York Times*. December 11, 2015
4. Wright J. Autism's lost generation *Atlantic*. December 10, 2015

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Women's Health Update

by Tori Hudson, ND
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Skin Solutions in Women

In keeping with the theme of this month's issue, this column focuses on select skin issues in women and select writings/publications over the last several years. These selections are based on skin problems that I encounter every day in my women's health practice of over 31 years. While the list could easily include acne vulgaris, acne rosacea, atopic dermatitis, psoriasis, and more, I have chosen to highlight radiation dermatitis in breast cancer patients, wound healing after C-section, and skin aging. I hope you find the information from these abstracts as useful in your clinical practice as I have.

Curcumin for Radiation Dermatitis in Breast Cancer Patients

This small randomized, double-blind, placebo-controlled clinical trial was conducted in 30 breast cancer patients to assess curcumin's ability to reduce the severity of radiation dermatitis. Women with non-inflammatory breast cancer or carcinoma in situ and who were receiving radiotherapy were randomized to receive either 2.0 grams 3 times per day of curcumin or placebo during their course of radiation treatments. The Radiation Dermatitis Severity (RDS) score was assessed weekly along with the presence of moist desquamation, redness, and scores on the McGill Pain Questionnaire-Short Form and Symptom Inventory questionnaires. The average age of the women was 58.1 and 90% were Caucasian.

Curcumin reduced RDS at the end of radiation therapy compared with placebo. The mean RDS scores for curcumin patients were 0.8 lower than the placebo-treated patients; that is, 2.6 vs. 3.4. There were also fewer curcumin-treated patients with moist desquamation (28.6% vs. 87.5%). There were no significant differences in pain scores in total sensory pain or intensity of pain at the treatment site, and oral curcumin did not reduce erythema. Curcumin was not effective at reducing the severity of radiation dermatitis in those women who had a total mastectomy prior to radiotherapy.

Comment: Radiation dermatitis is one of the most common side effects that patients acquire from radiotherapy. It occurs in approximately 95% of women receiving radiotherapy for breast cancer, and 10% of those are severe cases. Current conventional treatments include washing with lukewarm water and mild soap, and applying unscented lanolin-free, water-based moisturizers, hyaluronate cream, and possibly topical corticosteroids. Practitioners of natural medicine have been using many options, including topical aloe preparations, topical vitamin E, and topical calendula lotion. Calendula lotion in particular has one French study demonstrating efficacy.

Oral curcumin has low bioavailability, and according to at least one publication, an oral dose less than 4.0 grams is not detectable in the blood. In the current study, patients had to take 12 capsules per day to achieve the 6.0 grams per day. There are at least 5 technologies that enhance the bioavailability and thus would then require fewer capsules. These 5 technologies include:

1. curcumin phytosome (*Curcuma longa* extract (root)/phosphatidylcholine complex; e.g., Meriva)
2. turmeric essential oils standardized for curcuminoid complex (curcumin, demethoxycurcumin, and bisdemethoxycurcumin; e.g., BCM-95)
3. water-dispersible turmeric rhizome (e.g., Theracurmin)
4. turmeric root extract with standardized curcuminoids amount combined with black pepper fruit (e.g., Turmeric Supreme)
5. turmeric root extract/curcuminoids combined with piperine (numerous products available)

Ryan J, Heckler C, Ling M, et al. Curcumin for radiation dermatitis A randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients *Radiat Res.* 2013;180:34–43.

Topical *Aloe Vera* for Cesarean Section Wound Healing

The purpose of this study was to assess the effect of *Aloe vera* gel on the healing of cesarean section wounds. A REEDA (redness, edema, ecchymosis, drainage, and approximation) scale was used to measure the wound around the incision. The score for each of those symptoms ranged from 0 to 3, with a possible maximum score of 15. Higher score equates with poorer wound healing.

A total of 97 women were initially enrolled, but 7 were lost to follow-up, leaving 45 women for each group. There was a slight but significant difference in body mass index and blood pressure between the treatment and control groups. Women were between ages 18 and 36 years old and recruited from an Iranian Hospital. They were included if they had a full-term pregnancy and had a history of 0 to 2 previous cesarean sections. Women were excluded if there were delivery complications, if there was an abnormal fetus, if there was neonatal care requiring the infant to remain in the hospital, if the cesarean section was associated with a hysterectomy, or if severe bleeding or the cesarean section lasted longer than 90 minutes.

The *Aloe vera* leaf was sliced open and the mucilaginous gel was removed and applied to the cesarean section incision, which was then wrapped in sterile gauze. Individuals in the control group received no topical treatment, but the incisions were wrapped in sterile gauze. After 24 hours post cesarean section, the sterile gauze was removed and the wound was assessed using the REEDA scale. After 9 days, individuals returned to the hospital and the wound was assessed again.

The women treated with the *Aloe vera* gel had significantly lower REEDA scores (0.0 ± 0.0) than the control group (0.6 ± 1.3) All of the patients in the *Aloe vera* treatment group (45 women) received REEDA scores of 0, while 35 women in the control group received REEDA scores of 0, 24 hours after surgery.

Comment: Some of the complications of cesarean sections are infections associated with surgical incision, slow wound healing, and hematomas. Those who are familiar with traditional uses of *Aloe vera* know that it is used topically for healing of wounds and burns. The blinding procedure of this study leaves one asking, wouldn't the patients know they were not getting an application of a mucilaginous gel? Perhaps they were not awake when the application was done. It would have been easy to have a nonmedicated type of gel as a placebo. Nonetheless, I think that this treatment is a reasonable and safe and potentially helpful strategy in improving healing of incisions from cesarean sections (and perhaps, other surgical incisions).

Molazem Z, Mohseni F, Younesi M, Keshavarzi S. *Aloe vera* gel and cesarean wound healing; a randomized controlled clinical trial *Glob J Health Sci* August 2014;7(1) 203–209.

Topical Estradiol vs. Genistein for Skin Aging in Postmenopausal Women

The primary outcome of this prospective, randomized, double-blind study was to compare the effects of estradiol and genistein treatment on hyaluronic acid (HA) concentration in the facial skin of postmenopausal women. Collagen in the dermis is associated with glycosaminoglycans, and particularly HA, which is responsible for moisturizing the skin. HA performs important functions including hydration of spaces around cells, controlling molecules that circulate in the extracellular environment by activating or guiding cell migration, and providing a link with growth factors and proteins that signal cells.

A punch biopsy of facial skin from the preauricular area was taken at baseline and after the 24 weeks of intervention. Hormonal vaginal cytology was also collected at baseline and after weeks 6, 12, 18, and 24 weeks in addition to serum estradiol levels at baseline and again at the end of 24 weeks.

Eligible participants were included if they were ages 45 to 55, 2 to 5 years postmenopausal, nonsmokers; and had FSH levels > 40 mIU/mL, serum estradiol < 20 pg/mL, BMI < 30 kg/m^2, no treatment with estrogen or soy for the previous 12 months, and vaginal and endometrial atrophy. Thirty postmenopausal women were divided into two groups: group 1: 0.01% 17 beta estradiol gel (n = 15) and group 2: 4% genistein isoflavone gel (n = 15). Women applied the gel to their faces every night for 24 weeks. In the morning, they used gel sunscreen only. They were advised to avoid all other creams.

After the 24 weeks of intervention, HA concentration increased in both groups, but the effect was greater for estradiol gel than genistein gel. There was an increase in the number of stratified squamous epithelium layers and keratinization for both groups, but the women who used the estradiol gel had better organization of connective tissue components. Serum estrogen levels were maintained below 20 pg/mL in both groups, which assured that there was no meaningful systemic absorption or systemic estrogenic effect of either the topical estrogen or topical genistein.

Comment: As menopause marches on and hypoestrogenism continues, manifestations include skin dryness, skin atrophic changes, skin aging, fragile skin, and wrinkles and furrows. This wrinkling is particularly caused by a reduction in collagen, elastic fibers, and glycosaminoglycans, especially HA, which is the largest component of the extracellular matrix of the skin. Both systemic and topical estrogen improve the collagen, which then reduces the consequences of hypoestrogenism. Estrogen also stimulates HA synthesis by fibroblasts and increases the constituents of interstitial substance components. Other studies have demonstrated the effect of topical estrogen therapy and also found positive results.

The authors of this study were hoping that genistein from soy isoflavones with its affinity for the beta-type estrogen receptors would have similar outcomes to the estrogen. The estrogen receptor beta is predominant in the skin. When using this prescription, it is important to use the dose of 0.01% estradiol gel or something consistent with previous studies, which includes 0.01% estriol; and applied once daily. Gel or cream base would be options. While the results were not as good, there was still an effect with 4% genistein gel applied daily. Given that after 24 weeks, there was no change in serum estradiol levels and vaginal or endometrial atrophy, this implies no need to oppose the estrogen with a progestational agent, although 24 weeks is certainly not the same as long-term use. I would consider a pelvic ultrasound after 1 year of use. If there was ever an episode of postmenopausal bleeding during this treatment, I would then evaluate with pelvic ultrasound and/or endometrial biopsy.

Patriarca M, Barbosa de Moraes A, Nader H, et al. Hyaluronic acid concentration in postmenopausal facial skin after topical estradiol and genistein treatment: a double-blind, randomized clinical trial of efficacy. *Menopause* 2013 Mar,20(3) 336–341.

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Essential Fatty Acids and Skin Conditions: Selected Research

The role of fish oils in skin health ranges from something as simple as improving dry skin to influencing the skin aging process to diseases such as eczema and psoriasis. A short review of the research in this area can assist clinicians and patients/consumers in targeting the optimal dosing of essential fatty acids in preventing and treating these conditions.

There are several basic mechanisms involved in why omega-3 fatty acids from fish oils in particular have such an important role in skin health: eicosapentaenoic acid (EPA) promotes the production of anti-inflammatory prostaglandins. EPA also helps to inhibit the production of androgens, which then results in a decrease of sebum production, which can have a favorable effect on acne, and EPA helps to limit production of arachidonic acid, a pro-inflammatory agent found in higher amounts in people with such skin conditions as psoriasis.

The decrease in collagen that occurs after women reach age 40 affects the elasticity and resiliency of our skin. This atrophying effect is a major factor in the aging of skin. As women age, there is a decrease in the epidermis turnover rate that accounts for the doubling of time it might take to heal a wound. With age, the cell cycle slows down and cells cannot slough off quickly enough to make way for the new cells. This is what can cause the skin to become leathery and dull and more prone to the etching of wrinkles.

Fish oil has been shown to help prevent wrinkles and delay the aging process of the skin, according to recent research published in the *Journal of Lipid Research* in 2005.[1] Researchers applied eicosapentaenoic acid (EPA) omega-3 fatty acids to human skin cells and then subjected those cells to ultraviolet radiation, simulating exposure to the sun and sun damage. Cells getting the omega-3 EPA application were more resistant to signs of damage that lead to skin wrinkling. Using fish oils to limit skin damage that leads to wrinkling, could also be relevant with UV damage and skin cancers.

The manipulation of dietary fats is extremely important in the management of both eczema and psoriasis. With psoriasis, blood levels of free-fatty-acids are typically abnormal and most of the clinical research has utilized fish oils. Individuals with eczema also appear to have altered essential fatty acid (EFA) and prostaglandin metabolism. In eczema, there is a tendency for linoleic acid levels to be increased and gamma-linolenic acid (GLA) to be low. Supplementing the diet with evening primrose, borage, or blackcurrant oil can provide gamma-linolenic acid (GLA) that can correct the underlying metabolic defect. There have been many scientific studies using GLA with excellent benefits in improving the symptoms of eczema.[2-5] Dosages in the range of 0.5 to 3 grams of GLA are appropriate. Both evening primrose and borage oils have been used in these studies, but borage oil turns out to be a much richer source of GLA and therefore more efficient and cost effective. Borage oil typically contains 20% to 24% GLA, and evening primrose oil only 8% to 10% GLA. So borage oil contains twice as much GLA as evening primrose oil and is in fact nature's richest source.

A number of studies have shown that fish oil supplements may reduce inflammation and improve the itching and scaling associated with psoriasis, although not all studies have shown successful treatment effect. In psoriasis, overactive T cells trigger immune responses and cause an increased production of healthy skin cells and more T lymphocytes. The skin cells cannot slough off fast enough and then accumulate on the surface of the skin, creating the thick, scaly patches of psoriasis. EPA and DHA from fish oils reduce inflammation and suppress the body's response to T lymphocytes.

Several double-blind clinical studies have demonstrated that supplementing with 10 to 12 grams of fish oils rich in EPA and DHA (providing 1.8 grams of EPA and 1.2 grams of DHA) can result in

Coming in the May Issue on Heart Health...

Sugar Toxicity – A Silent Epidemic

by David Edwards, MD, and Jean Malik, MD

Think you know everything about the perils of eating sugar and carbs?

Maybe not.

Edwards and Malik are concerned about the unfolding pathology that is devastating to our circulation by our current dietary laissez-faire of eating limitless sugar. While the medical community focuses on the dire consequences of cholesterol, it ignores the far more serious risks of the metabolic syndrome. An elevated glucose is concerning and an elevated hemoglobin-A1c is even more so. For Edwards and Malik, a hemoglobin-A1c of 6.4 should cause alarm.

Edwards and Malik present the horror story of microvascular atherosclerosis. This is not the plaque that you can see on angiography or by tomography. This is the stiffening of capillaries that really can't be measured. When the microcirculation develops a "sugar glaze" in the endothelium, circulation comes to a standstill. This is the pathology that brings on the heart attack, the stroke, and the gangrene in the extremities.

significant improvement in psoriasis lesions.[6–8] Individuals who have psoriasis produce many times more leukotrienes, which are inflammatory compounds. Fish oils bind to receptor sites and inhibit the production of these inflammatory compounds, thereby reducing the buildup of skin cells that have replicated too rapidly in psoriatic individuals. In one of these clinical trials, 28 patients with psoriasis were randomized into two groups, with one group receiving 10 fish oil capsules per day containing 1.8 g of EPA and the other 10 olive oil capsules per day for 12 weeks.[16] After 8 weeks, there was a reduction in itching, erythema, and scales and a decreased surface area of skin affected by the disease in the fish oil group. There were no significant changes in the placebo group.

In a negative randomized, double-blind, placebo-controlled trial, patients received 10 fish oil or olive oil capsules 3 times per day for the whole study, along with an application of a topical steroid to their psoriasis plaques for the first 3 weeks. Most of the patients had a worsening of their psoriasis after discontinuation of the topical steroid cream. There also was no apparent difference between the fish oil and the olive oil group.[1]

Intravenous infusions of fish oils emulsion have proved to be effective in treating symptoms of chronic psoriasis. In a European study of 54 men and 29 women with psoriasis, one group received 2 infusions of fish oil emulsion per day (100 ml of 10% emulsion) and the second group received 2 infusions of a placebo emulsion.[2] After 2 weeks, 16 of the patients (37%) receiving fish oil showed a 50% or greater improvement compared with only 9 patients (23%) who received the placebo.

A Japanese study combined the use of low-dose etretinate (0.3–0.5 mg/kg per day) and EPA and compared it with the high-dose etretinate.[3] The clinical trial included 40 psoriasis patients who were randomly assigned to receive either 20 mg etretinate capsules daily or 20 mg etretinate plus 1800 mg of EPA per day. After 12 weeks 45% of the patients in the combination group showed a greater than 75% improvement compared with 15% in the pure etretinate group. The combination group also achieved a 50% improvement in a shorter amount of time (5.1 weeks) than the medication only group (7.6 weeks).

Topically applied fish oil can also be an important strategy in alleviating the itching, scaling, and erythema of psoriasis. One of the main characteristics of psoriasis is an increased concentration of arachidonic acid and its metabolite, leukotriene B4, in and around psoriatic plaque. Fish oils are known to suppress the formation of leukotriene B4. Researchers in Buenos Aires investigated topical fish oil to psoriasis lesions to determine its effect on symptom management.[1] Twenty-five patients with psoriasis were randomly assigned to apply either fish oil or liquid paraffin to their psoriatic plaques and were then instructed to leave them covered for 6 hours overnight under an occlusive dressing. This treatment was repeated daily for a 4-week period. Fish oil proved highly effective in reducing scaling (on a scale of 0 to 4, an average rating of 2.91 down to 0.32), reducing plaque thickness (from a rating of 2.21 to 0.52), and erythema (from a rating of 2.71 to 0.90). The fish oil treatment had no effect on itching. While the 4-week liquid paraffin treatment was also effective in reducing erythema, it was significantly less effective than the fish oil treatment in reducing scaling and had no significant effect on itching or plaque thickness.

Essential fatty acid supplementation should also be considered to provide the skin with the proper oils and moisture, thereby preventing and reversing dry skin, preventing and reversing sun and age damage, and other environmental oxidative damage. Seed oils are known to modulate dermal properties. In one study, two groups of women ingested flaxseed or borage oil for 12 weeks.[1] The placebo group received medium-chain fatty acids. Skin reddening was diminished in both the borage and flax oil groups. Skin hydration was also significantly increased with flax oil and borage oil and transepidermal water loss was decreased by about 10% after 12 weeks of treatment. Roughness and scaling of the skin were significantly decreased with both flax oil and borage oil. None of these factors were affected by the placebo, except for hydration.

Whether it is dry skin, aging skin, eczema, or psoriasis, using supplemental EFAs in the form of specific amounts of EPA/DHA from fish oils and selected seed oils is an invaluable tool to alter the course of the condition.

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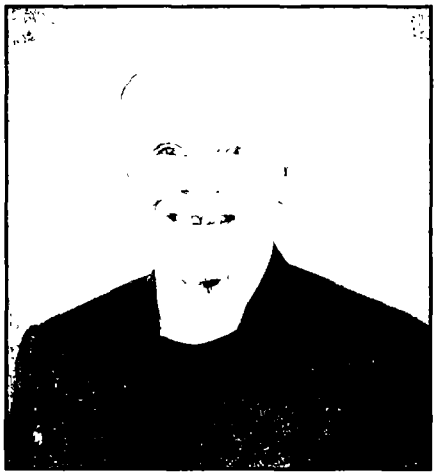

Eyes So Dry, Makes Me Want to Cry

As this issue of the *Townsend Letter* is focusing on eye conditions, it got me thinking about one of my favorite ophthalmological remedies: vitamin A eyedrops for the treatment of dry eye syndrome (also called sicca syndrome or keratoconjunctivitis sicca). In two uncontrolled trials, and 1 double-blind trial, application of eyedrops containing vitamin A resulted in improvement of dry eyes in most cases.[1–3] In another trial, vitamin A eyedrops were of similar efficacy to 0.05% cyclosporine eyedrops (Restasis) in improving tear production, blurred vision, and goblet cell density. The frequency of adverse events was lower with vitamin A eyedrops than with Restasis (4% vs. 10%).[4] In addition, vitamin A eyedrops cost only about $10 per month, as compared with about $400 per month for Restasis.

However, there is one major problem with vitamin A eyedrops: you can't get them anymore (unless you have them compounded by a pharmacist). The US Food and Drug Administration (FDA), after years of harassing the small company that was manufacturing these eyedrops, has now in effect shut them down. The story of the FDA versus vitamin A eyedrops is a classic example of how this government agency, whose job it is to protect the public, has instead harmed us.

When vitamin A eyedrops first entered the market a few decades ago, the product was called Vita-A drops. However, as told to me by the inventor of the product (now deceased), the FDA banned the sale of Vita-A drops on the grounds that the name constituted a de facto health claim. The FDA prohibits most health claims for natural products, and when "unapproved" claims are made, the agency considers the product to be a "misbranded drug," which cannot legally be sold. According to the FDA's way of thinking, there is no reason to put vitamin A in an eyedrop other than to treat an eye disorder. The public would know that a product named Vita-A eyedrops contains vitamin A, and they would assume that the vitamin was added to improve an eye disorder; ergo, the claim is in the name. After an extended legal battle and tens of thousands of dollars of legal fees, the FDA allowed the product to return to the market under a new name, Viva-Drops.

Several years passed, during which Viva-Drops were readily available and many people suffering from dry eyes were able to benefit. Then, the harassment started again. In 2011, the FDA sent a warning letter to Dakota Laboratories (the manufacturer of Viva-Drops), alleging that the company's manufacturing procedures were in violation of the current good manufacturing practice (cGMP) regulations for Finished Pharmaceuticals. An example of one of the alleged violations was:

> Your firm has not established appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile ... For example ... your aseptically manufactured products are filled into 15mL bottles; however, your process simulation studies (i.e., media fills) were conducted using 10mL and 12mL bottles which did not represent the products that would be manufactured. In your response, your firm states that two of the three media fills were successfully completed by the time the product was shipped to the customer. Your response is inadequate because you have not provided any assurances that your aseptic process was in a state of control during the manufacture of sterile drug products which were subsequently distributed.

Now, I'm not a microbiologist and I'm not an expert in the area of quality control, but while reading through the list of alleged violations, I could not help but think the FDA was purposely trying to create a scenario of "death by 1000 nitpicks." The FDA could easily have shown Dakota Laboratories how better to comply with cGMP regulations, but instead the agency apparently chose to use those regulations as a blunt weapon.

On August 26, 2013, the US Justice Department filed suit on behalf of the FDA, seeking to prevent Dakota Laboratories from producing sterile eyedrops until it addressed the alleged cGMP violations. Had the suit gone to trial, the government would have had to prove by a preponderance of the evidence that Dakota Laboratories was violating the regulations. And it is noteworthy that the FDA had not received a single report of harm related to the use of any Dakota Laboratories product. However, in order to avoid another round of massive legal fees, the company agreed to a settlement, which essentially shut it down.

So, now Allergan is happily raking in a billion dollars a year from Restasis, while we the people no longer have access to a product that works just as well, causes fewer side effects, and is much less expensive. It doesn't have to be this way.

Alan R. Gaby, MD

Notes

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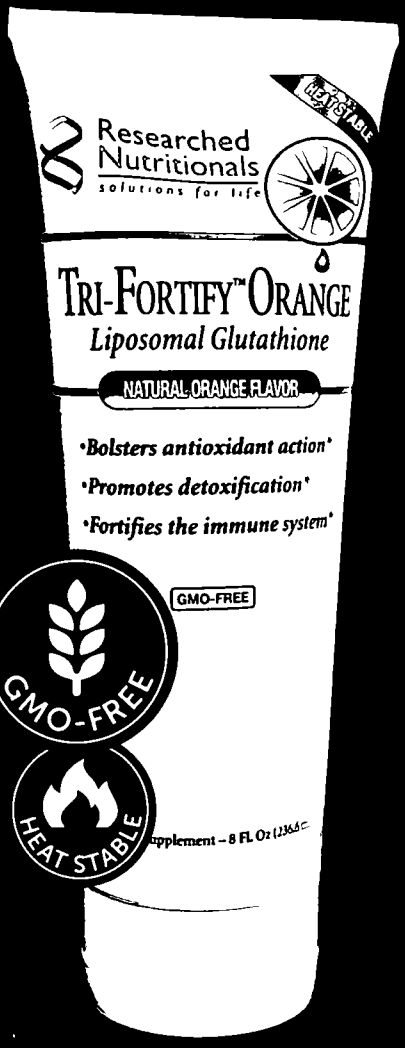

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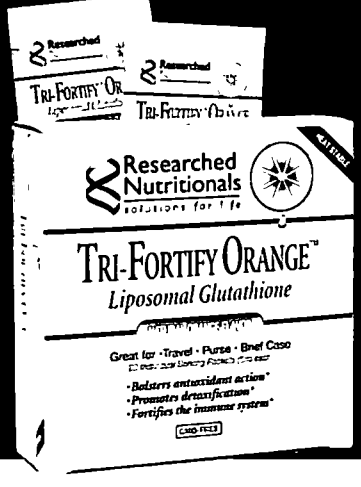

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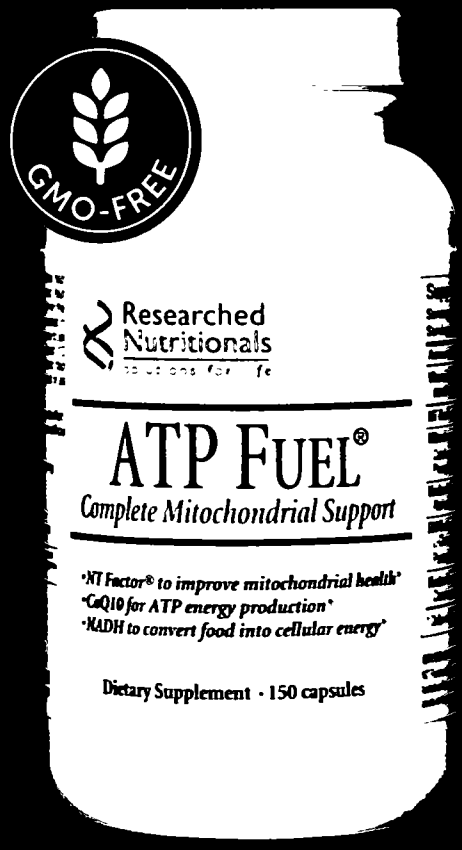

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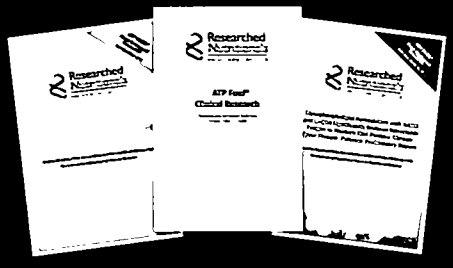

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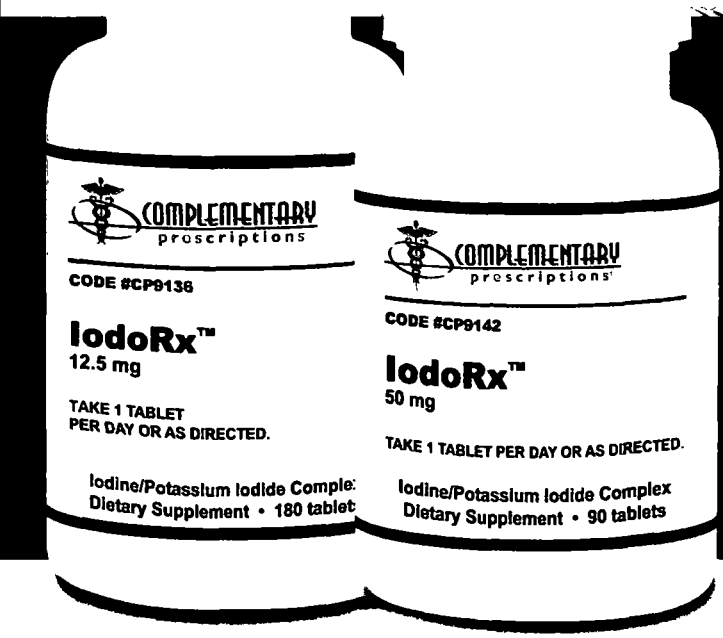

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