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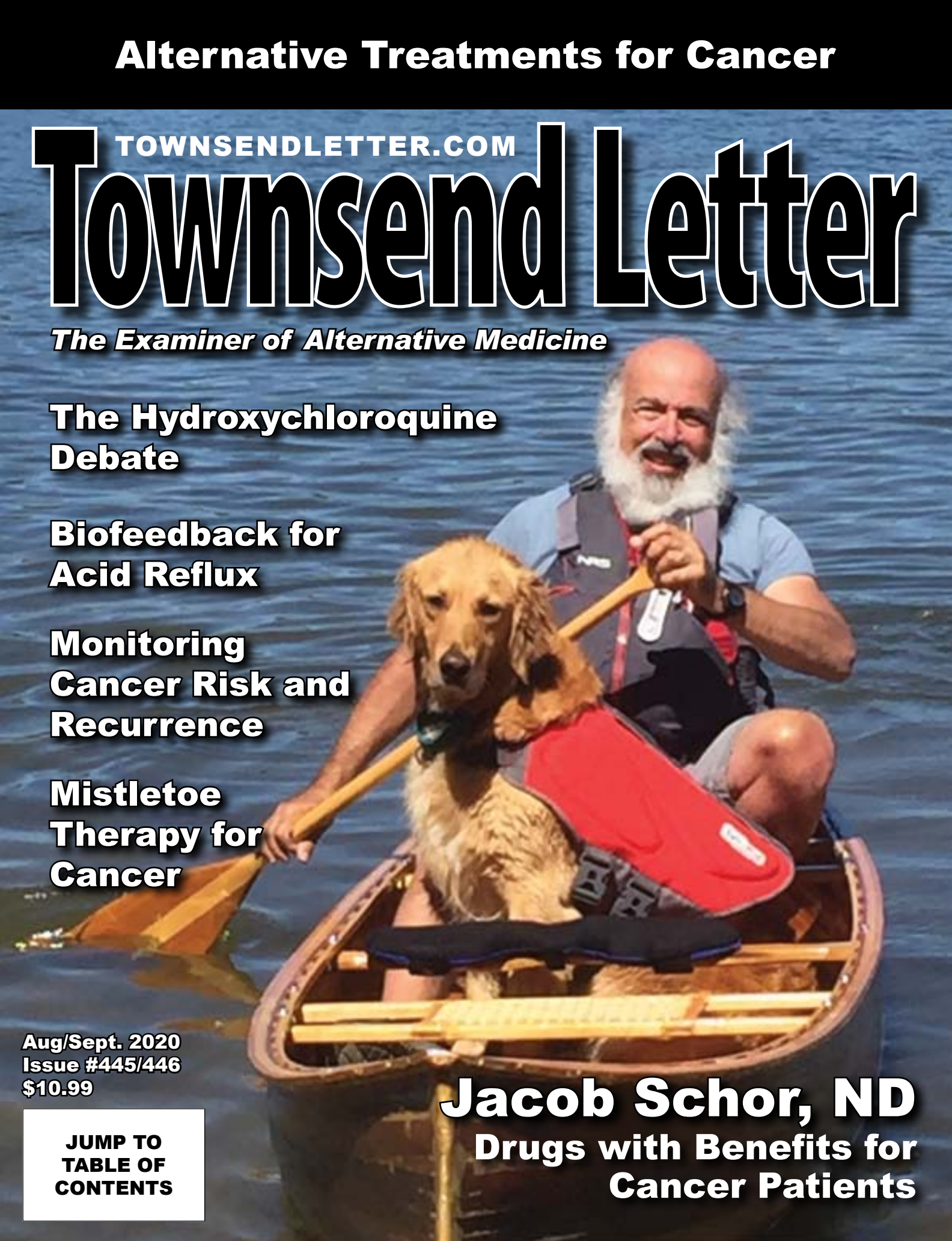

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Jacob Schor, ND

Drugs with Benefits for Cancer Patients

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From the Publisher

The Irrationality of Managing COVID-19

You wouldn't think so, but pandemic movies have been a hot item during the last several months. Imagine lying sick in bed with the SARS-CoV-2 virus experiencing all the "delights" of a virus unleashing a cytokine storm in your body while watching folks experiencing the plague on your home big screen. Movie critic Anthony Lane did just that viewing *Contagion* ("Our Fever for Plague Movies, NewYorker.com, May 15, 2020). The celebrity A-List taking part in the 2011 movie eerily mirrored much of what we have gone through this Spring; however, the flick portrayed a much more desperate scenario with food supplies disappearing entirely overnight, military personnel blocking interstate travel, folks with guns doing home invasions, and infected individuals decompensating more like Ebola victims than corona ones. (Poor Gwyneth Paltrow depicts "Patient Zero" after noshing on an infected pig in the Chinese countryside; the pigs were noshing on bat droppings.)

For those who like this sort of thing, Emma Thompson gets the rare honor of being responsible for the greatest decimation of humankind in the 2007 *I Am Legend*; her experimental cancer cure based on a genetically-engineered measles

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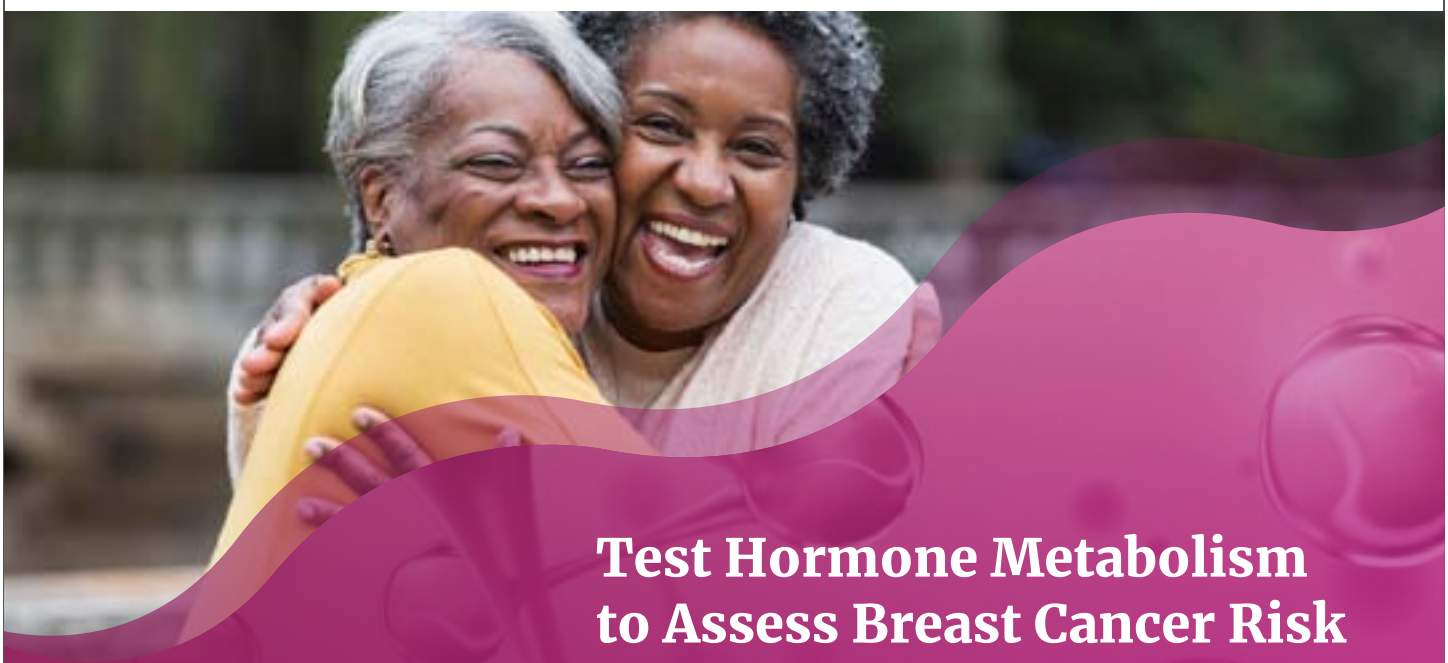

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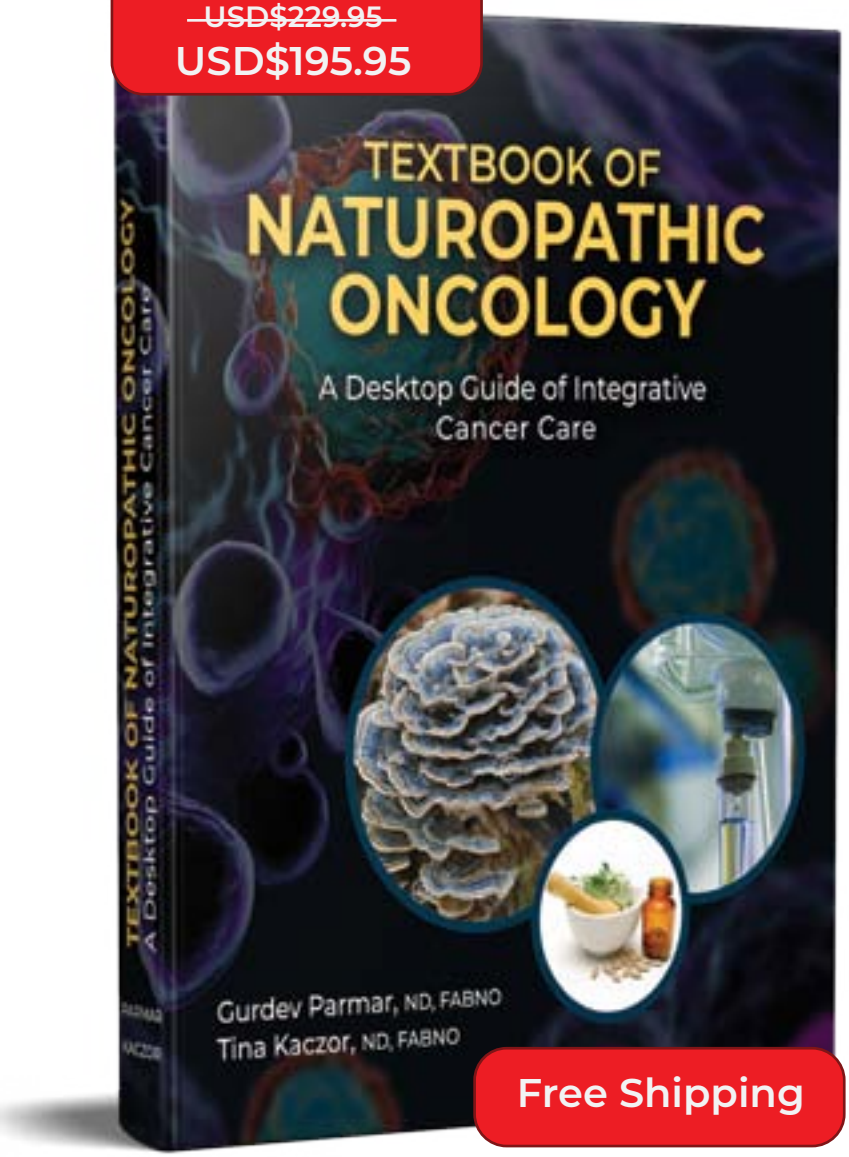

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Letter from the Publisher

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vaccine goes tragically awry decimating 3.5 billion, unleashing the ultimate population of zombies. (How's that for a plug for the so-called novel coronavirus vaccines we are being promised to be made available in the months ahead? All in?) Lane apparently survived his infection without complications – perhaps we should add watching sci-fi disease films to the treatment protocol.

It is a well-accepted tenet of economics that the wealthy are able to make hay out of any situation, good or bad, while the poor only find themselves getting even more screwed. Before the pandemic resulted in lockdown, savvy investors were shorting stocks and making fortunes. A month into the nationwide quarantine, these same day-traders were purchasing "volatility" options – not whether the stock would go up or down, but just that the stocks would wildly gyrate up and down on a week-to-week basis. Of course, the folks who have always enjoyed big tax advantages on their capital gains, hedge funds, are deeply involved now in volatility options. These individuals are actually counting on COVID-19 craziness continuing big-time in the weeks and months (and years) ahead. Why not? Aren't these captains of Wall Street entitled to make millions while the middle-class suffers and the lower-class completely goes insolvent and starves? Of course, let me not just blame rich traders, when the California Public Employees Retirement System is also betting on volatility (Banerji, G. Investors Bet on Volatility. *WSJ*. June 13-14, 2020). If you have a few bucks to make a very risky investment, you can place a bet (make an investment) on ProShares Ultra VIX Short-Term Futures ETF, traded as UVXY. Realize that you'll be betting that COVID-19 management continues to be irrational.

From my perspective, the Alice in Wonderland aspects of public health policy remains the notion that the way to control this ongoing pandemic is social isolation so that the population as a whole is not exposed to the virus. How is that possible? SARS-CoV-2 is not going away. If we are not exposed today, we will be exposed tomorrow; if not tomorrow, the day after. It is eventually going to happen. Clearly it is not going away. The big lotto prize is that we invent a vaccine, one that is likely to be genetically engineered, and that immunization will make us immune. Well, if you buy that lotteries are winnable, then you will agree to self-isolate until a vaccine appears this winter, or the next, or the next. However, if you are not a lotto man/woman, you should maintain a steady course of vitamin D, vitamin C, vitamin A, zinc, elderberry, garlic, mushroom fractions, proteolytic enzymes, get a regular IV infusion of vitamin C or Meyer's cocktail, and be socially distant as prudent. Eventually you will contract the virus. And that will be a good thing. We do need herd immunity, and that will require 70% of the population to develop antibodies. We aren't going to get there by staying at home and being couch potatoes.

And those folks who think masks are our best protection are sadly missing out on the protection conferred by using nutrient supplementation. It is a sad state of affairs that medical authorities ignore the value of vitamin C and nutrients

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Letter from the Publisher

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in preventing viral infection, but that is the intransigence of evidence-based medicine.

Is the p53 Tumor Suppressor Gene a Cancer Marker That Has Been Underutilized in Cancer Care?

Lisbon-based physician Serge Jurasunas has spent over a decade studying the role that the p53 gene plays in cancer care. Jurasunas has reviewed how the gene functions in numerous articles published in the *Townsend Letter.* In the best of times when there is no cancer, p53 signals the immune system to maintain its surveillance of cancer cells and activates metabolic pathways inducing cell apoptosis. The gene ensures mitochondrial functioning remains aerobic utilizing the Kreb's cycle for ATP production, rather than anaerobic, producing ATP by glycolysis. From Jurasunas' perspective unimpaired p53 activity makes the critical difference between the body's ability to find and shut down incipient cancer and its inability to control a malignancy that grows aggressively if the gene is defective.

For reasons that remain unclear, standard of care in oncology ignores p53 gene activity assessment. p53 activates genes such as Bax and BcL2 that are responsible for upregulating or downregulating tumor cell activity and metabolic functioning as well as growth, migration, and apoptosis. Unlike "wild-type" p53 present in non-cancer cells, a mutant form of p53 is a strongly active metabolic signaler in tumor cells. Such a mutant form of p53 induces the intensive glucose uptake needed to maintain the energetically inefficient process of glycolysis in neoplastic cells. Both p53 and mutant p53 gene activity and proteins can be measured. Elevated mutant p53 levels are associated with increasing cancer activity and tumor growth and metastasis.

In this issue Jurasunas introduces us to the role that the nucleotide-adding telomere enzyme, telomerase, plays in assessing tumor cell activity. In life-aging research maintaining cellular telomere activity is considered critical if one is to achieve longevity. Unfortunately, that same telomere preservation is critical to neoplastic cell "immortality." Unlike normal cells, cancer cell telomerase activity is prodigious and matches the activity of the p53 suppressor gene. Jurasunas measures p53 gene activity and compares it to telomerase activity. When the p53 gene activity is greater than telomerase, cancer activity is being controlled; when the p53 is lower than telomerase, the tumor is actively metastasizing.

Jurasunas has reviewed, in his earlier work in the *Townsend Letter,* how treatment can increase p53 activity using herbals and nutrients. He invites readers to further examine his work on his blog.

Cover Article: Jacob Schor, ND, Argues that Repurposed Drugs Should Be Included in Naturopathic Oncology Care

From the 1970s to late 1990s, there was a sharp schism between alternative cancer treatment and conventional cancer

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Letter from the Publisher

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management. The latter approach consisted only of surgery, chemotherapy, and radiation; the former one espoused diet, supplementation, and unapproved "treatments." For patients and practitioners there was a line in the sand – one either underwent conventional care covered by insurance or one engaged in alternative treatment, which was not reimbursable. Of course, for most patients, alternative medicine was only sought after conventional cancer treatment failed. Being in the advanced stages of cancer with widespread metastasis, most patients receiving alternative cancer care did poorly as well. Of course, a minority of patients experiencing late stage cancer did reverse their disease following alternative therapies. The hope that one could beat cancer using diet and herbals did maintain the schism between alternative and conventional camps.

In the early 2010s conventional cancer care was transformed by the introduction of novel cancer drugs targeting pathways vital for cancer cell metabolism and growth. Targeted immunotherapies for individual cancers promised to change cancer survival. At the same time research began in earnest to discover whether well-established drugs, such as metformin, might have a role in arresting cancer activity. Metformin, the most widely used drug in the treatment of diabetes as well as pre-diabetes, has been studied for its anti-cancer effect in numerous human malignancies. Similarly, other common drugs have demonstrated significant effectiveness, including aspirin, omeprazole, doxycycline, cimetidine, propranolol, coumadin, even sildenafil. (How's that for a reason to get a Viagra prescription?)

Jacob Schor, ND, has challenged our absolute sense of the propriety of naturopathic medicine and distrust of conventional medicine in his *Townsend Letter* column, Curmudgeon's Corner. Many truths that we hold sacrosanct because they have been passed down by our elders and have always been believed do not necessarily hold up under careful scrutiny. Unfortunately, evidence-based medicine does justify our reconsideration of a diagnostic or treatment that fails to be effective. Of course, some studies are faulty and should not nullify what we find valuable in our care. Schor argues that simply because an effective treatment is a drug should not automatically exclude it from the protocol we provide to our cancer patients. If the antibiotic, doxycycline, could increase our breast cancer patient's chances of survival, it should be part of the regimen. To say to the patient that the only treatment to be used is diet and herbals is a disservice.

It is 2020 and the schism between natural medicine and conventional medical care is over. We need to employ the best of both in cancer treatment.

Jonathan Collin, MD

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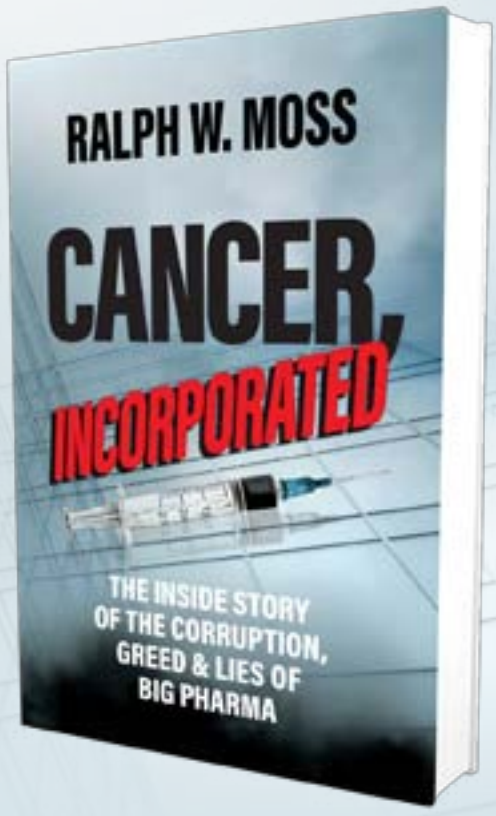

Immunotherapy: The Battle Within

by Ralph W. Moss, PhD©2020

Over the past year and a half, I have been working as the writer and narrator of an hour-long documentary, *Immunotherapy: The Battle Within*. Creating this film has been a three-generation affair, with my son, Ben Moss, serving as producer, and my grandson, Jacob Moss, directing, filming, and editing the film. The overall project has been co-sponsored by the Center for Integrative Oncology and Moss Reports.

This film shows how cancer itself often involves an internal fight within the patient between rogue cancer cells and one's own immune system – a "Battle Within." But that internal battle also refers to a struggle within science, spanning more than a century, over the fundamental direction of cancer treatment.

There are three basic elements to the film. We certainly acknowledge the importance of modern-day immunotherapy, with excerpts from our interview with James P. Allison, PhD, co-recipient of the 2018 Nobel Prize for his discovery of immune checkpoint inhibitors. But long before its acceptance by mainstream medicine, immunotherapy survived as a popular complementary or alternative approach to cancer.

We remind our viewers of the controversy over the treatment of cancer by Lawrence Burton, PhD, of Freeport, The Bahamas, which I discussed on *60 Minutes* in 1980. We then take the viewer on a tour of European cancer clinics that practice innovative forms of immunotherapy. These include clinics in Vienna, Austria, and Duderstadt, Cologne, and Prien, Germany. Each of these practices a unique form of treatment, sometimes including the use of hyperthermia (heat therapy) and immune-stimulating drugs, such as mistletoe and interleukin-2. We then fly back to the United States to tour American cancer clinics that practice non-conventional approaches to immunotherapy.

A continuous presence in the film is the Coley family, the unsung heroes of cancer immunotherapy. This includes William B. Coley, MD (1862-1936) and his daughter, Helen Coley Nauts (1907-2001).

In their remarkable careers, spanning over a century, they showed that the injection of a mixture of two bacterial byproducts (popularly called "Coley's toxins") could have a profound effect on the progression of cancer. While Coley's contribution to immunotherapy is often given lip service today, Mrs. Nauts is almost totally unknown. Yet she systematically tracked down and published the outcome of all known cases of cancer treated with her father's treatment – more than a thousand individuals! A surprising number of these had long remissions, which were sometimes tantamount to a cure.

In 18 detailed monographs and numerous papers, Mrs. Nauts and her medical co-authors compiled a record of Coley toxin's successes – as well as its failures – over a period of 110 years from the 1890s to Mrs. Naut's death in 2001. It would require a book of its own to fully explain the scope of this treatment.

Mrs. Nauts also identified the factors that greatly increased the likelihood of a favorable outcome. This represented a valuable intellectual heritage, a heritage that is now in danger of being totally lost through not-so-benign neglect. One purpose of the timely documentary is to rescue Coley's toxins from the frequent misrepresentations one finds on the internet and in popular books on cancer.

Immunotherapy: The Battle Within shows the enormous promise of enhancing and mobilizing the immune system in the fight against cancer. It is a battle that has been waged for over a century. But the full story of its development has never been told before in such an exciting and engaging way.

The film should be released by the publication date of this issue of *Townsend Letter*. You can watch the film and find out more at https://www.immunotherapyfilm.com.

◆

Emerging Development of *Viscum album* Therapy and "Best Practices Training"

By Dr. Steven M. Johnson, DO, and Dr. Nasha Winters, ND, FABNO

Mistletoe or *Viscum album* extracts (VAEs) represent a potential salutogenic paradigm for the modern practice of clinical oncology. VAEs are demonstrating multifaceted therapeutic outcomes. For instance, heightened immune editing and apoptosis of tumor cells, as well as diverse palliative care and quality of life benefits, were demonstrated in 22 out of 26 controlled research trials with minimal evidence of serious side effects or drug interactions, even at high infusion doses. There are now over one hundred studies on the effects of VAEs in animals and humans. Interest in the adjunctive role of VAE treatment is steadily growing, and individual case studies continue to support efficacy in the clinical setting.

VAE applications have expanded and evolved a great deal in Europe and the United States over the last two decades. Interest has also spread to over 21 countries around the world. Celebrating a one-hundred-year anniversary alongside Anthroposophic medicine, we are seeing resurging interest in VAEs supported by higher-quality controlled research trials. There was a great deal of discussion about VAE research during the past Society for Integrative Oncology (SIO) meetings, and several suggestions to improve mistletoe research in the future were outlined there. Currently three new trials are in progress involving pancreatic and bladder cancer via bladder infusions of VAE.

The field of precision and translational medicine is well suited to the implications and applications of mistletoe therapy in standard, integrative, and vitalistic healthcare models. Taking biological and physiological principles, validated with evidence-based and evidence-informed research, from the bench to the bedside and to the community is key to changing healthcare in general and cancer care in particular by moving beyond a single target and treatment into a more comprehensive, individualized approach.

At a time when the real overlooked pandemic is a cancer diagnosis killing more than 1600 people per day in the US alone and expected to impact nearly 50% of us in our lifetime worldwide, and where the needle on the dial has barely moved with regards to cancer statistics and outcomes, it is time to take a more integrative and innovative approach to how we care for the terrain beyond the tumor.

The use of mistletoe in medicine dates back to the Greek physician, Dioscorides (40-90 AD) though it was Hippocrates (460-377 BC) and his students that applied it to treat diseases of the spleen and complaints associated with menstruation. It has long been used as a plaster to reduce pain, swelling, carcinoids, scrofula and abscesses, and has a warming, softening, and astringent quality. In modern times, Dr. Ita Wegman, the first woman to study and practice medicine in Switzerland, began to treat cancer patients in Zurich with mistletoe injections in 1917 and was the first to use it specifically for tumor treatment at a time when chemotherapy was not available (and wouldn't be until after WWII) and surgery and radiotherapy were regarded as brutal and barbaric.

Rudolf Steiner, the founder of Anthroposophy who observed three years of Dr. Wegman's clinical outcomes, formally recognized mistletoe as a cancer therapy in 1920, making this year the 100th birthday. Mistletoe has since been studied extensively with various results suggesting positive outcomes from improved quality of life, lowered cancer fatigue, maintained bone marrow function throughout standard of care treatment, lowered angiogenesis and inflammation, and immune system regulation with stimulation of apoptosis and NK cell function to name a few. VAE has proven to work beneficially via both the innate and adaptive immune response.

An excellent book regarding its history, mechanism of action, and medicinal constituents is *Mistletoe: From Mythology to Evidence-Based Medicine* edited by K.S. Zanker and S.V. Kaveri. This small primer, published in 2015, gives a glimpse of this powerful substance. A more comprehensive book – bringing in more clinical relevance and deeper dive into the immune system, status of research around the world (in particular in the US), and modernized applications and integrations with other therapies – is currently in the works with an expected release by Christmas time! How apropros!

Though widely used around the world as an adjuvant therapy in cancer care, it still falls into obscurity in the United States. A Phase I clinical trial on subcutaneous application for safety along with Gemcitabine was published in 2013, showing it to be well tolerated; no botanical/drug interactions were observed, and clinical response was similar to Gemcitabine alone.[1] It remains elusive and difficult to obtain for patients in the US. Currently, at Johns Hopkins University, a Phase I clinical trial is underway using intravenous application of mistletoe[2]; and though results are preliminary, it is promising in safety as well as improved clinical outcomes with expectations of moving through Phase II and III.

In addition to the Johns Hopkins and other clinical trials, the pending book publication, and a growing number of patients and practitioners requesting access to this traditional, yet novel therapy here in the United States, there has been a clear lack of standardized quality education for the physician. That has changed over the last few years with an international Helixor-sponsored (a German VAE manufacturer) training program for physicians every other year in Germany. Also, currently a collective of seven expert

faculty members from around the world have developed a diverse curriculum "best practices" mistletoe and integrative oncology course, teaching how to use basic and advanced European clinical methods of mistletoe application alongside conventional and integrative oncology strategies. **The next course is open for enrollment to be held in Denver, Colorado, October 15-18, 2020**.

In a world that has seemingly experienced more separation and isolation over the years, with more divisiveness in politics and medicine, it is refreshing and hopeful to see a plant medicine unify Anthroposophic-trained MDs, naturopathic doctors and other allied health professionals as we share in the vision of better quality of life and clinical outcomes for our patients who may be met with a cancer diagnosis and treatment in their lifetimes.

The scientific studies and the deep traditional foundations of salutogenic thinking that lie behind the VAEs are a clear opportunity to bridge the science and art of medicine back together. How many of us as physicians would welcome the opportunity to bridge these paradigms in a dynamic and rational way for both our patients and ourselves? The training course this coming October will be a special opportunity to meet with other colleagues to learn and share about this emerging integrative paradigm for the future.

The uses in Europe have expanded with new approaches to administration methods that extend beyond the well-known subcutaneous applications. While some physicians are trying to market oral forms of this medicine, it should be mentioned here that there is "no" good clinical evidence of efficacy on specific tumor types. Researchers have worked diligently to keep the integrity of VAE therapy intact, without allowing it to succumb to false claims and marketing methods.

The "best practices" course mentioned above is an attempt to maintain standards of responsible and effective clinical care for our patients and to offer everyone the highest chance of good therapeutic outcomes, hopefully generating a larger body of case studies in the future. Also, it is an intention to review up-to-date research and to be open to new emerging applications that have merit and need further study.

For information on ordering the recently translated (German to English) Mistletoe Vademecum, which gives a wide oversite of the Viscum therapy, as well as access to other training materials and research websites, please visit https://anthroposophicmedicine.org/Mistletoe and fill out the materials request form. This is available to all licensed clinical practitioners. Additional information is also available at https://www.mistletoe-therapy.org/.

A lot has evolved since many of you may have read about VAE therapy in the past. We hope this short review will inspire both new and experienced clinicians to consider exploring this special and evolving paradigm of integrative oncology support. We invite you to get to know the properties of this fascinating medicine and to offer the benefit of improved clinical outcomes and quality of life for your patients.

Dr. Nasha Winters, ND, FABNO, is a global healthcare authority in integrative cancer research. She is co-author of the best-selling *The Metabolic Approach to Cancer*, which has received many accolades, and is a co-facilitator of *Viscum album* extract training in the US. www.drnasha.com

Dr. Steven Johnson, DO, has lectured frequently in Europe and the United States on integrative medicine and oncology, with a focus on mistletoe therapies, biological and nutritional modalities, as well as running a large integrative medical clinic for 14 years. He is currently the president of the Physicians' Association for Anthroposophic Medicine and a consultant for Uriel Pharmacy.

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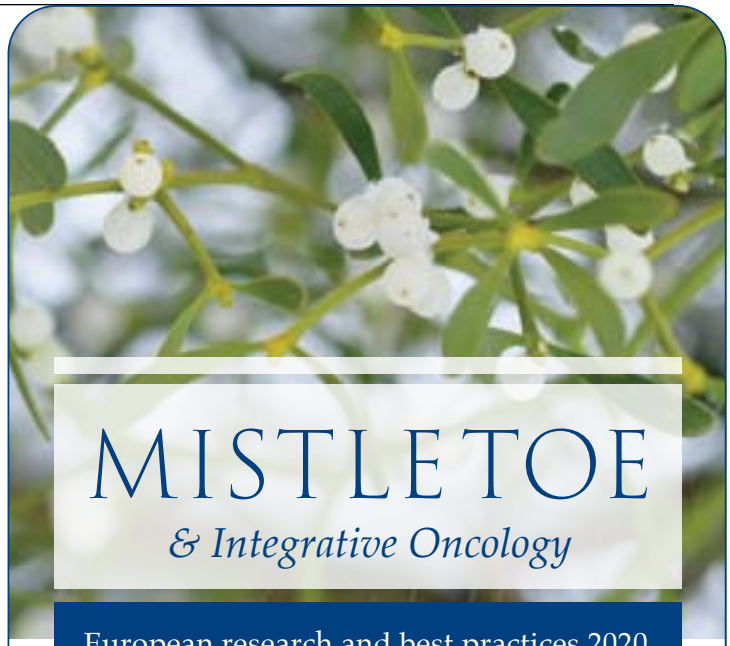

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Vitamin C Saves Wuhan Family from COVID-19

by Richard Cheng, MD, PhD
Orthomolecular Medicine News Service

Ms. N lives in Wuhan, China. She takes special care about the well-being of her entire family, including her chronically ill mother, aged 71. Ms. N has always been interested in nutrition, and she recently learned about vitamin C's antiviral effects.

I am an American physician currently residing in Shanghai. I interviewed Ms. N by telephone after I received a forwarded story that she posted on Chinese social media, WeChat. I made an effort to connect with Ms. N to verify the story and below is what she told me.

Ms. N lives with her child in the epicenter of COVID-19 pandemic. She is close to her parents and her brother and his wife. The six of them visit each other on a regular basis. Her mother has diabetes and heart disease with stents placed, in addition to several other chronic illnesses, including reflux esophagitis.

Right before the Chinese New Year, around January 21st, her mother developed flu-like symptoms with a low-grade fever of 38C. Based on her knowledge. Ms. N advised all members of the family to take oral vitamin C. She herself has been taking about 20,000 mg daily in divided-up doses. Her mother reluctantly took a smaller dose, probably half or less of what her daughter's been taking.

Her mother's condition was stable for 9-10 days. But on January 30th, without deteriorating, her mother decided to go to Wuhan Union Hospital, a hospital prominent not only in Wuhan, but in all of China. She wanted to check out if she was infected with the Wuhan pneumonia virus. At the hospital, she was diagnosed with what is now known as COVID-19 pneumonia. The second day upon admission, her fever started going up, as high as 39.6°C. In about 10 days on February 10th, she was admitted to the intensive care unit and went on the heart-lung machine as a final attempt to save her life.

At this time Ms. N learned of the clinical trials with vitamin C, administered by infusion (IVC; intravenous vitamin C). Immediately she requested the person in charge on the ICU to use large dose IVC on her mother. The attending physician agreed but would go only to around 10,000 mg. After 20 days in ICU, her mother improved and was discharged to a regular ward, continuing the IVC treatment, as insisted by Ms. N.

While in hospital, Miss N, her brother, and sister-in-law took turns to visit and take care of her mother. They were wearing very simple protection: gloves and masks. Also noted is that while her mother got sick at home, none of the five other family members was wearing any mask for several days. But all of them went on oral vitamin C tablets. None of them developed COVID-19 infection.

I summarize the story below with a few take-home messages:

- Vitamin C tablets at high doses daily may be the reason why the family didn't catch the infection.
- Given her age, history of chronic disease, and the high mortality of COVID-19 on seniors, IVC may have played a large role in her mother's improvement.
- The news of official IVC clinical trials has definitely had a positive impact in this case, as the attending physician was emboldened to use IVC.
- A well-functioning immune system is of the utmost importance to keep away the viral infection. And, vitamin C may support the defense against the COVID-19 virus, most importantly in chronically ill patients with a weakened immune system.

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Abridged Articles

Notice: To get more articles published in the print magazine we need to abridge some articles and print references online.

Abridged Articles in August/September 2020 Issue:

"Estrogen Vindication" by Devaki Lindsey Berkson, DC
"Can Acid Reflux Be Reduced by Breathing?" by Eric Peper, PhD, et al.
"The Curcumin Conundrum" by Douglas Lobay, ND
"Cancer Update" by Prof. Serge Jurasunas, ND

Plasmanex1 – A Functional Food for Metabolic Disorders

by Fred Pescatore, MD

Abstract

Natto, soybeans fermented with natto bacteria, is a specific fermented food that has been regularly consumed in Japan for many years. The health-supportive effects of natto has attracted growing attention in recent years. In order to evaluate the effect of Plasmanex1, a functional food derived from *Bacillus subtilis* var. *natto*, on metabolic disorders, Plasmanex1 capsules were administered to 13 subjects with metabolic disorders at one capsule twice/day (Bacillopeptidase F Proprietary Blend (BFPB) 250 mg/day) for 12 weeks. The results of this study showed that total cholesterol, LDL cholesterol, and triglycerides were significantly reduced, and significant decreases in fibrinogen were observed. These results suggest that this product may possess lipid-metabolism improvement and blood-flow-viscosity reduction activities. Additionally, significant decreases were also observed in HgbA1c, hs-CRP, and body weight, suggesting that it has anti-diabetic, anti-inflammatory, and body-weight reduction potentials.

Introduction

Metabolic syndrome, variously known also as syndrome X, insulin resistance, etc., is defined by WHO as a pathologic condition characterized by abdominal obesity, insulin resistance, hypertension, and hyperlipidemia. With the successful conquest of communicable infectious diseases in most of the world, this new non-communicable disease (NCD) has become the major health hazard of modern living. Though it started in the West, with the spread of the Western lifestyle across the globe, it has become a global problem.

The two basic forces spreading this malady are the increase in consumption of high calorie, low fiber fast food and the decrease in physical activity and increase in more sedentary forms of leisure time activities.

The syndrome feeds into the spread of diseases like type 2 diabetes, coronary diseases, stroke, and other disabilities. The total cost, including the cost of health care and loss of potential economic activity, is in the trillions. The present trend is not sustainable unless a magic cure is found (unlikely) or concerted global/governmental/societal efforts are made to change the lifestyle that is promoting it. Revitalizing old fashioned healthier lifestyle, promoting old-fashioned foods using healthy herbs rather than oil and sugar, and educating people about choosing healthy/wholesome food over junk are among the steps that can be considered.

Metabolic syndrome is defined as the presence of any three or more of the following:

- Blood glucose greater than 5.6 mmol/L (100 mg/dl) or drug treatment for elevated blood glucose
- HDL cholesterol <1.0 mmol/L (40 mg/dl) in men, <1.3 mmol/L (50 mg/dl) in women or drug treatment for low HDL-C
- Blood triglycerides >1.7 mmol/L (150 mg/dl) or drug treatment for elevated triglycerides
- Waist >102 cm (40 inches) (men) or >88 cm (34.5 inches) (women)
- Blood pressure >130/85 mmHg or drug treatment for hypertension

The global prevalence of metabolic syndrome is estimated to be about one quarter of the world population – so over 1 billion people are now affected with metabolic syndrome.

Natto, soybeans fermented with *Bacillus subtilis* var. *natto*, is a traditional Japanese fermented food. Natto contains a wide variety of peptides, amino acids, and vitamins. Because of these properties, natto has attracted much attention in the nutraceutical field. A recent cohort study in Japan on the effect of fermented soybean food on mortality reported a direct correlation between the greater consumption of fermented soybean food (natto) and lower mortality rate.[1] This effect was not observed in non-fermented soybean foods. Examples of fermented soybean foods eaten in Japan include natto and miso, and both are attracting greater attention as functional foods. ➤

Table 1. Effects of Plasmanex1 on blood parameters and body weight

Parameters	Normal Range	Baseline ave. ± SD	End ave. ± SD	p (paired t-test)
Total cholesterol (mg/dL)	130-220	231.8 ± 42.5	207.2 ± 32.0	0.0056
HDL (mg/dL)	46-65	65.3 ± 19.4	62.4 ± 16.3	0.1895
LDL	60-140	139.7 ± 34.9	122.2 ± 28.6	0.0178
Triglycerides (mg/dL)	50-149	140.3 ± 131.8	89.7 ± 65.9	0.0336
Fibrinogen (mg/dL)	200-400	415.2 ± 72.0	383.3 ± 75.2	0.0442
HgbA1c (%)	4.6-6.2	5.89 ± 1.60	5.34 ± 0.84	0.0369
hs-CRP (mg/dl)	0.3-0.5	2.334 ± 1.881	1.159 ± 1.144	0.0045
Body weight (pound)	—	187.4 ± 34.3	171.1 ± 34.8	1.9×10^{-8}

Plasmanex1

➤

Plasmanex1 is a functional food containing bacillopeptidase F (BFPB), which is a serine protease produced by *Bacillus subtilis* var. *natto*. BFPB is reported to possess anticoagulant, blood-viscosity reduction, and thrombolytic activities.[2,3] This substance is also shown to lower blood pressure and to improve shoulder stiffness, low back pain, and coldness in extremities, in a study on patients with lifestyle diseases.[4,5] Additionally, a clinical study on healthy subjects, with no underlying pre-existing health conditions demonstrated that BFPB improved headache, reduced muscle stiffness, and increased skin surface temperature, demonstrating that this substance possesses blood-flow-improving capability.[6] In this study, we examined total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride, ESR, fibrinogen, HgbA1c, high sensitivity CRP (hs-CRP), and body weight, in order to evaluate the effect of Plasmanex1 on patients with metabolic syndrome.

Methods

Test design was an open study on 13 subjects with metabolic disorders (5 males, 8 females, age range 19 to 78 years, average age 47.7). Plasmanex 1 was administered at 1 capsule twice per day (BFPB 250 mg/day) for 12 weeks. Total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride, fibrinogen, HgbA1c, hs-CRP, and body weight were measured at baseline and at the end of the study period. All patients were given adequate information about the trial and the study product to allow them to provide informed consent prior to the study. The acquired data was statistically processed by t-test which was applicable, and p-value was regarded as significant at < 0.05.

Results

The results of the study are shown in Table 1 (page 13). Total cholesterol, LDL cholesterol, and triglycerides were significantly reduced. Total cholesterol was reduced in 10 of 13 subjects. Of seven subjects whose total cholesterol level was higher than the normal range at baseline, three subjects showed decreases to within the normal range. LDL cholesterol was reduced in nine subjects. Of six subjects whose LDL cholesterol level was higher than the normal range, four subjects showed decreases to within the normal range.

Fibrinogen was reduced in nine subjects. Of six subjects whose fibrinogen level exceeded the normal range at baseline, four subjects showed decreases to within the normal range after the study period.

Furthermore, HgbA1c, hs-CRP, and body weight significantly decreased. Among the 13 subjects, a decrease in HgbA1c was seen in 10 subjects, in hs-CRP for 10 subjects, and in body weight for 13 subjects, respectively.

Discussion

Total cholesterol, LDL cholesterol, and triglycerides were significantly reduced, suggesting that Plasmanex1 possesses lipid-metabolism-improving potentials. A significant decrease in HgbA1c was observed, suggesting its potential in diabetes and pre-diabetes. A significant decrease in hs-CRP was also observed, suggesting its anti-inflammatory potential. Furthermore, body weight was significantly reduced, suggesting its body-weight reduction potential.

This study was a small-scaled, open test, and further research is required. However, this study suggests that Plasmanex1 possesses lipid-metabolism improvement, blood-viscosity reduction, anti-diabetes, anti-inflammatory, and body-weight reduction potentials, and can contribute to improvement of metabolic disorders and metabolic syndrome.

While it is still necessary to be acutely aware of communicable diseases, this modern era is markedly characterized by lifestyle diseases. Lifestyle diseases are defined as diseases linked with the way people live their life. These are non-communicable diseases. This is commonly caused by lack of physical activity, unhealthy eating, alcohol, drugs, and smoking. Diseases that mostly have an effect on our lifestyle are heart disease, stroke, obesity, and type II diabetes.

Plasmanex1 appears to have properties that can contribute to curbing the metabolic biologic markers associated with our current lifestyles. Further research is needed to ascertain who are the best candidates and including a dietary trial along with Plasmanex1 to see if the outcomes are even stronger.

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Fred Pescatore, MD. MPH, CCN, is a Manhattan-based traditionally trained physician and internist who specializes in nutritional medicine. He is a globally renowned health, nutrition, and weight loss expert, as well as the author of seven books, including the *New York Times* bestsellers *The Hamptons Diet* and newly released *The A-List Diet*. He is the president of the International and American Association of Clinical Nutritionists and a member of the College for the Advancement of Medicine. Dr. Pescatore's extraordinary background in complementary medicine led him to open his globally recognized medical center, Medicine 369, in New York City. The rapidly expanding practice is credited as one of the most effective and successful integrative medical centers worldwide. He has studied in America, Southeast Asia, India, Japan, Africa, and Europe and is sought after as one of the frontline educators and visionaries improving health care and human life.

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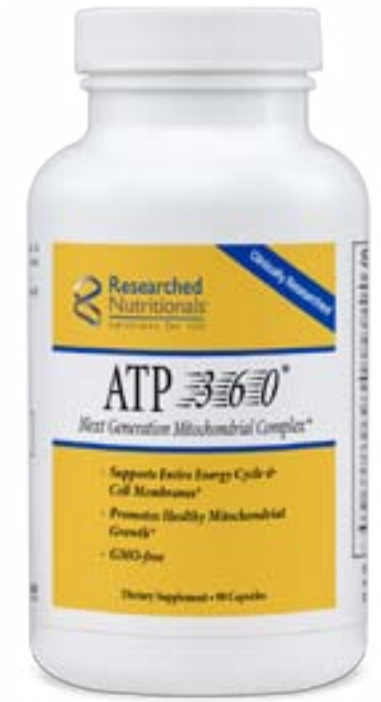

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ON THE COVER: Jacob Schor, ND – Drugs with Benefits for Cancer Patients (pg. 28); Biofeedback for Acid Reflux (pg. 44); Monitoring Cancer Risk and Recurrence (pgs. 40 and 58); Mistletoe Therapy for Cancer (pg. 10); The Hydroxychloroquine Debate (pg. 96)

Shorts

briefed by Jule Klotter
jule@townsendletter.com

Questions About CPIs and Immunotherapy

"Why do the majority of patients not respond at all, or only partially or transiently, to immunotherapy?" asks Angus G. Dalgleish in a recent *Expert Review of Anticancer Therapy* editorial. Dr. Dalgleish is a professor of oncology at St George's University in London, United Kingdom. For over two decades, he has investigated the use of biological substances to increase the body's immune response against cancers. The field of immunotherapy has expanded far beyond the use of killed bacteria, like William Coley's toxins, and now includes cytokines (e.g., interleukin 2), and checkpoint inhibitors (CPIs), such as pembrolizumab (Keytruda), Ipilimumab (Yervoy), and atezolizumab (Tecentriq). "The response to immunotherapy is often dramatic but relatively uncommon," Dr. Dalgleish writes, "and until recently difficult to improve upon."

Checkpoint inhibitors (CPIs), which are monoclonal antibodies, have increased survival of some people with melanoma and some other cancers. Immune checkpoints are molecules on certain immune cells that need to be activated (or inactivated) to start an immune response, according to the American Cancer Society website. Some cancer cells develop ways to use these checkpoints to prevent immune system attack. For example, the checkpoint protein PD-1 found on T-cells works as an off switch; when that protein attaches to a protein (PD-L1) on another cell's surface, it protects the cell from attack: "Some cancer cells have large amounts of PD-L1, which helps them hide from an immune attack." Unfortunately, CPIs have "significant toxicity," according to Dalgleish. Adverse effects include diarrhea, inflammation of the lungs, rashes, itchiness, hormonal effects, and kidney infections.

After years of trying to figure out why some patients respond to immunotherapy and others do not, Dr. Dalgleish and colleagues came to realized that non-responders show more biomedical signs of inflammation before treatment: "…whereas there is no single predictive biomarker to predict possible patient response to a CPI-based treatment, there is an exciting trend that a signature of several chronic inflammatory markers is associated with non-responsiveness."

Chronic inflammation causes cell mediated immunosuppression and increased angiogenic and wound healing activity, making it more difficult for the body to fight cancer. Dalgleish and colleagues have begun to investigate the use of non-steroidal anti-inflammatory agents and immune modulators before using checkpoint inhibitor treatment.

Gastrointestinal microbiome composition is another, perhaps related, factor that affects a patient's response to CPI treatment. In some cases, CPI response has improved after the patient receives fecal transplants. Dalgleish notes that a healthy microbiome is associated with a healthy diet and less inflammation.

Dalgleish and colleagues have also observed that patients who had received treatment with the immune modulator IMM-101 had a faster and better response to subsequent CPI treatment. IMM-101 a heat-killed *Mycobacterium obuense* preparation, provokes innate immune activity (i.e., NK cells and gamma delta T-cells).

"The sequence of treatments may be more important than combination," Dalgleish writes, "…and this may well apply to any treatment that activates and sheds antigens, such as radiotherapy (RT) ablations and certain chemotherapy regimens." In addition to using anti-inflammatory agents and immune modulators to prime the body before using CPIs, Dalgleish says that CPI dosage needs to be investigated: "…more is not always better, a situation that has not been fully explored with CPIs, given that overweight patients seem to do better with CPIs in a number of cancer types, compared to their non-overweight counterparts."

A clinical trial with unresectable stage III and stage IV melanoma patients is underway to investigate the use of IMM-101 before CPI treatment (NCT03711188).

Dalgleish AG. Why do the majority of patients not respond at all, or only partially or transiently, to immunotherapy? *Expert Review of Anticancer Therapy.* 2019;19(12):1001-1003.

Fasting and Vitamin C for Cancer

In vitro and mouse studies indicate that a fasting-mimicking diet (FMD) increases the anti-cancer effect of high-dose vitamin C therapy in KRAS-mutated colon cancer, according to a 2020 study. The team of Italian and US researchers report that the diet-vitamin combination delayed tumor progression in mice injected with KRAS-mutated colon cancer cells. The KRAS (or K-RAS) gene produces a protein that has a role in cell growth, maturation, and death. These mutant cells are more susceptible to vitamin C's anti-cancer effects than KRAS wild-type cancer cells. Mutated forms of this gene have been found in colon cancer, non-small cell lung cancer, and pancreatic cancer.

KRAS-mutant cancer cells need iron to grow and proliferate. The fasting-mimicking diet inhibits vitamin C-induced heme-oxygenase-1 (HO-1) upregulation in KRAS-mutant cells. HO-1 is an enzyme that degrades heme to iron, carbon monoxide, and bilirubin. By inhibiting the cancer cells' access to iron, the

diet makes KRAS-mutated cells more susceptible to vitamin C's anticancer effects. Fasting/FDM can also sensitize cancer cells to chemotherapy, according to laboratory studies. The researchers say: "Of note, the FMD + vitamin C combination was as effective as oxaliplatin + FMD or oxaliplatin + vitamin C….Moreover, triple treatment (FMD + vitamin C + chemotherapy) was the most active therapeutic intervention in delaying tumor progression…and extending survival" in the mice.

The question is whether a fasting-mimicking diet and high-dose vitamin C, both of which have low toxicity, will have the same effect on humans. Randomized clinical trials involving patients with KRAS-mutated colorectal and, possibly, other tumors are needed.

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Metformin in Non-Diabetic Cancer Patients

Metformin, an oral medication for type 2 diabetes, has shown a number of anti-cancer mechanisms in laboratory studies, including mTOR inhibition, cytotoxic effects, and immunomodulation. In addition, observational studies have shown decreased cancer risk, improved response to cancer therapy, and lower all-cause mortality in cancer patients who take the drug for diabetes. Studies are now being conducted to see if metformin has the same benefits for cancer patients who do not have diabetes. At this point, "the results are controversial," write Kailin Chen and colleagues in their 2020 review article.

A few studies indicate that metformin may help prevent colorectal and endometrial cancers in nondiabetic people. A randomized, placebo-controlled, phase 3 trial found a statistically significant reduction in polyps and adenoma recurrence in nondiabetic patients who took low dose metformin (250 mg/day) for a year-long study (*Lancet Oncol.* 2016;17:475-83). In other studies, women who took metformin in the month preceding surgery for breast cancer or endometrial cancer had "decreased cellular proliferation in tumors" than those in the control groups. But overall, Chen et al say, "…the outcomes in the clinical trials, especially for nondiabetic patients with cancer, are not as satisfactory as expected."

The authors suggest several reasons for the lackluster clinical study results. First, optimal dose, schedule, and duration for metformin use in nondiabetic cancer patients or those at-risk for cancer have not been determined. Dosages in the reviewed studies varied from 250 mg/day, 850 mg/day, 500 mg twice daily, to 1700 mg/day; and treatment length varied as well. In addition, metformin's effect may differ with the cancer's histological subtype and/or genotype. For instance, metformin "induced significant apoptosis only in the small cell carcinoma cell line but not in other human lung cancer cell lines." Also, it may be that metformin is most effective in combination with some other treatment(s).

Metformin is an inexpensive drug and relatively safe with a low risk of lactic acidosis, according to the authors. "The risk of lactic acidosis increases with renal or hepatic impairment, aged 65 years or older, having a radiological study with contrast, surgery, or other procedures, hypoxic states, and excessive alcohol intake," according to Drugs.com. Gastrointestinal symptoms, including anorexia, nausea, abdominal discomfort, and diarrhea are the most common side effects. Also, metformin can cause vitamin B12 deficiency in some patients, so patients' B12 status needs to be monitored.

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Transparency Lawsuit Against FDA

On February 25, 2020, Federal Judge Naomi Reice Buchwald ruled that the Food and Drug Administration (FDA), National Institutes of Health (NIH), and Department of Health and Human Services (HHS) misinterpreted a 2007 law that required clinical drug trial results to be posted on ClinicalTrials.gov. This government-funded database was approved by Congress in 1997, in an effort to increase transparency. Studies that show product ineffectiveness or poor safety are rarely published. In fact, negative information about a drug or device often remains hidden unless a lawsuit and the process of discovery brings the information to light. ClinicalTrials.gov was viewed as a possible solution to the lack of transparency.

ClinicalTrials.gov did not work as hoped, however. So, Congress passed the 2007 Food and Drug Administration Amendments Act (FDAAA); it requires basic, summary results for all FDA-approved drug and medical device clinical trials be posted on the website – even if the study did not conclude until after FDA approval of the product. HHS did not publish its regulation on how to interpret this law until 2017, and that document exempted studies completed or approved before January 2017, leaving 10 years of data hidden. In those ten years, universities, companies, and research institutions (including NIH) had repeatedly missed reporting deadlines, according to an investigative article in *Science.* FDA has not enforced the 2007 law with fines (up to $12,103/day), and NIH continues to give research grants to offenders. This lack of transparency and accountability led to the lawsuit.

The lawsuit was filed by two student law clinics, Yale Media Freedom and Information Access (MFIA) and NYU Technology Law and Police (TLP), with the help of the Yale Collaboration for Research Integrity and Transparency. Charles Seife, an investigative science and technology journalist at NYU, and Peter Lurie, MD, president of the Center for Science in the Public Interest and a former associate commissioner of the FDA, were the plaintiffs. Judge Buchwald's ruling requires the government agencies to collect and post study results for the clinical trials conducted after the 2007 law went into effect.

In addition to increasing transparency needed to make informed medical and research decisions, the ruling may help increase FDA accountability. A 2020 *JAMA* article by Jonathan J. Darrow, JD, Jerry Avorn, MD, and Aaron S. Kesselheim, MD, JD, reports: "The number of [FDA] expedited development and approval programs has expanded greatly since 1983, reducing the amount of evidence available at the time of approval and increasing uncertainty about the existence or amount of clinical benefit." The agency is now using less data, fewer pivotal studies, and more surrogate measures to approve medical drugs and devices than it did twenty years ago. Yet, the amount of Prescription Drug User Fee Act fees, paid to the agency by industry, has exploded from $66 million (annual mean) in 1993-1997 to $820 million in 2013-2017; "…in 2018, user fees accounted for approximately 80% of the salaries of review personnel responsible for the approval of new drugs." Transparency is one battle; conflict-of-interest is another.

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VITAMIN C PROMOTES IMMUNE RESILIENCY

It is well-known that vitamin C, which the human body needs but does not manufacture, plays a key role in immune function. There is some controversy, however, regarding whether high or low-dose vitamin C therapy is most advantageous.

High-dose advocates cite human clinical trials in which doses of intravenous vitamin C many times higher than the RDA have shown promising results in immuno-compromised individuals.

Those that favor the low-dose approach emphasize that since intravenous vitamin C has considerable financial, time, and convenience burdens, it is not practical for most people. They also cite the vitamin's diminishing returns at higher oral doses (the more you take, the less you absorb) and the fact that mega-doses of vitamin C can cause gastrointestinal distress.

According to Dr. Lucie Kotlarova, Director of the Integrative Safe Treatment Center in the Czech Republic, both high and low doses are appropriate at different times, depending on the circumstances.

VITAMIN C: IMMUNITY, DEFICIENCY, & CHANGING NEEDS

Vitamin C is essential to a properly functioning immune system because it influences multiple pathways that enhance the production and activity of white blood cells, such as T-cells, B-cells, and natural killer cells. It also helps modulate the production of cytokines and acts as an antioxidant.

While vitamin C is plentiful in most fruits and vegetables, deficiency is more prevalent than commonly thought. In fact, it is the fourth-most common nutrient deficiency in the United States.

The body's baseline need for vitamin C varies as well. Daily low-dose vitamin C is effective for shortening the duration of immune challenges. However, if the immune system is activated against a threat, metabolic demand for vitamin C increases. Similarly, if the body launches an inflammatory response, oxidative stress rises, increasing the need for antioxidants like C. As Dr. Kotlarova explains, "Prophylactic use of vitamin C requires dosing in the milligram range, whereas addressing a current threat requires dosing in the gram range."

BENEFITS OF ORAL LIPOSOMAL VITAMIN C

Vitamin C in a liposomal form offers a solution for overcoming the two main obstacles with traditional oral vitamin C: limited bioavailability and gastrointestinal distress. Lipid metabolites form a protective sphere around the vitamin molecule, allowing it to travel intact through the stomach and into the intestines and liver, where they enhance its entry into the cells. Because liposomal vitamin C is 10-20 times more bioavailable than ascorbic acid, there is no need to take extremely high doses.

"The liposomal delivery is much more effective because of its advanced absorption and the fact that it doesn't cause any damage to the stomach and digestive tract that non-lipid coated vitamin C creates," Dr. Kotlarova explains.

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Literature Review & Commentary

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

Inositol Hexaphosphate and Inositol Induce Remission in Stage IV Melanoma

A 59-year-old man was treated surgically in 2012 for stage IIIB melanoma on the left foot. Around a year later another melanoma lesion was excised from his left shin. In January 2015 he developed a new melanoma lesion on his left thigh, and was found to have mediastinal and hilar lymphadenopathy with multiple pulmonary nodules. At that time he was in stage IVB. He declined immunotherapy and targeted therapy and instead began taking 4,000 mg of inositol hexaphosphate (IP6) and 1,100 mg of inositol twice a day. Six months later, there was significant improvement, including a decrease in the size of the hilar and mediastinal lymph nodes and the lesion on the thigh. He went into complete clinical and radiological remission after being on IP6 and inositol for 2 years. He continued the treatment for another year and remained in remission at the time of this report.

Comment: IP6 (also known as phytate) occurs naturally in corn, soy, wheat bran, nuts, and other high-fiber foods. It is also found in mammalian cells and regulates a number of different biochemical processes. It inhibited many different tumor cell lines *in vitro*, including colon, breast, and melanoma. Inositol has also demonstrated anticancer properties. In animal studies, the combination of IP6 and inositol had anticancer effects that were greater than those seen with each individual compound. In the present case report, treatment with IP6 and inositol was associated with a complete remission in a patient with advanced melanoma. Controlled trials are needed to confirm these promising findings.

Khurana S, et al. Inositol hexaphosphate plus inositol induced complete remission in stage IV melanoma: a case report. *Melanoma Res*. 2019;29:322-324.

Fasting Followed by Plant-Foods Diet for Lymphoma

A 42-year-old woman presented with a palpable mass in the right inguinal region and was diagnosed by excisional biopsy with stage IIIa, grade 1 follicular lymphoma. She refused conventional therapy and underwent a medically supervised 21-day water fast, after which the enlarged lymph nodes were substantially smaller. The patient then consumed a diet consisting entirely of whole plant foods free of added sugar, oil and salt. At six- and nine-month follow-up visits, the patient's lymph nodes were non-palpable, and she remained asymptomatic. CT and PET scans conducted after three years found no evidence of active disease.

Comment: In this case report, a 21-day water fast followed by a diet of whole plant foods appeared to induce remission in a patient with stage IIIa, grade 1 follicular lymphoma. Controlled trials are needed to confirm these promising findings. The mechanism of action of this treatment is not known.

Myers TR, et al. Follow-up of water-only fasting and an exclusively plant food diet in the management of stage IIIa, low-grade follicular lymphoma. *BMJ Case Rep*. 2018;2018:bcr-2018-225520.
Goldhamer AC, et al. Water-only fasting and an exclusively plant foods diet in the management of stage IIIa, low-grade follicular lymphoma. *BMJ Case Rep*. 2015;2015:bcr2015211582.

Does Eating Tomatoes Prevent Prostate Cancer?

The association between consumption of tomato products and risk of prostate cancer was examined in a prospective cohort study of 27,934 Adventist men (aged 30 years or older) living in the United States or Canada. The Adventist church recommends a healthy lifestyle, including avoidance of alcohol and smoking, and consumption of a plant-based diet. During 7.9 years of follow-up, 1,226 incident cases of prostate cancer were documented. Consumption of canned and cooked tomatoes more than four times a week, as compared with never consuming this food, was associated with a 28% lower risk of developing prostate cancer ($p = 0.02$).

Comment: This study is consistent with several other observational studies in which higher intake of tomato products was associated with a lower risk of prostate cancer. The possible anti-cancer effect of tomatoes is thought to be due at least in part to its high content of lycopene, a carotenoid that is known to enhance immune function. Tomatoes also contain a saponin called alpha-tomatine, which inhibited the growth of human prostate cancer cells *in vitro*.[1]

Fraser GE, et al. Tomato consumption and intake of lycopene as predictors of the incidence of prostate cancer: the Adventist Health Study-2. *Cancer Causes Control*. 2020;31:341-351.

Association Between Meat Consumption, Cooking Methods, and Colorectal Cancer

The association between red and processed meat consumption and risk of colorectal cancer was examined in a prospective cohort study of 48,704 women (aged 35-74 years) in the United States and

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Gaby's Literature Review

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Puerto Rico who had a sister diagnosed with breast cancer. During a median follow-up period of 8.7 years, 216 colorectal cancer cases were documented. There was an increased risk of colorectal cancer when comparing the highest vs. the lowest quartile of processed meat consumption (hazard ratio [HR] = 1.52; p for trend = 0.02). A similar association was seen for specific meat products, including breakfast sausages and bacon. There was little evidence of an association between red meat consumption and colorectal cancer risk. However, there was a positive association with specific red meat products when cooking methods were considered; for example, grilled/barbequed steaks (HR = 2.23; 95% confidence interval [CI], 1.20-4.14) and hamburgers [HR = 1.98; 95% CI, 1.00-3.91).

Comment: In this study, consumption of processed meat or of red meat cooked at high temperatures was associated with an increased risk of developing colorectal cancer. Many processed meats are preserved by adding nitrites. Nitrites can be converted to carcinogenic nitrosamines in the stomach or during the cooking process. Nitrosamines appear to play a role in the pathogenesis of gastric cancer. In addition, an observational study found that higher intake of nitrosamines was associated with an increased risk of colorectal cancer.[2] The association between high-temperature cooking of meat and colorectal cancer might be explained in part by the fact that high-temperature cooking of meat results in the formation of carcinogens such as heterocyclic amines and polycyclic aromatic hydrocarbons.

Mehta SS, et al. A prospective analysis of red and processed meat consumption and risk of colorectal cancer in women. *Cancer Epidemiol Biomarkers Prev*. 2020;29:141-150.

Ketogenic Diet and Breast Cancer

Sixty Iranian women with locally advanced (n=44) or metastatic (n=16) breast cancer were randomly assigned to consume a medium-chain triglyceride-based ketogenic diet or a standard diet during the first three months of chemotherapy. In the patients with locally advanced cancer, Kaplan-Meier analysis conducted over a period of 25 months showed a significantly higher survival rate in those consuming the ketogenic diet than in the control group (p=0.04).

Comment: Those of you who have followed my writings in the *Townsend Letter* know that I suspect that most of the nutrition research coming from Iran is fraudulent. There are two issues about the present study that lead me to question its credibility.

First, it does not seem possible to have conducted a 25-month survival analysis. Patients were enrolled between July 2017 and October 2018, and the paper was submitted to the journal on February 12, 2019. The patients who were enrolled near the end of the enrollment period could not have been followed up for more than 5 months. I emailed the man who was listed as having written the paper, and I asked him for clarification. He stated that the follow-up period lasted until June 2019, not February 12, 2019, because one of the reviewers asked him to add a survival analysis and to re-submit the paper. While that could be true, journals typically mention both the date the manuscript was originally received and the date the revisions were received. In this paper, there was no mention of a revised version being received. Even if one accepts the statement that the follow-up period was extended by 4 months, patients who were enrolled near the end of the enrollment period could not have been followed up for more than 9 months.

continued on page 25 ➤

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Dr. Jennifer Miele is the co-founder and clinical director of the BAJA MEDGATE clinic in San Diego, and in Tijuana, Mexico. Jennifer focuses on medical research and development of new protocols based on an integrative approach involving a focus of PDT/Photodynamic Therapy in oncology, immunotherapy, regenerative medicine, endocrinology, infectious diseases, autoimmune diseases, and nutrition. They have experienced the effectiveness of the Relax Sauna in their clinics and recommend them to their patients.

Jennifer recently enthusiastically confided to us, ***"I Love the Relax Sauna, and frankly, the wood infrared saunas just do not penetrate as much as the Relax Sauna."***

Washington Cancer Clinic uses the Relax Sauna while doing IV Therapy

A Washington cancer clinic has informed us that they have been able to increase the effectiveness of their IV Therapy by putting many of their patients in the Relax Sauna while their "IV arm" sticks out of the armhole. They usually increase core temperature 4.2° in 1 hour, and are excited with their results.

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Rebecca Harder runs the Taos Hyperbaric Wellness Center, and Colon Care Hydrotherapy Clinic in Portland, and is the author of ***"Gastra Girl: Saving America One Colon at a Time"*** which is an inspiring compendium of innovative health articles on hyperbaric oxygen, ozone, far infrared saunas, vaccines, etc., and includes articles written by Paul Harsh, Dietrich Klinghardt, Sherry Tenpenny, and Russell Blaylock and others. Chapter 10 is entitled, "Why Infrared Saunas are an Absolute Necessity for Everyone." She intones, "I realized the Relax Sauna was head and shoulders above all the rest to recommend."

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After "turning her nose" at the Relax Sauna for 10 years (having wooden infrared Saunas in her pristine clinics), Rebecca finally experienced the Relax Sauna. In 3 minutes she was sold, because of the instant relaxation and the difference she felt. She tells us, "NO OTHER SAUNA feels as good as the Relax Sauna or gives you the benefits as this one does in such a short amount of time because of its pure infrared light with no negative EMF.

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➤ *continued from page 22*

Second, in the Author Contribution section of the paper, the man with whom I corresponded was listed as having written the paper by himself, although 2 other contributors reviewed the manuscript. In reading this paper, I found it to be fairly well written in terms of grammar, sentence structure, and overall command of the English language. In contrast, the emails sent to me by this author demonstrated a poor grasp of English, containing sentences such as, ". . . we analysed data accord positive and negative. data accord row shown no accord column. . . . Because in metastatic patients diagnosis time differ to admit time to study." Given the evidence that numerous companies in Iran are in the paper-selling business,[3] one wonders who actually wrote this paper.

Khodabakhshi A, et al. Feasibility, safety, and beneficial effects of MCT-based ketogenic diet for breast cancer treatment: a randomized controlled trial study. *Nutr Cancer*. 2020;72:627-634.

Heating Extra-Virgin Olive Oil Decreases Its Polyphenol Content

Extra-virgin olive oil was processed at two different temperatures (120°C and 170°C), either for a short time (30 minutes for 120°C, 15 minutes for 170°C) or a long time (60 minutes for 120°C, 30 minutes for 170°C), to simulate common pan-frying conditions in a home kitchen. The mean polyphenol content decreased by 40% at 120°C and by 75% at 170°C, compared with raw olive oil. Increasing the cooking time decreased the content of hydroxytyrosol but had no significant effect on the content of total polyphenols.

Comment: Some of the beneficial effects of extra-virgin olive oil are thought to be due to hydroxytyrosol and other polyphenols. Hydroxytyrosol functions as an antioxidant and anti-inflammatory agent, as well as an inhibitor of platelet aggregation. Extra-virgin olive is preferable to refined olive oil because most of the polyphenols are lost in the refining process. Olive oil is often recommended for cooking because of its high concentration of monounsaturated fatty acids, which are resistant to heat-induced oxidation. In contrast, oils with high concentrations of polyunsaturated fatty acids (such as sunflower, safflower, and corn oil) are thought to be less safe for cooking because subjecting polyunsaturated fatty acids to high temperatures leads to the formation of potentially atherogenic lipid peroxides.

The present study demonstrates that heating extra-virgin olive oil results in the depletion of one or more of its beneficial constituents. While olive oil may still be preferable to other oils for cooking, the results of this study suggest that the greatest benefits are derived from consuming extra-virgin olive oil uncooked.

Lozano-Castellon J, et al. Domestic sauteing with EVOO: change in the phenolic profile. *Antioxidants*. 2020;9:E77.

Fish Oil and Cardiovascular Disease: Possible Influence of Polychlorinated Biphenyls

The association between consumption of omega-3 fatty acids from fish (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]), dietary exposure to polychlorinated biphenyls (PCBs), and risk of cardiovascular disease was examined in a prospective cohort study of 32,952 women and 36,545 men in Sweden. During a mean follow-up period of 15.5 years, after adjustment for PCBs intake, there was a significant inverse association between EPA/DHA intake and risk of cardiovascular disease (hazard ratio [HR] comparing extreme quintiles, 0.79; p for trend = 0.04). After adjustment for EPA/DHA intake, there was a significant positive association between PCBs intake and risk of cardiovascular disease (HR comparing extreme quintiles, 1.31; p for trend = 0.005).

Gaby's Literature Review

Comment: PCBs are organochlorine compounds that were used for various industrial and chemical applications. They were banned in the Western world in the 1970s, but they persist in the environment and are detectable in human tissues. PCBs are known to bioaccumulate in fish. In epidemiological studies, exposure to PCBs was associated with increased risk of cardiovascular disease, hypertension, obesity, and diabetes. In the present study, the beneficial effect of fish consumption on cardiovascular disease risk appeared to be compromised by co-exposure to PCBs. This interaction might explain in part the conflicting results in studies that examined the association between fish consumption and cardiovascular disease risk.

Regular use of a sauna may be effective for removing PCBs from the body. The concentration of PCBs in sweat after using a sauna is substantially higher than the concentration in urine. Regular sauna use has been associated with a decreased risk of cardiovascular disease, an effect that might be related in part to the removal of PCBs and other toxic compounds from the body.

Donat-Vargas C, et al. Cardiovascular and cancer mortality in relation to dietary polychlorinated biphenyls and marine polyunsaturated fatty acids: a nutritional-toxicological aspect of fish consumption. *J Intern Med*. 2020;287:197-209.

Possible Risk Associated with Tartrate-Containing Nutritional Supplements

The authors of this study analyzed the composition of previously unidentified urinary stones from the Mayo metals laboratory database between 2010 and 2018. Thirty-five calcium tartrate stones were identified in 25 patients from the Mayo database, and two others were identified from the authors' institution, for a total of 37 calcium tartrate stones in 27 patients. Thirty stones were pure calcium tartrate and the rest had elements of more common stones. The authors were able to locate and question three of the 27 patients. All three reported routine consumption of an energy drink (Spark), typically two-to-four servings per day for periods of one-to-three years. Spark contains (per serving) 500 mg of choline (as bitartrate and citrate) and 10 mg of L-carnitine (as tartrate).

Comment: Tartrate (the salt of tartaric acid) occurs naturally in some fruits and wine. It is also used as a preservative and flavoring agent (it gives foods a sharp, tart flavor). In addition, tartrate is added to some carbonated beverages and fruit jellies. The present study raises the possibility that excessive consumption of tartrate can lead to the formation of calcium tartrate kidney stones. For people supplementing with large amounts of choline or L-carnitine, it might be preferable to use forms other than tartrate or bitartrate salts.

Kleinguetl C, et al. Uncovering a novel stone in 27 patients: calcium tartrate tetrahydrate. *Urology*. 2019;126:49-53.

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2. Knekt P, et al. Risk of colorectal and other gastro-intestinal cancers after exposure to nitrate, nitrite and N-nitroso compounds: a follow-up study. *Int J Cancer*. 1999;80:852-856.
3. Stone R. In Iran, a shady market for papers flourishes. Science 2016;353:1197.

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Integrative Oncology Research Update from KNOWoncology.org

by Jen Green, ND

KNOWoncology.org is an integrative oncology database and educational platform created and maintained by the Oncology Association of Naturopathic Physicians. KNOWoncology is a revolutionary tool that supports clinical decision making, creation of patient handouts, authoring of mini systematic reviews, and staying up to date on the human research on natural health products in cancer care. Because the volume of human studies is increasing each year, it is necessary to have a website like KNOW to stay abreast of new and relevant international research.

Methodology: Twice or more yearly, a medical librarian systematically searches Medline and EMBASE for all human studies on natural health products and cancer care. Then KNOW uses a double screening process to identify records that meet criteria (human studies, English language, natural agent used with or without conventional therapies). Articles are then summarized by a team of research assistants and tagged according to tumor type, natural therapy (eg, probiotics, green tea), conventional therapy (eg, radiation, Taxol), and side effects of conventional care (eg, neuropathy, nausea, diarrhea). This allows each study to be fully searchable within the KNOW website.

Search Results: When you search in KNOW, studies result on the screen according to level of evidence (ie. systematic review, then controlled trials, then observational studies and case reports). Most of the studies that have closed access (you have to pay for them) are summarized in a more detailed way so that clinicians can quickly learn the precise population, natural product type, dose and duration, and outcomes of the study. There is also an export button to copy either the whole summary or just the citation into patient recommendations, letters to oncology teams, patient handouts, presentations, or articles.

Comparing KNOW to a PubMed Search: EMBASE, which is the European version of PubMed, has many studies on natural health products and cancer care that are conducted in France, Japan, Southeast Asia, and the Middle East. These studies are missed in a typical PubMed search. In two quality appraisal studies of KNOW, a search in KNOW consistently resulted in a more complete list of human studies than a search in PubMed.[1]

Applications of KNOW: KNOWoncology.org is both a clinical tool to support evidence-informed decisionmaking, as well as an academic tool to support mini systematic reviews and other evidence-based content. An example of content powered by KNOWoncology.org are three patient brochures (IV Vitamin C in Cancer Care, Tamoxifen Support, and Protecting Your Heart During Adriamycin Chemotherapy), which were done in collaboration with bbct.ngo and OICC.ca: https://oncanp.org/patient-resources/

KNOWoncology.org is up to date and empowers clinicians with current best evidence. To gain access, sign up as a new OncANP member at https://oncanp.org/join-now and get 10% off membership using code "Townsend2020"

Cancer Studies from 2018/2019 to KNOW About

Breast Cancer.

In a double blind RCT, 48 women with stage IIIb breast cancer being treated with neoadjuvant cyclophosphamide-doxorubicin-5FU who took omega 3 fatty acids 1 g/day (EPA and DHA dose not specified) during chemotherapy had a significantly greater reduction in Ki67 expression and VEGF expression post-treatment compared to placebo. Disease-free survival at one year was improved (P=.044) and overall survival was significantly better in the fish oil group (P=.048).[2]

Comments: This is one of many studies supporting the use of fish oil during chemotherapy for breast cancer. It is also the second trial to show a survival benefit for fish oil in stage III/IV breast cancer. The first RCT by Bougnoux P et al, 2011 was a smaller trial with more advanced patients, where 1.8 g of DHA alongside chemotherapy showed greatly improved survival (P=.007).[3] Fish oil likely also decreases side effects from chemotherapy. In a double blind RCT, 1 g DHA during paclitaxel chemotherapy decreased incidence of peripheral neuropathy.[4] In an RCT, breast cancer patients taking fish oil 4 g daily concurrent with chemotherapy had better lung strength and endurance.[5]

Two new systematic reviews, worth reading, on managing side effects in breast cancer discuss the following:

- Treatments for aromatase inhibitor-associated arthralgia in breast cancer survivors: acupuncture, aerobic exercise, omega-3 fatty acids[6]
- Natural approaches to cancer-related fatigue in breast cancer: guarana, acetyl-L-carnitine, co-enzyme Q10 and diet rich in whole foods, omega-3 fatty acids, fruits, and vegetables[7]

Colon Cancer.

In a small RCT (n=28), patients with stage IV colorectal cancer who took C3 curcumin 2 g/d along with FOLFOX +/- bevacizumab had improved overall survival compared to placebo. No significant difference was found between arms for quality of life or neurotoxicity. The HR for OS was 0.34 (95% CI: 0.14, 0.82; *P* = 0.02) median of 200 d for FOLFOX and 502 d for CUFOX.[8]

Comments: Until this study, it was unclear whether curcumin was safe to combine with FOLFOX chemotherapy. Although these findings cannot be extrapolated to other types of chemotherapy

or other types of curcumin, it provides a strong rationale that C3 curcumin is safe to use during FOLFOX chemotherapy. It's also thrilling to see a chemotherapy acronym, CUFOX, to show the integration of a natural health product into cancer care.

In an RCT (n=73), patients undergoing colorectal cancer surgery who took synbiotics (*Lactobacillus paracasei, Lactobacillus rhamnosus, Lactobacillus acidophilus* and *Bifidobacterium lactis* plus FOS) for seven days before surgery had reduced inflammation (CRP, IL-6, $P < 0.001$), less postoperative infections (2.8% vs 18.9%, $P = 0.02$), lower antibiotic use ($P < 0.001$) and shorter length of hospital stay ($P < 0.001$).[9]

Comments: A previous double blind RCT of synbiotics before colorectal surgery had shown that synbiotics reduced post-operative infections.[10] This short, simple intervention with only seven days of probiotics plus FOS showed strong benefits in clinical outcomes and also levels of inflammation.

Ovarian Cancer.

In a controlled trial, women with advanced stage III and IV ovarian cancer were divided into five treatment arms of neoadjuvant (before surgery) platinum-taxane with and without long-term platinum-taxane chemotherapy after surgery, and with or without Indole 3 carbinol (I3C) alone, or I3C and EGCG. The group that took I3C alone, or I3C (200 mg BID) and EGCG (200 mg BID) alongside neoadjuvant platinum-taxane chemotherapy as maintenance therapy had significantly statistically better five-year survival (60 vs 44 months, $p<.0001$), lower CA-125 tumor markers, improved progression-free survival, and less ascites compared with those who did not use I3C/EGCG. There were no adverse events found for I3C and EGCG.[11]

Comments: While this trial was not randomized due to recruitment challenges, it was a controlled trial and the groups were very similar at baseline. The researchers in this study selected I3C and EGCG to try to target cancer stem cells. I3C and EGCG were proven safe to combine with carboplatin-Taxol chemotherapy, and they improved treatment outcomes. This study is the first of its kind to suggest more broadly that I3C (400 mg) and EGCG (400 mg) are safe to combine with carboplatin-Taxol.

Prostate Cancer.

In a systematic review of four RCTs, use of green tea catechins by patients with high grade prostate intraepithelial neoplasia or atypical small acinar proliferation prevented development of prostate cancer.[12]

In a systematic review of fish oil for prostate cancer, fish oil did not impact PSA; however in cohort studies, there was an association between higher intake of fish and decreased risk of prostate cancer–related death.[13]

In an RCT, wood mallow and marshmallow flower powder infusion prevented anal discomfort and diarrhea caused by prostate radiation.[14]

Pediatric Cancers.

(Note that KNOWoncology.org has a search function to select all pediatric studies regardless of tumor type.)

A systematic review of integrative clinical trials for supportive care in pediatric oncology from the International Society of Pediatric Oncology, traditional and complementary medicine collaborative, included 44 RCTs.[15]

KNOW contains two additional RCTs published after this systematic review. In an RCT, children with acute lymphoblastic leukemia (ALL), who received 420 mg silymarin daily for a week following each doxorubicin dose, had improved cardiac tests compared to placebo.[16] In an RCT, children with ALL were given 30 g/day soy or cowpea nut powder for 12 weeks. The soy powder significantly improved physical activity level, body weight, body mass index, number of red blood cells, hemoglobin/hematocrit levels, and fatigue.[17]

Systematic Reviews on Cancer Treatment Side Effects

In a systematic review of herbs for mental health in cancer survivors, 100 RCTs of 38 botanicals were included (St John's wort was excluded due to concerns about drug interactions). Herbs with minimal risk of series side effects with demonstrated effectiveness for anxiety and depression are black cohosh, chamomile, lavender essential oil internally, passionflower, saffron and chasteberry. The herbs with two or more RCTs were saffron, kava kava, gingko, lavender essential oil internally, bacopa, and passionflower.[18]

This database offers up-to-date best evidence for integrative care.

In a systematic review on natural agents for mucositis, 26 RCTs were included. Effective agents included aloe vera juice, *Calendula officinalis*, chamomile, yarrow, low level laser, olive oil, placental extract, propolis, royal jelly, indigowood root, and *Glycyrrhiza glabra*. Natural therapy was reported to have better patient compliance with fewer side effects. Manuka honey was not tolerated by patients due to nausea and vomiting.[19]

In a systematic review of herbal treatment for xerostoma, 25 RCTs were included. A total of 24 formulas were included in the trials, but most were insufficiently reported in the methodology section. Five traditional Chinese formulas were shown to significantly improve the salivary flow rate compared to comparators (Shennongbaijie decoction, Xuanmaizengyehuadu decoction, Yunnanbaiyao capsule with Niancianchuanqipipa gel, Jiaweizengye decoction, and Sanganhuayin decoction).[20]

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On the cover

Repurposed Drugs for Cancer

by Jacob Schor, ND, FABNO

A rapidly growing subcategory in the chemotherapeutic treatment of cancer is the utilization of prescription drugs originally approved for treating conditions other than cancer. Such off-label use of drugs has taken the world of integrative oncology by storm. This strategy has potential for increasing efficacy of treatment. At the same time, it raises deep questions on how we define naturopathic medicine, natural medicine, and our role as physicians. Will using pharmaceutical drugs to prolong a patient's life fit into who we claim to be as naturopathic physicians?

One of the earliest non-cancer drugs noted to have anticancer side effect was cimetidine. Cimetidine was an early H-2 agonist approved for treating gastric ulcers in the late 1970s. Reports of an anticancer effect appeared not long afterward; the earliest was likely Armitage and Sidner's 1979 paper,[1] but Burtin's 1988 trial usually receives the credit. Burtin reported that cimetidine or ranitidine combined with subcutaneous histamine improved survival of gastric cancer patients to the degree that patients survived six times longer than patients receiving palliative treatment alone.[2] A double blind, placebo-controlled trial by Tonnesen, published the next year, showed that cimetidine alone at a normal dosage significantly prolonged survival in gastric cancer.[3] Cimetidine is now reported helpful against a range of cancers, including renal, melanoma, gastric, and colorectal carcinomas.[4] In Ali's 2018 study, patients starting cimetidine after surgery for colorectal cancer delayed cancer recurrence.[5]

If cimetidine is the drug longest known for secondary usage in cancer, the best-known drug is likely metformin, the glucose-lowering agent that is first-line treatment for type-2 diabetes. Metformin decreases hepatic gluconeogenesis and improves insulin sensitivity. It was approved for treatment of type-2 diabetes in France in 1957, in the UK in 1958, Canada in 1972, and finally, in the US in 1994.[6] During the early 2000s metformin also became the drug of choice for treating hyperinsulinemia and metabolic abnormalities associated with polycystic ovarian syndrome (PCOS). The first major report that associated metformin with lower cancer risk may have been Josie Evan's 2005 study that examined medical records of over 300,000 people in Scotland. Just under 12,000 of these individuals had type-2 diabetes. Of these individuals, 923 were eventually diagnosed with malignant cancers. Those who had taken metformin had a significantly lower risk of being diagnosed with cancer [OR 0.79 (0.67 to 0.93)].[7]

Since then numerous papers have been published on metformin's possible benefit in cancer. Observational studies, systematic reviews, and multiple meta-analyses of case-control and cohort studies suggest metformin use is associated with a 10-40% overall decrease in cancer incidence along with a similar decrease in mortality.[6,8]

Many of us were first exposed to the idea of using prescription drug cocktails to treat cancer by Ben Williams. Mr. Williams was diagnosed with glioblastoma in March 1995. He availed himself of a drug and supplement protocol that proved to be effective. He chronicled these treatment choices first on a website[9] and in his 2002 book, *Surviving Terminal Cancer: Clinical Trials, Drug Cocktails, and Other Treatments Your Oncologist Won't Tell You About.* The protocol he followed stood out not just because of the many nutritional supplements but also because he took multiple

off-label drugs. When he first posted these protocols, I ignored the drugs, as they were not 'naturopathic.' I turn back to his list now with interest. What he did worked. Williams took a range of drugs including Accutane, Actos, and Celebrex that evidence suggested might have an additive or synergistic effect against glioblastoma. His list of supplements became the foundation that we have used with brain tumors.

The phrase 'repurposing drugs' first shows up in the medical literature in 2005 with two papers by D. W. Carley.[10] In 2009, eight papers were published on the subject. These focused on the prohibitively high cost ($800 million) and long time (20-27 years) that it took to bring a new cancer drug to market and suggested that older, already approved drugs might have new uses and proposed ways to screen for anticancer action.[11] In 2011, Vazquez-Martin suggested that metformin might be 'repositioned' to utilize its ability to target and eliminate cancer stem cells at preinvasive stages.[12] Then in 2012, Michele Holmes and Wendy Chen at Harvard wrote their classic review: "Hiding in plain view: the potential for commonly used drugs to reduce breast cancer mortality." In this paper, they "… presented and evaluated the evidence for several commonly used over-the-counter and prescription medications – including aspirin (and other non-steroidal anti-inflammatory drugs), beta-blockers, angiotensin-converting enzyme inhibitors, statins, digoxin, and metformin, all of which have been evaluated among breast cancer survivors in prospective studies. Substantial scientific evidence supports the idea that some of these common and relatively safe drugs may reduce breast cancer mortality among those with the disease by an amount that rivals the mortality reduction gained by currently used therapies. In particular, the evidence is strongest for aspirin (approximately 50% reduction), statins (approximately 25% reduction), and metformin (approximately 50% reduction). As these drugs are generic and inexpensive, there is little incentive for the pharmaceutical industry to fund the randomized trials that would show their effectiveness definitively….Because of the multiple potential pathways that can be involved with cancer growth and metastases, tremendous interest remains in whether currently used non-cancer medications may potentially have anti-cancer effects."[13]

This paper was the last calm before the storm; thereafter interest in repurposed drugs exploded. While this was an obscure idea in 2009, PubMed lists 247 citations for 'repurposing drugs' in 2017 and 312 for the following year. One might argue that this is due to a collective realization by researchers that this is an excellent idea. The excitement is in part due to a man in Belgium named Luc Verelst, whose sister was diagnosed with endometrial cancer in the summer of 2008. Like many of our patients, Verelst searched to find the best and most reliable treatments; and like them, he was overwhelmed, frustrated, and confused by the complex and contradictory information he found. In 2009, Mr. Verelst founded a non-profit organization called Reliable Cancer Therapies (RCT) to publicly share information on cancer treatments and to investigate new treatment options. He founded a second organization in 2013, the Anticancer Fund (ACF), with the ambitious goal of discovering a cure for cancer. As part of their mission, the ACF scientists took on the task of researching this concept of drug repurposing They have cataloged potential repurposed drugs on a website (http://www.redo-project.org), produced summaries on many of these drugs, and are funding research on promising candidates.

Older already approved drugs are being screened for anti-cancer actions.

Pan Pantziarka is the lead author on many of the papers produced by the "redo" scientists.[14] Both Dr. Pantziarka's first wife and son George had Li-Fraumeni Syndrome, a rare, autosomal dominant disorder linked to mutations in the p53 tumor suppressor gene that pre-disposes carriers to cancer; both died of cancer at young ages. Pantziarka is now the program director for drug repurposing at the Anticancer Fund and the coordinator of the Repurposing Drugs in Oncology (ReDO) project.

By February 2020, the ReDo-project database listed 310 drugs, sold for other uses, that might have potential efficacy in cancer care. Of these, half are supported by relevant human data and a fifth are supported by data from at least one positive clinical trial. The ReDO project is summed up in a 2018 paper by Pan Pantziarka et al. The full text is available online.[15]

Many patients find this entire concept exciting. But for us naturopaths, it is disturbing. There is no reason to assume using prescription drugs would be acceptable to my "drugless practitioner" naturopathic colleagues. Patients come to us because they want alternatives to taking drugs, in particular chemotherapy; even patients who have acquiesced to the oncological standards of care, still urgently want to avoid using further drugs. The business of repurposing pharmaceuticals seems to go against our profession's underlying philosophy, and our patients will not hesitate to speak up to remind us.

The medical oncologists who work with our patients are usually unfamiliar with the concept of repurposed drugs and are rarely aware that there is research supporting such uses. A search on PubMed for "metformin AND cancer" (May 30, 2019) yielded 4,432 citations. Yet I cannot recall any medical oncologist ever suggesting to a patient that they take metformin because they have cancer.

Most of us were drawn to practice naturopathy by a deep trust in nature, though the word 'trust' does not do justice to our deep sense that nature can be relied on to heal the sick and injured. Perhaps faith would be a better word. Even as we talk about evidence-based medicine, we retain that faith in the Vis Medicatrix Naturae, We may have enrolled in naturopathic school to become nature doctors;

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but upon graduation, we became physicians, who specialize in naturopathy, but physicians, nevertheless. To quote Ryan Blum writing in the *Journal of Ethics* in 2009, "Physicians' responsibilities to the patient are the same whether they utilize naturopathic, osteopathic, or allopathic diagnostics and treatments."[16] We may profess philosophical tenets about natural healing, but our obligation is to our patient's best interest and some days that may be standard of care treatment. I have listened to patients profess our own naturopathic creed, "I believe that nature can heal all illness, that if we just discover the cause, I can cure my cancer naturally," and I've been forced to admit an unwillingness to bet their survival on it

ASCO reported in October 2018 that 40% of the American public is certain that cancer can be cured naturally.[17] Among our naturopathic patient population, probably double that number believe this. Sadly, this does not seem to be the reality. We find ourselves in the awkward situation of sharing with the patient what we know from experience, that spontaneous remissions triggered by natural therapies are rare and not dependable. Their best chance of survival is often a combination of natural therapies alongside the standard of care therapies offered by medical oncologists. And even then, positive outcomes are not certain. By adopting the title physician, we elevated ourselves into the modern era of evidence-based medicine and the responsibilities that come with believing in science, statistics, and peer reviewed publications.

The line patients draw between the pharmaceutical treatment of cancer using chemotherapy that sets it apart from the natural treatments is difficult to define. The simplest delineation is that materials that require a prescription are bad and that things sold in health food stores are good. My college chemistry teacher defined organic as "any chemical compound that contains a carbon atom." That's not how we use the term organic anymore. It is no easier to define what the "natural treatment of cancer" means. Many chemotherapy agents are naturally derived substances. Doxorubicin, the drug used to treat breast cancer, is derived from soil micro-organisms native to southern France. Taxol, used to treat breast and ovarian cancer, originated in the bark of the Pacific yew tree. Vincristine was derived from the periwinkle flower. You can't find more natural treatments than these.

Patients will object that these natural chemo drugs have lost their true nature through chemical refinement, that during concentration or synthesis in an artificial process divorced from nature, their essence has been lost. If we tour the modern health food store and examine the shelves of natural supplements, only a scarce few meet this bar set for 'natural'. Whether we are talking about amino acids, digestive enzymes, herbal extracts or vitamins, few still fulfill the old definition of natural being something one can cook up in their home kitchen.

This line between chemo and natural brings to mind that 1964 quotation from United States Supreme Court Justice Potter Stewart in Jacobellis v. Ohio. In attempting to define a threshold test for obscenity, Justice Stewart said, "I know it when I see it."

Wade Boyle defined the difference between allopathic and naturopathic herbalism years ago in a way that might help (I paraphrase from distant memory): "The allopaths use herbs to control and suppress symptoms. Naturopaths use herbs to stimulate the patient's Vital Force, to tonify organ systems and so to heal the patient." A parallel distinction might apply to naturopathic cancer treatment.

We might say that allopathic physicians attempt to eradicate cancer cells while naturopathic physicians stimulate the body to fight the cancer. Every cancer patient comes to us hoping we will enlist their immune system to fight their cancer, what we might call the Holy Grail of Oncology. Yet tell a patient about the history of Coley's toxins and how he isolated and cultivated bacteria from human excrement and used it via injection to stimulate an immune response and often as not, chemotherapy no longer sounds so bad to them. The new immunotherapy drugs, pembrolizumab is an example, that urge on the immune system to recognize cancer come with significant risks of provoking overreactions and creating autoimmune disease. Are these drugs natural in that they trigger a natural defense against cancer?

Patients come in seeing the world as black and white and wanting to choose one side over the other. So accustomed to modern political and social divisions, they expect a similar divide in our office and are drawn to online viewpoints that push for a similar medical dichotomy. Yet biology and medicine are more grey than black or white.

As physicians our obligation is to the patient's well-being, and we must advocate for what will help them achieve both a longer and better life. We are obligated to use every tool at our disposal and enlist every resource available on behalf of our patients. To do less is to not act in their best interest. Otherwise we should stop calling ourselves physicians. I have lost my initial hesitancy about suggesting these repurposed drugs.

One approach I have found useful is to find already existing reasons for patients to take these drugs. For example, many cancer patients have type-2 diabetes. Yet few take metformin because treating diabetes has taken a backseat to treating their cancer. We check hemoglobin A1c status on all our cancer patients. The medical standard of care is to prescribe metformin for anyone with a 5.8% or higher A1c. Few patients or doctors follow these guidelines. If a patient's results are in 'metformin range', it takes moments to find a study on PubMed reporting metformin's benefit against their particular cancer.

If the patient has heartburn or gastric discomfort during chemotherapy, we explore the use of either cimetidine[18] or a proton pump inhibitor such as omeprazole.[19] While there is reason to be cautious about using PPIs with prostate cancer[20] and with drugs that, like capecitabine, require

stomach acid for absorption,[21] in general PPIs relieve discomfort and bring a good argument that they may have anti-cancer action.

Most cancer patients during treatment are encouraged to keep a supply of antibiotics at home just in case. Not all antibiotics are equal when it comes to limiting cancer growth and I've taken to suggesting if they need to reach for one of these drugs that they try clarithromycin first.[22]

Many naturopathic patients have never let go of the idea that *Candida* overgrowth is the cause of all illness, including cancer; and with these people, it is easy to lobby for itraconazole.[23] These same patients are often concerned about other types of parasites. Rather than just running an O&P, they could pretreat using mebendazole.[24]

If patients complain of inflammation after they are taking the anti-inflammatory supplements, like curcumin and Boswellia, they should consider diclofenac. Diclofenac is a potent inhibitor of COX-2 and prostaglandin E2 synthesis and has desirable effects on the immune system, the angiogenic cascade, chemo- and radio-sensitivity, and tumor metabolism.[25]

Patients with hypertension, especially those with ovarian cancer, should consider a betablocker like propranolol.[26] A November 2018 study suggested betablockers positively affected ovarian cancer survival. Patients 60 or older who had taken betablockers for a year or more had a significantly better chance of outliving those not taking the betablockers. About half of the users were taking non-selective beta blockers (NSBB) while the rest were taking selective beta blockers (SBB). The NSBB acted faster, having a significant impact in about six months compared with two years for the SBB drugs to show effect. Risk of dying for those taking betablockers was about half of what it was for women not taking them.[27]

Artemisia has become popular and many patients are eager to be treated with it. They overlook the fact that the other antimalarial agents have stronger evidence in support, and are cheaper and easier to take, in particular chloroquine or hydroxychloroquine.[28]

In the case of patients who display symptoms of cardiovascular disease, in particularly angina, they should protect themselves during chemo and radiation by taking nitroglycerine or a slow release nitrate.[29] Then there are the PDE-5 inhibitors, angina drugs repurposed to treat erectile dysfunction, to consider.[30] One can come up with creative arguments for their use.

There is another approach to using the ReDo database, which I call the Chinese menu approach. I grew up at a time when Chinese restaurants had fixed price meals but gave the diner options for different courses. One got to pick an appetizer from column A, a main dish from column B, a rice or noodle dish from column C and so on.

Although the Redo database lists drugs alphabetically, we can re-group them by action. For example, a number of different drugs listed increase nitric oxide. The list includes several antianginal drugs, including nitroglycerine,[29] atenolol, bepridil, dalteparin, ranolazine, trimetazidine, and verapamil. As mentioned, the classic PDE5 inhibitors used to treat ED, including sildenafil, tadalafil and vardenafil are listed. Publications suggest a list of potential anticancer effects for these PDE5 inhibitors against a range of cancer cell lines using in vitro, and ex vivo xenograft animal models, including CLL,[31] prostate,[32] colorectal,[33] gliosarcoma,[34] breast,[35] melanoma,[36] multiple myeloma,[37]

Some drugs that treat diabetes, heartburn, and cardiovascular disease have anti-cancer effects.

lung,[38] lymphoma,[39] liver,[40] head and neck,[41] et cetera. There is human evidence suggesting benefit in treating Waldenstrom's macroglobulinemia, penile squamous cell carcinoma, multiple myeloma, and to suppress MDSC numbers.

The recurrent theme here is that use of these PDE5 inhibitors potentiates or enhances the cytotoxicity of chemotherapy drugs. The same is true for the antianginal drugs. All increase blood flow and this action may be how they potentiate chemotherapy; they aid delivery of chemotherapy to poorly perfused tumors. During radiotherapy these drugs help oxygenate hypoxic tumor cells, so they become more responsive to radiation.

The lesson learned may be that we should proactively increase nitric oxide levels during active treatment and any one of these drugs might help. Translating this into naturopathic approaches might be to advocate for nutritional supplements that increase nitric oxide such as beet extracts or l-arginine. Think of vasodilation as our column A.

Metformin, of course, is on the list of repurposed drugs but so are other antidiabetic medications for type 2 disease, including canagliflozin, epalrestat (a reversible aldose reductase inhibitor used for the treatment of diabetic neuropathy), the sulfonylurea drugs glibenclamide and glipizide, the GLP-1 receptor agonist, liraglutide, pioglitazone, and repaglinide. These drugs display a range of mechanisms suggesting that their benefit may be due to lowering blood sugar, lowering insulin overproduction, or by increasing insulin sensitivity. Translating this might mean weight loss, exercise, or even berberine.

The Chinese restaurant approach would have us pick a vasodilator, then second, treat diabetes under column B.

Scanning the ReDo list again, one might notice numerous antifungal medications, including clotrimazole, griseofulvin, itraconazole,[23] ketoconazole, posaconazole, and tioconazole.

Itraconazole is the best documented of these drugs. Clinical trials have shown that patients with prostate, lung, and basal cell carcinoma have benefited from treatment with

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itraconazole, and there are additional reports of activity in leukemia, ovarian, breast, and pancreatic cancers. Focus on itraconazole has suggested a potential role as a potentiator for chemotherapeutic drugs, particularly as a possible agent to reverse multi-drug resistance (MDR) (though be cautious using it with rituximab in lymphoma[42]).

The benefit from these antifungals is probably the result of various mechanisms, including inhibition of multidrug resistance, inhibition of Hedgehog signaling[43] and inhibition of angiogenesis[44] rather than their basic action of reducing fungal populations. Yet as mentioned, many of our patients worry about fungal infections and this may inspire them to want to take these types of drug.

If Column C on the menu is itraconazole, we might want to include berberine not just because it acts like metformin but because berberine has a synergistic effect with itraconazole at killing yeast.[45]

There are several blood thinners on the list: anticoagulant drugs used post myocardial infarction or with heart arrythmias to reduce clotting, including aspirin, warfarin, bemiparin, clopidogrel, dalteparin, ticagrelor, tinzaparin and ticlopidine. A blood thinner might be our column D on the menu, even something as simple as fish oil.

While nothing prohibits naturopathic treatment that target each of our menu categories, we must remember the evidence supports the drugs rather than our substitutions. We may not be ready to actively encourage use of these drugs, but at the same time we should be careful not to discourage their use, especially if there are already clinical indications for our patients to take them for other conditions.

This is a work in progress. This is all so new that we hardly have more than anecdotal evidence to support the idea of using multiple repurposed drugs together at the same time, yet this is what many researchers now advocate.

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Jacob Schor is a 1991 graduate of National College of Naturopathic Medicine in Portland, Oregon, and practiced in Denver, Colorado, until June 2019. He also has a BS degree in food science from Cornell University in Ithaca, New York. This earlier training in food chemistry and nutrition has influenced and informed his approach to naturopathic medicine throughout his career as a naturopathic doctor. He is a past president of the Colorado Association of Naturopathic Physicians and the Oncology Association of Naturopathic Physicians and also served on the board of directors of both associations as well as the American Association of Naturopathic Physicians. He is an associate editor for the *Natural Medicine Journal* and a regular contributor to the *Townsend Letter*.

HYPERCOAGULATION

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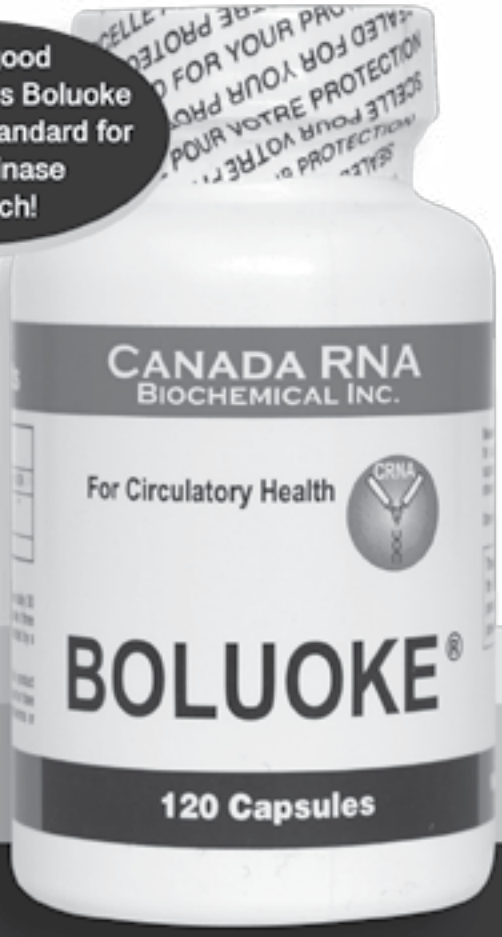

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Ancient Herbs: Potential Cancer Treatment in a New Clinical Trial

by Paul Richard Saunders, PhD, ND, DHANP

Arum palaestinum (Black Calla), *Curcuma longa* or turmeric, garlic (*Allium sativum)* and vanilla (*Vanilla planifolia)* and have long been used in traditional medical systems for a variety of clinical conditions. In this article we will explore recent research that suggests, when used in combination, these plants offer a promising cancer treatment based on cell and animal data. In fact, so promising that they are now being trusted in human trials.

Arum palaestinum is a member of the Araceae family whose closest North American relative is Jack-in-the-Pulpit (*A. triphyllum*). It has a dark purple spathe arising from a red spadix and long green leaves. The fruit, in which its seeds are contained, is a brilliant red. It is native to the Mediterranean basin but has been naturalized in North America, North Africa, Europe, Western Asia, and Australia. It can be an irritant to mucous membranes, but when properly prepared the leaves are often consumed as food with lemon and flat bread or bulgur. Its traditional uses are multiple, including cancer, worms, kidney stones, skin sores, rheumatism, tuberculosis, diarrhea, and cough among others. In a 2008 article *Arum* was reported to be consumed by over half of the residents of the West Bank of the Dead Sea.[1] Its active constituents include some 180 compounds of which isovanillin, linolenic acid, and beta-sitosterol have been the focus of considerable research.[2]

Curcuma longa is a member of the Zingiberaceae family. The other well-known member is common ginger or *Zingiber officinale.* Both species are native to India, but they can be found growing in China, Japan, and India as well as Polynesia and Micronesia, presumably spread by trade and human travel. Turmeric is a large perennial plant from which the root is harvested after 7-10 months of growth. The root is used fresh, boiled, or can be dried and ground where it provides both color and a bitter-peppery flavor to curry dishes and related spices and seasonings. The research on turmeric is extensive and was prompted by its extensive use in Ayurvedic, Siddha, traditional Chinese, and Unani medicines.[3] Its constituents include curcumin, demethoxycurcumin, bisdemethoxycurcumin and thirty-four essential oils, including tumerone, atlantone and zingiberene.[4,5] The bulk of the research points to its potential as an anti-inflammatory to reduce the risk or treat cancer as well as in osteoarthritis, ulcerative colitis, *H. pylori* infections, cataracts, and cardiovascular disease prevention.[3]

Allium sativum is a member of the Amaryllidaceae family. Garlic is native to central Asia and northeastern Iran; but as a result of trade and travel and widespread culinary use, it is planted the world over. Left on its own, garlic will naturalize and grow in the wild as a common weed. Its use in medicine probably began in China thousands of years ago. It contains small amounts of the B-complex vitamins and at least nine nutritive minerals.[6] Garlic has been researched for it use in cardiovascular disease prevention,[7] cancer,[8] and the common cold.[9] The constituents of garlic include alliin, ajoene, diallyl polysulfides, S-allylcysteine, saponins, and flavonoids.[10] When garlic is consumed, the sulfur containing compounds are metabolized into allyl methyl sulfide (AMS). Humans cannot digest AMS, so it is carried into the bloodstream, lungs, and skin from which it is excreted over several hours as the famous "garlic breath" and "garlic sweat."[11]

Vanilla planifolia or common vanilla is a vine and a member of the Orchidaceae family. It is the second most expensive spice after saffron (*Crocus sativus*). It was brought to Spain by the conqueror of the Aztecs, Don Hernan Cortes. Vanilla essence is extracted from the seedpod, contains several hundred compounds, including vanillin, which was synthesized in 1874.[12] Vanilla can lower cholesterol, contains antioxidants, calms and relieves stress, aids digestion, and may protect diabetic kidneys.[13]

Peganum harmala or Syrian rue is a member of the Nitrariaceae family and a source of harmala. The harmala alkaloids may increase serotonin and norepinephrine, and have been shown to be cytotoxic to multiple cancer cell lines. It does this by inhibiting angiogenesis, reducing expression of

vascular endothelial growth factor, and inhibiting nuclear factor-K-beta, cAMP, and activating transcription factor-2.[14,15]

Beta-sitosterol is a plant sterol similar in structure to cholesterol. It is found in many plants such as vegetable oils, nuts, and avocados.[16] Beta-sitosterol has been investigated in benign prostatic hyperplasia where it was found to improve urinary symptoms and urinary flow.[17]

Hyatt Life Sciences Herbal Research

Dr. Gene Zaid, founder of Hyatt Life Sciences, is now a very successful chemist with over 50 patents despite the fact that his life began in a Palestine refugee camp. He founded JACAM Chemical Company in his family garage in 1982 and later sold the chemical company and decided to invest in the use of plants from his native land to help people. Hyatt Life Sciences is a research-based company that produces both over–the-counter products and pharmaceutical grade products for serious health conditions such as cancer. Zaid's company has developed products using concentrated forms of the above ingredients that are called Afaya Plus and GZ17. The latter has been shown to significantly reduce both prostate cancer cell number in vitro and when implanted in mice.[2] GZ17 has also shown effect on breast cancer MCF7 and lymphoblastic leukemia 1301 cell lines. The GZ17-6.02 version has shown significant effect against head and neck squamous cell carcinoma, patient derived xenografts, and mouse syngeneic tumors *in vivo*.[18] In an open label phase I trial that began in March 2019, GZ17-6.02 is given to patients with advanced solid tumors and lymphoma.[19] The trial is expected to be completed in August 2020.

In summary, six plants or constituents of plants from Palestine and the Middle East have been combined in such a way that they have shown benefit against prostate cancer, lymphoblastic leukemia, a breast cancer cell line, and head and neck squamous cell carcinoma. An advanced form of that product is now being used in a phase I clinical trial in patients with advanced solid tumors and lymphoma. The future for plants in the treatment of cancer looks bright indeed.

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Dr Gene Zaid, founder of Hyatt Life Sciences that developed the product being researched

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Estrogen Vindication, Part 1: Estrogen and the WHI

by Devaki Lindsey Berkson, DC

This article has been abridged from the original. Full article and references available at www.townsendletter.com

Summary

Estrogen was once an extremely popular hormone. Estrogen replacement was used as an anti-aging drug by multiple millions of women in the United States and all over the world. Estrogen therapy was even standard of care to treat certain breast cancers. However, once the Women's Health Initiative (WHI) hormone trials were prematurely stopped due to early negative conclusions (July 9, 2002) claiming prescribed estrogen caused cancer and heart disease, these scary headlines prompted many doctors and women to become *estrogen-phobic*.

Nonetheless, as crazy as it seems, within only months after the WHI first published negative estrogen news, re-analyses started to emerge from scientists and statisticians at prestigious institutions. These new "look-sees" of the WHI statistical data painted completely different stories.

But the emerging "good news" never made headlines like the initial "bad news." The bad news? Estrogen can "cause" breast cancer. This turned out to be "wrong news."

The good news: Estrogen therapy in healthy women significantly "protects against" breast cancer. This good news continued to accumulate over the past two decades, without influencing "standard of care," without entering the clinical trenches of most doctors or the understanding of most women – until December 2019.

In December 2019, a 19-year reanalysis – looking back from an almost 20-year vantage point with new statistical in-depth collaborative investigation – was presented at the San Antonio yearly breast cancer symposium. Conclusions by a consortium of 12 highly respected cancer centers stated – once and for all – estrogen protects breasts. This re-analysis makes it finally undeniable that estrogen is not the enemy; rather, it *protects* breasts from cancer. Unfortunately, many doctors and women continue to not know about this news nor translate it into their practices or lives.

Even though no one knows exactly how breast cancer starts, it does not seem to be due to estrogen, but rather to *cancer stem cells* – a totally different kind of cell that has nothing to do with estrogen. Most older women, who naturally have less estrogen, have higher risks of being diagnosed with breast cancer than younger more estrogenized females. Pregnancy, which is the "highest estrogenic time" of life in any woman, is protective *against* breast cancer. In fact, there is a 70% decrease in breast cancer risk associated with a full-term pregnancy before the age of 18. It's also been shown that pregnancy is safe after treatment of breast cancer, even among estrogen receptor–positive women patients (ER+ means pathologists identify *estrogen receptors* in the tumor). Also, no benefits have been proven for aborting at the time of pregnancy in breast cancer patients, so lowering the levels of estrogen didn't cause further improvement in outcomes.

Medical practitioners thought tamoxifen worked because it was an anti-estrogen. But tamoxifen works in a wide variety of anti-cancer mechanisms, not just by tamping down estrogen. In fact, tamoxifen can often raise estrogen levels. In the HABITs study (which concluded that hormones cause breast cancer), only the women on tamoxifen turned out to have higher risk of recurrences (though this was not easy to read within the inner depths of the study and was thus was not noticed by many doctors).

The appreciation of estrogen as "foundational" in protecting many aspects of health is rapidly growing. A few examples are estrogen protects bones from fracture, blood vessels from hardening, brain from dementia, shields mitochondria (energy-producing cells) from damage, allows bodies to benefit from lifestyle changes as it promotes epigenetics, makes it easier to keep a smaller waistline, and maintains heart and kidney health.

Estrogen therapy is as close to an effective anti-aging tool that we have, even maintaining life-promoting telomere length. The longer and healthier our telomeres (the tips on our DNA), the longer and healthier we live. In fact, estrogen reduces premature death from quite a large number of possible causes.

My Story

Twenty-six years ago, I was diagnosed with breast cancer. This was not found by mammogram but by self-palpation while in the shower. I was the very first

woman in the US diagnosed with a pure mucinous cancer, a very rare cancer back then, more common now. Neither my radiologist nor oncologist had ever treated a pure mucinous cancer at that time.

I was a DES (diethylstilbestrol) daughter, meaning my mother had been given this drug when pregnant with me. DES was banned in 1971 as the most cancer-causing substance ever invented at that time. DES was the first synthetic estrogen (50 times stronger than bio-available estrogen) and given to pregnant women from 1938 to 1971 as a prenatal vitamin or to stop threatened miscarriages. Many DES daughters turned out to manifest breast cancer in their mid-40's. I was one of the very first ones.

As no one had ever treated breast cancer in a DES daughter before, I kept asking, "How do you know that what you are recommending is right for me?"

They suggested I do standard protocol, like radiation. However, even though my doctors had never treated pure mucinous tumors before, or ever treated a documented DES daughter before, after several weeks of sleuthing (pre-Internet), I found the only two groups (in the Netherlands) with human studies at that time on this type of tumor.

Due to the time changes, I had to call the principal leaders on these investigations in the middle of the night and leave messages about my circumstance. As the fickle finger of fate would have it, one head investigator didn't call me back until a very dramatic moment: I was sitting on the table getting the grid put on my chest for my first radiation treatment.

This doctor/scientist firmly recommended, "If I were you, I would not do radiation. We have learned that radiation causes fibrosis, which makes it impossible to palpate a tumor in the breast if cancer returns. Totally pure mucinous tumors are never picked up by mammograms, only by palpation. If you have radiation, you won't be able to monitor yourself appropriately. That's what we advise all our pure mucinous breast cancer patients to do: not get radiation and do vigilant breast exams."

I got off the table and told the radiologist I wasn't going to do radiation therapy. I explained to this female radiologist (wife of one of the local cancer docs) what the experienced researcher had told me. I further explained that this scientist was one of the only two research teams in the world (at that time) studying this unique tumor type. They had published a study on 95 patients with this unique tumor, and understood protective details for patients with this unique tumor.

The data clearly indicate that estrogen significantly *decreases* breast cancer incidence and deaths from breast cancer.

The radiologist spat angrily back, "F… him!" (I kid you not.) "If you don't do this radiation, you are certainly going to die!" That was 26 years ago.

Then my cancer doctors told me that I didn't need chemotherapy. *Hmmm*. Reading the science, it was becoming clearer to me (even way back then) that *stem cells* caused cancer more than the daughter cells found mostly in primary tumor loads. I decided to do my own chemo. After a lot of investigation, I found a black-market chemo from Switzerland (called "Ukraine") that was supposed to eradicate both daughter cancer cells and cancer stem cells, but not harm healthy cells. So, I did 40 rounds of this chemo with a willing local doctor.

Then my cancer doctors recommended tamoxifen. But I was one-of-a-kind – a lone woman with a pure mucinous tumor and a history of DES – so it seemed they didn't really know if it would help me and this special situation…or not. They were fitting me into the same box that all other breast cancer patients were in.

So I called Craig Jordan, the man who put tamoxifen on the map. Grateful to get him on the phone, I asked: "I have this rare tumor and this rare in-utero exposure to DES. Do you think I'm really a candidate for tamoxifen?" Dr. Jordan was thoughtful and candid, "I have to be honest with you. No one in your situation has ever asked me that. Let me look into this. I'll get back to you in a week."

To his credit Dr. Jordan indeed called back within a week and humbly explained, "If I were you, I wouldn't take tamoxifen. I think it might make DES daughters worse. Not sure, but I don't have a good feeling about it." Stunningly enough, I still get yelled at by cancer doctors today telling me I made a mistake not taking it, even though its main scientist suggested otherwise!

After all I read, it made sense to me to take estrogen therapies, even though not one of my colleagues (functional or conventional) agreed with me. I was on my own. I waited five years just to be safe, but at year six Dr. Wright wrote me the first bioidentical script for 2-methoxyestradiol (2 MEO), which I had figured out would reverse the immunosuppressive issues started by DES in the womb. I was the first person in the US to take bioidentical 2 MEO, so Dr. Wright and I had to figure out the dosage. I also began hormonal therapies of estradiol, estriol, progesterone, and testosterone.

When I saw my breast cancer doc for yearly exams over the past two decades, she would say, "You look better than any of my other patients. But stop taking estrogen. It will kill you."

Thank god, I've been well. At my ripe age, when many are winding down, I'm still winding up. My breast cancer doctor is 20 years younger than I am, but truthfully, as smart and nice as she is, she looks 20 years older as she hasn't taken hormone therapies.

This 19-year reanalysis of the Women's Health Initiative confirms my own research. (For those who want to know, I take 125 mcg/2MEO methoxyestradiol/day, along with .35 mg estradiol/.75 mg estriol BID labially, along with 3 mg testosterone/day mucosally.)

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By the way, there are a lot of nuances to taking 2 MEO. I have a webinar on it available at drlindseyberkson.com. It's hard to get. I am trying to write the monograph that the FDA requires to help move this along.

I worked at a hormone/nutritional family practice clinic, the Wiseman Family Practice clinic, in Cedar Park, Texas, for six years. I asked Dr. Richard Wiseman, who had been in practice for almost 50 years, what he thought about hormones. He ran several Ironman marathons a year, looked like he stepped out of an Irish Spring commercial, and had been prescribing bioidentical hormones all those years. Dr. Wiseman said, "If you took 100 people who all exercised and ate well, you could still pick out those who were on hormones: they will have shinier skin, more youthful voices, straighter posture, thinner waistlines, look younger, and even appear more confident."

Hormones protect so many organs – from the collagen in our skin to the volume of our hippocampus (where our memories live in the brain).

I am honored to be able to write this article to spread the word that the science shows estrogen is once again okay to prescribe and safe to take.

Summary of Criticisms of the WHI

- It only used one protocol of hormones (not individualized or diverse options).
- The age of the participants was older, many years away from hormone exposure.
- The majority of women were obese (which is a significant risk factor for breast cancer).
- The study had an extreme number of dropouts of participants.
- The recommendations could not be validly generalized to all women.
- Many of the WHI's conclusions were ultimately found to be inaccurate.

Worst kicker of all has just been realized in 2020! The WHI had huge design flaws that when analyzed, the flaws themselves pointed to the protection of estrogen on breast tissue. Dr. Avrum Bluming wrote about these serious statistical defects in the editorial section of *The ASCO Post*, in early 2020, just after the 19-year re-analysis was presented in San Antonio. Dr. Bluming wrote:

> An explanation of the hormone replacement therapy "anomaly' [huge flaw, Berkson's comment] was published in 2018. It was caused by a *lower-than-expected risk in the control group*, against whom the combination hormone replacement therapy population was measured. This lowered risk appears to have resulted from including within the placebo group women who had taken estrogen prior to joining the study and who were randomly assigned to that placebo arm. When the risk was recalculated after these women were excluded, the increased risk observed among those randomly assigned to combination hormone replacement therapy had disappeared.

In other words, some of the women in the control group had taken estrogen therapies earlier in their lives. This protected them against breast cancer. This gave the control group a lower incidence. This made the group on hormones falsely "appear" to have an increased incidence! What a statistical kettle of fish!

"This remarkable analysis," further states Dr. Bluming, "should have been incorporated into the 19-year interpretation of the results presented in San Antonio and published in *The ASCO Post* article."

Wow. This shows just had difficult it is to run randomized trails without "confounding factors" that make results nothing but questionable. Dr. Bluming also states that this may take progestins out of the picture as risk factors for breast cancer. However, there are plenty of articles linking synthetic progestins to many increased downstream health consequences.

Decline in Breast Cancer

One of the clinchers in the media and even in scientific studies that the WHI's conclusions were sacrosanct, was the recent decline in breast cancer incidence. Many said, "See, when women went off hormones (after the WHI) they got less breast cancer. This proves the HRT-breast cancer link."

I realized early on, about 2004 and 2005, that women were going to be missing out on hormones. Scouring the literature, I saw the reanalyzes that were not making headline news. I became passionate about getting the accurate science "out" so women wouldn't miss out on lifesaving and breast-saving hormones. That's why I wrote *Safe Hormones, Smart Women*. All the information inside that book has been vindicated.

As I took a deep dive into the incidence data, it became clear that breast cancer rates started to slow down *before* the WHI results came out and use of HRT went down! This is critical to understand. They did not go down because estrogen scripts went down. They went down because our surveillance has gone up.

The conclusion that going off hormones secondary to the WHI started the decline in breast cancer incidence is wrong. But this is not known by many doctors, patients, or pharmacists.

Dr. Christopher L. Li from the Division of Public Health Science at the Fred Hutchinson Cancer Research Center (one of the cancer center names on the WHI 19-year reanalysis) looked at data from 13 cancer registries from 1995 to 2004 to get a handle on what was causing reduced incidence of breast cancer cases.

They found that breast cancer rates started to go down around 1998, *well before 2002* when the WHI brouhaha hit the media. The decline, they stated, was mostly likely due to more and improved breast cancer screening. The WHI didn't start the decline, though in fact, now that we see how protective estrogen therapy is on breast tissue, it may very well have contributed to breast cancer incidence by denying women protective hormonal therapies.

WHI Re-Analyzed by 12 Prestigious Cancer Centers

From 1993 to 1998, more than 27,000 postmenopausal women, aged 50 to 79 years, with no prior breast cancer, enrolled in one of two randomized, placebo-controlled WHI

trials implemented at 40 US centers, with follow-up through September 2016.

- Women with an intact uterus received conjugated equine estrogens (CEE; 0.625 mg/day) plus MPA (2.5 mg/day) or placebo (n = 8102) for a median of 5.6 years.
- Women with prior hysterectomy received CEE alone (n = 5310) or placebo (n = 5429) for a median of 7.2 years.
- After about 19 years of follow-up, CEE+MPA resulted in a *significant 29% increased* risk of breast cancer.
- Whereas CEE alone resulted in a *significant 23% reduction* in breast cancer incidence.
- There was a *significant 44% reduction* in deaths from breast cancer with Premarin.
- There was a *45% increase* (borderline significance) in breast cancer deaths with CEE+MPA (Premarin plus the synthetic progestin MPA).

Re-Analysis Presented in San Antonio

On December 13, 2019, at the San Antonio Breast Cancer Symposium (SABCS), an abstract was presented that summarized the 19-year follow-up of the Women Health Initiative. (You can read the entire abstract in the Appendix.) Medscape published an article entitled "Remarkable New Data on Menopausal Hormone Therapy," summarizing the new research, headed by lead investigator Dr. Rowan T. Chlebowski, MD, PhD, from Harbor-UCLA Medical Center, Torrance, California, and funded by the National Institutes of Health (NIH).

Chlebowski has been a consultant for AstraZeneca, Novartis, Amgen, Genentech, Pfizer, Puma, Immunomedics, and has received NIH grant funding. So Dr. Chlebowski has been studying breast cancer and hormones for a long time from many different perspectives.

The data are "remarkable," said Dr. Chlebowski. The reanalysis study concluded:

- Estrogens are breast protective a*gainst* breast cancer, (and this protection can last up to two decades).
- Synthetic progestins *promote* breast cancer, slightly but significantly. (Other animal and human studies have implicated synthetic progesterone in increasing the risk of heart disease; estrogens do not share the same increased risk.)

Dr. Chlebowski was asked if this should change how doctors and patients look at estrogen and how it is prescribed to menopausal women. Dr. Chlebowski replied, "Yes, I would hope so! Women considering estrogen alone should know it's safe and there may be a *breast cancer benefit* associated with its use."

Dr. Chlebowski pointed out:

> …none of the approved agents for breast cancer risk reduction . . . have been able to demonstrate a reduction in deaths from breast cancer . . . so this is a very unique finding.
>
> Women should be reassured if they had short-term estrogen exposure they are not at increased risk. In fact, the data suggest there is decreased risk.

Who is saying this besides Dr. Chlebowski? The following esteemed institutions agreed with these findings and put their names on them!

- The Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center, Torrance, California;
- Fred Hutchinson Cancer Research Center, Seattle, Washington;
- Brigham and Women's Hospital, Boston, Massachusetts;
- Stanford Prevention Research Center, Stanford, California;
- University of Washington, Seattle, Washington;
- Pitt Public Health, Pittsburgh, Pennsylvania;
- Karmanos Cancer Institute, Detroit, Michigan;
- Stony Brook University, Stony Brook, New York;
- University of Tennessee Health Science Center, Memphis, Tennessee;
- Albert Einstein Cancer Center, Bronx, New York;
- The Ohio State University, Columbus, Ohio, and
- The UF Health Internal Medicine, Gainesville, Florida.

Their consensus clearly states: after 19 years of the WHI being looked at from 360 degrees, there are two different types of menopausal hormone therapy – estrogen alone and estrogen plus progestin – which have "opposite" effects on breast cancer incidence.

Of note, these effects persist long after stopping treatment (up to ten and possibly 19 years).

The data clearly indicate that estrogen – in this case horse estrogen (conjugated equine estrogens, CEE) alone (without synthetic progestins) – significantly *decreases* breast cancer incidence and deaths from breast cancer.

In contrast, CEE plus a synthetic progestin (MPA, medroxyprogesterone acetate) significantly *increases* the risk of developing the disease. In both instances, these effects linger for decades after discontinuation.

Part II of this article will discuss the physiology of estrogen and breast cancer, and the WHI and Million Women Study.

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D. Lindsey Berkson, DC, has been a leader in functional medicine, with an emphasis on the gut, hormones, and the environment for several decades. Dr. Berkson has been teaching certification relicensing courses for MDs, pharmacists, NPs, NDs and chiropractors for decades – in the last few years focusing on the gastroenterology module for A4M and hormones and oxytocin for PCCA.

Dr. Berkson formulated Metagenic's first female nutrient line for physicians. Dr. Berkson was a scholar at an estrogen think tank at Tulane University where she worked with the top scientists that discovered "receptor physiology" and growing epidemic of competitive inhibitors found in endocrine disruptors.

Dr. Berkson has authored 21 books; several have been best sellers. She also hosts the Dr. Berkson's Best Health Radio, writes the Berkson Blog (@ DrLindseyBerkson.com), and is a research fellow with Health Sciences Collegium.

Diagnostic Tests for Early Detection of Cancer: An Integrative Approach

by Leigh Erin Connealy, MD

The American Cancer Society's annual estimates of cancer diagnoses and deaths provided some good news during a year dominated by COVID-19 headlines. *Cancer Statistics, 2020* reported that the cancer death rate decreased by 29 percent between 1991 and 2017, and the decline of 2.2 percent from 2016 to 2017 was the greatest ever annual drop in cancer mortality.[1]

These positive trends were attributed to a number of causes, including declines in smoking; advancements in treatment, especially for hematopoietic and lymphoid cancers; and improvements in early detection. However, the researchers also pointed out that progress is slowing for prostate, breast, colorectal, and cervical cancers, which are common targets of screening. Furthermore, for cancers such as liver, lung, pancreas, esophagus, and ovarian that are generally not diagnosed until later stages, prognosis remains poor.

This underscores the need for more sensitive tests for the early detection of cancer. Cancer begins developing in the body years before it becomes symptomatic or can be picked up by the usual screening and diagnostic tests. Very early detection with tests that are often overlooked by conventional doctors gives physicians and patients the best opportunity to halt cancer progression and even reverse abnormal cellular changes before they develop into full-blown malignancy.

The Cancer Profile

The Cancer Profile is a comprehensive blood test that measures a number of hormones, cancer antigens, proteins, and enzymes. Analyzed as a whole, these markers reveal biochemical changes that occur when cancer is present or developing anywhere in the body.

Tests include human chorionic gonadotropin (hCG), which is produced not only during pregnancy but also by cancer cells. Any amount of hCG in the blood or urine may be indicative of cancer.[2] Another is phosphohexose isomerase (PHI), also called autocrine motility factor. PHI is an enzyme that regulates anaerobic metabolism. An elevated PHI suggests that cellular metabolism may be shifting towards low-oxygen glycolysis, which makes the body more hospitable to cancer growth.[3]

Thyroid stimulating hormone (TSH) is included because thyroid hormones' essential role in growth, differentiation, and metabolism has a significant effect on the development of cancer.[4] The Cancer Profile measures gamma-glutamyl transpeptidase (GGTP), a marker of liver disease that is also an early predictor of several types of cancer.[5] In addition, it tests carcinoembryonic antigen (CEA), which is elevated in most types of cancer, and dehydroepiandrosterone sulfate (DHEA-S), an adrenal hormone linked with immune function and resistance to stress.

Developed by Emil Schandl, PhD, founder of American Metabolic Laboratories, the Cancer Profile can identify cancer in its early developmental stages, ten to 12 years before it shows up on routine tests.[6] Because it provides warnings that cancer may be brewing, it is one of the best tools for cancer prevention. It is also useful for monitoring the effectiveness of cancer treatments and detecting early signs of recurrence.

RGCC Oncotrace

One of the problems with conventional cancer tests and treatments is that they fail to detect and eliminate circulating tumor cells (CTCs) and cancer stem cells (CSCs). CTCs are cancer cells that are shed from tumors and released into the vascular system. As these cells circulate through the body, they may nest in various organs and are therefore a major source of metastasis and cancer recurrence. CSCs are residual cells with stem cell-like properties that make them resistant to drugs and other treatments that kill most cancer cells.[7] Together, CTCs and CSCs are responsible for 95 percent of metastatic cancer and cancer deaths.

Oncotrace is a blood test developed by RGCC, an international medical genetics company. Referred to as a "liquid biopsy," it uses multiple cell markers to identify CTCs and CSCs in the blood.[8] This may be the most important test for detecting metastasis and cancer recurrence. A patient could be declared cancer-free following treatment, but the only way to be sure is to test for CTCs and CSCs.

RGCC also offers blood panels that evaluate the sensitivity of each patient's cancer cells to dozens of common chemotherapy drugs and natural anticancer agents.[9] This allows physicians to develop personalized treatment plans that target each patient's genetically unique cancer.

Nagalase Test

Alpha-N-acetylgalactosaminidase, commonly called nagalase, is an enzyme secreted by cancerous cells that shuts down a key aspect of the immune response that keep cancer

in check. It interferes with the conversion of precursor proteins to Gc macrophage-activating factor (GcMAF), a protein that triggers macrophage activity. An increase in nagalase levels in the blood has been directly correlated with tumor burden, cancer aggressiveness, and disease progression in a wide range of cancer types.[10]

Testing serum nagalase levels is a reliable means of detecting cancer, monitoring progression and treatment response, and fine-tuning treatment protocols. Interestingly, a GcMAF-based immunotherapy has been developed that has proven effective in reducing serum nagalase levels and improving clinical outcomes in patients with various stages and numerous types of cancer.[11] Nagalase levels are also increased in certain viral infections, including HIV, HSV-1, and HSV-2, suggesting additional applications for this test. It is available through Health Diagnostics and Research Institute.[12]

Comprehensive Blood Tests

All doctors order blood tests for their patients, but many of them are unaware of the insights that some of these tests reveal about cancer risk and progression. For instance, a complete blood count (CBC) provides valuable information about cancer risk and response to treatment. Studies have shown that even a modestly elevated hemoglobin A1c (HbA1c) is associated with an increased risk of most types of cancer.[13] A high HbA1c level signals the need for diet changes and other interventions to control blood sugar, since diabetes is a well-established risk factor for cancer.[14]

Because excessive inflammation is present not only in cancer but in many chronic degenerative diseases, high-sensitivity C-reactive protein (CRP) is by no means a rule-out test for cancer.[15] Nevertheless, cancer should be considered in patients with elevated inflammatory markers, and normalizing inflammation is an important goal in prevention and treatment. Multiple studies link a low blood level of vitamin D with an increased risk of cancer.[16] Bringing the 25-hydroxy vitamin D level into the optimal range of 50–75 ng/mL with supplemental vitamin D3 is a cornerstone of a nutritional approach to cancer prevention.

Other blood tests that provide actionable information include natural killer (NK) cell function test, which measures the activity of critical immune cells, and beta-hCG (also called quantitative hCG), a tumor marker as discussed above. All told, comprehensive blood tests provide signs of early disease and can help doctors devise prevention and treatment strategies.

Heavy Metal Testing

Acute heavy metal poisoning, usually due to workplace or accidental exposure, is a medical emergency that presents with obvious symptoms such as abdominal pain, vomiting, chills, and shortness of breath. Low-level exposure to mercury, lead, cadmium, arsenic, and other heavy metals also has cumulative adverse effects and can cause organ damage and increase the risk of multiple diseases, including cancer.[17]

Although acute poisoning is rare, we are all exposed to toxic heavy metals in the air we breathe, the water we drink, the food we eat, the personal care products we use, and the amalgam fillings in our mouths. Unfortunately, low-level exposure often goes unnoticed, and the resultant fatigue, headaches, aches and pains, and attention and memory problems are usually attributed to other causes. A number of labs, including Doctors Data, test heavy metal concentrations in blood, urine, stool, and/or hair samples. Taking steps to lighten patients' toxic burden via removal of amalgams, dietary changes, targeted supplements, and/or oral or intravenous chelation therapy often improves symptoms and reduces the risk of serious disease.

Food Sensitivity Testing

Diet is an important determinant of health, and poor dietary habits go a long way toward explaining our epidemic of obesity and chronic diseases. Even a reasonably good diet can stress the body if it contains foods that cause an allergic or hypersensitive response. Therefore, identifying problematic foods and cleaning up the diet is an important step in the prevention and treatment of cancer and other diseases.

Early detection permits the use of strategies and lifestyle measures to prevent full-blown cancer.

Food allergies were once believed to be relatively rare. But a 2019 study involving more than 40,000 adults found that 10.8 percent of participants had symptoms after eating specific foods that were consistent with IgE-mediated immune reactions – and 38 percent of them reported at least one food allergy-related emergency room visit.[18] Skin-prick, scratch, and blood tests for IgE antibodies are reliable tests for diagnosing food allergies, and strict avoidance of the offending foods is the only treatment.

Nineteen percent of participants in the above survey thought they had a food allergy, but based on symptoms, the researchers concluded it was more likely a sensitivity or intolerance. Food intolerances have many causes and trigger many symptoms. Lactose intolerance, for example, is a genetic lactase deficiency that causes bloating and gas, while non-celiac gluten sensitivity may manifest as anything from brain fog and migraines to joint pain and digestive disorders. These problems are also common signs of other conditions, so they are rarely attributed to diet.[19]

While IgE testing is a proven means of identifying allergies, it does not pick up food intolerances. Breath tests can determine intolerances to fermentable carbohydrates such as fructose and lactose, and Meridian Valley Lab, US BioTek, and other companies offer blood panels that test for IgG and other non-IgE-mediated reactions to scores of foods. Another method is the elimination diet, which is quite reliable, especially when done under the guidance of a healthcare professional.

Cologuard Stool DNA Test

With early detection, the five-year survival rate of patients diagnosed with colorectal cancer exceeds 90 percent. Yet screening rates lag far behind the CDC's stated goals, and colorectal cancer is the third-leading cause of cancer deaths

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in the US.[20] The most common screening tests for men and women of average risk, beginning at age 45, are annual fecal occult blood tests (FOBT) or colonoscopy every 10 years. In recent years, stool DNA testing has been approved as another alternative.

Cologuard is a test that analyzes DNA in cells collected from a stool sample. It identifies DNA changes suggestive of colon cancer or precancerous polyps as well as blood in the stool, another potential sign of cancer. Even though it is not as accurate as colonoscopy, which is the gold standard for colorectal cancer screening, it is more sensitive than FOBT. In a study published in the *New England Journal of Medicine,* the stool DNA test detected 92 percent of colon cancers, although it was less effective at detecting precancerous polyps, plus 13 percent of tests were false positives and 8 percent were false negatives.[21]

Stool DNA testing is not recommended for anyone with a personal or family history of colorectal cancer or previous abnormal findings on colonoscopy. However, because it can be done at home with a mailable test kit, is covered by Medicare and many insurers, and requires no diet restrictions, bowel prep, or anesthesia, stool DNA testing is a good option for early detection.

Thermography

Thermography is a method of screening for breast cancer that uses infrared imaging technology to measure heat, inflammation, and vascular changes within the breast that are indicative of cancer. Researchers report that thermography can detect 86 percent of nonpalpable breast cancers, find some cancers that were missed by mammography, and identify abnormal findings eight to 10 years before a mass could be detected on a mammogram.[22] For instance, vascular patterns such as an asymmetrical increase in vein development in one breast suggests that the body may be creating new blood vessels to feed a nascent tumor.[23]

There is some controversy about thermography as a screening tool, and some studies have found it to be less accurate than mammography. But mammograms have a number of shortcomings. They miss about 20 percent of breast cancers; and false positives, which lead to unnecessary testing and overtreatment, are even more common. In addition, repeat mammograms expose patients to potentially harmful radiation that could potentially cause cancer.[24]

For all these reasons and more, thermography is, in my opinion, a preferable tool for breast cancer screening, early detection, and tracking progress of patients during and after treatment.

Ultrasound, PET, MRI, and CT Scans

The screening and diagnostic scans that are common tools of conventional oncology provide a wealth of information. Positron emission tomography (PET) scans, which "light up" cancer cells and other areas of heightened metabolic activity, are great for diagnosing cancer and metastasis. Magnetic resonance imaging (MRI) uses magnetic fields and radio waves to provide extraordinarily detailed images that help pinpoint tumor location and stage cancer. Computed tomography (CT) scans produce in-depth images of organs, soft tissues, and tumors by taking multiple X-rays from different angles. Ultrasound, an exceptionally safe technology, uses high-frequency sound waves to visualize tumors, cysts, and other soft tissue structures in the body.

Although PET, MRI, CT, and ultrasound are useful for guiding treatment, they can only visualize cancers that have reached a certain size – and a tumor becomes apparent only after it has been growing for years and has amassed tens of billions of cells.[25] In addition, these scans are unable to identify circulating tumor cells and cancer stem cells until they have nested and grown to an appreciable size. By the time a tumor can be detected, it is quite far along on the cancer developmental trajectory.

Another drawback with CT and PET scans is that they expose patients to hundreds of times more radiation than a chest X-ray, and excess exposure to medical radiation has been linked with an increased risk of developing cancer.[26] Of course, these scans are sometimes necessary, especially for patients with more advanced disease. For early detection, however, they are of limited value.

BioImmune Survey Bioenergetic Testing

Bioenergetic testing is an underutilized type of testing that measures the flow of energy through the body's meridians, or energy pathways. The BioImmune Survey we use at my clinic involves a computerized electrodermal screening device that tests the galvanic skin response and monitors energy imbalances suggestive of problems and their precise locations in the body.

The goal of bioenergetic testing is early detection and disease prevention. Subtle imbalances show up on bioenergetic testing long before they become evident on conventional bloodwork and scans. This test detects the presence of low-level infections, toxins, parasites, nutrient deficiencies, and other abnormalities that pave the way for the development or progression of cancer and other diseases. Bioenergetic testing also suggests specific remedies, lifestyle changes, and treatments that are most likely to be of benefit for boosting immune function and enhancing overall health.

Leigh Erin Connealy, MD, is the medical director of the Cancer Center For Healing and the Center For New Medicine in Irvine, California. Dr. Connealy's multidisciplinary treatment protocols, team of healthcare professionals, and holistic approach to health and healing have made the Centers the largest integrative/functional medicine clinic in North America, visited by more than 47,000 patients from all over the world. Author of *The Cancer Revolution* and *Be Perfectly Healthy* and a sought-after speaker who has appeared on numerous TV and radio shows, webinars, and podcasts, Dr. Connealy has been named one of the top functional and integrative doctors in the US.

Cancer Center for Healing, 6 Hughes, Irvine, CA 92618; 949-581-HOPE (4673); https://www.cancercenterforhealing.com/

Conventional doctors look askance at bioenergetic testing, and it is not embraced by all integrative physicians. However, in my 30-plus years of practicing medicine, I have found it to be an excellent adjunct to other tests.

Nutritional Testing

Nutrition is a foundation of integrative medicine, which underscores the importance of personalized nutritional counseling and testing for food allergies and intolerances. However, diet is not the only determinant of nutritional status. Genetics, gut health, age, and underlying disease burden are also key factors.

A number of tests are available for evaluating nutritional status. One is SpectraCell's Micronutrient Test. Rather than simply measuring blood levels of various nutrients, this test assesses functional deficiencies by determining how effectively 31 essential vitamins, minerals, amino acids, fatty acids, antioxidants, and metabolites are utilized within the white blood cells. This provides a clear picture of how various nutrients are functioning in the body.

Another is Genova Diagnostics NutrEval, a comprehensive test that includes both urine and blood analyses. Tests include organic acids, which provides insight into dysbiosis and malabsorption, mitochondrial and neurotransmitter metabolism, and toxin exposure. Amino acid and fatty acid analyses assess protein digestion and absorption and reveal imbalances in the ratios of omega 3, 6, and 9 and other fatty acids. Markers of oxidative stress and measurements of coenzyme Q10, glutathione, and other antioxidants are included, along with intracellular levels of nutritionally important minerals as well as toxic heavy metals.

Even subtle deficiencies of vital micronutrients can make the body more vulnerable to cancer and other diseases. The results of these two tests allow practitioners to recommend a therapeutic nutritional supplement program based on each patient's unique biochemical individuality.

Conclusion

Despite the recent advances in death rates, cancer remains a fearsome disease. More than 1.8 million new diagnoses of cancer and 606,520 cancer deaths are predicted in the United States in 2020.[1]

It is not only cancer itself that is frightening but also the conventional treatments and all their attendant adverse effects. Safer, more effective treatments are obviously needed, but that alone will not be enough to truly turn the tide. Only with widespread adoption of preventive strategies such as lifestyle changes plus early detection, when the best outcomes are possible, will cancer cease to be the formidable disease it is today.

Diagnostic Tests for Cancer

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Can Acid Reflux Be Reduced by Breathing?

by Erik Peper, PhD, BCB; Lauren Mason; Richard Harvey, PhD; Lisa Wolski; and Jasmine Torres

San Francisco State University

This article has been abridged from the original. Full article, figures, and references available at www.townsendletter.com

Gastroesophageal reflux disease (GERD), more commonly known as acid reflux, is a common and chronic disorder that affects up to 20% of people living in the US. GERD is defined as the regurgitation or retrograde movement of stomach acid and gastric fluids into the esophagus. The symptoms of GERD often include severe chest pains, heartburns, and can later result in the development of mucosal damage. Mucosal damage and chronic reflux in the esophagus often are precursors to esophageal cancer and can cause further complications. As the prevalence of GERD increases, so do the risks of damage due to chronic exposure to stomach acid (e.g. acid reflux).

Unsurprisingly, symptoms of acid reflux mostly occur if someone begins lying down shortly after a meal, when stomach acid may more easily move to the esophagus with gravity. In addition, sleeping on a slanted bed with the head higher than the feet, so that the stomach content flows downward, often reduces GERD symptoms at night. Predictably, some behavioral recommendations for patients with GERD are to avoid lying down shortly after meals as well as sleeping on a slanted bed.

Acid reflux most commonly affects people over the age of forty, and males tend to have higher rates of complications. Diet, obesity, tobacco, and alcohol, among other factors such as genetics, are higher risk factors to the development of chronic acid reflux. Recommended lifestyle changes include dietary modifications, weight loss, and body position; thus, health care providers often advise obese patients to lose weight since it can significantly reduce GERD. Because treatment options for GERD not only include medications and surgery, but also lifestyle changes, some treatment options will be discussed next.

Treatment Options for GERD

There are generally three categories of treatment options for GERD patients: lifestyle changes, medication, and surgery. Lifestyle changes are typically the first line of treatment. This includes eating small bites of food, avoiding fatty or acidic foods, or any foods that may irritate or worsen symptoms of GERD. Weight loss in patients who are overweight has been associated with symptom reduction, as well as avoiding alcohol and tobacco use, especially around mealtimes.

Acid-suppressive medication most often include antacids, histamine-receptor antagonists, and proton-pump inhibitors. Both antacids and histamine-receptor antagonists work to neutralize stomach pH. Although both of these medication types are generally prescribed for GERD patients, tolerability varies as there are some adverse side effects such as nausea, vomiting, and other side effects that lead to exacerbated gastrointestinal issues. Aside from side effects, these medications also cause pH to deviate from normal stomach pH that can cause other digestive complications. Rather than decreasing stomach pH, proton pump inhibitors work to decrease the production of stomach bile. This treatment responds more poorly than antacids or histamine-receptor antagonists, has many more complications, and has a rising safety concern for its use. Anti-reflux surgery is an effective treatment option for long-term therapy but is not without complications. Disadvantages of surgical interventions include long-term medical maintenance, alongside complications such as dysphagia, bloating, as well as the risk of recurrence.

Systemic Stress-Reduction Interventions

Behavioral interventions aim to reduce stress that is associated with acid flow up into the esophagus. Stress reactions related to acid reflux may be reduced by enhancing vagal tone through training such as heart rate variability biofeedback. For example, Sowder et al (2010) as well as Sun et al, (2016) demonstrated that functional abdominal pain can be reduced with heart rate variability feedback training. In most cases, the increased vagal tone was achieved by breathing at about six breaths per minute.

Although many factors contribute to acid reflux, one common theme associated with behavioral interventions

is to reduce the compressive forces on the stomach that would push the stomach acid into the esophagus. Furthermore, decreasing activities such as coughing or increasing pressure gradient across the diaphragm can reduce triggering acid reflux. An under-recognized compressive factor not listed is the pattern of respiration that involves the pressure and muscles around the stomach and esophagus. For example, during inhalation, the diaphragm flattens and descends, thereby pushing down on the abdominal content downward. If the abdomen cannot expand or extend fully, then the stomach becomes squeezed. In some cases, this causes the stomach content to be pushed upward into the esophagus resulting in heartburn and acid reflux. The factors that tend to restrict abdominal expansion include restrictive clothing, abdominal wall tightening, and obesity, in addition to the stress-breathing patterns that could be triggered by fear—all which may contribute to somatic discomfort and adverse symptoms.

Educating Clients About the Hydraulic Model

Informing patients about the role of abdominal expansion during inhalation is seldom included in medical treatment approaches for two main reasons: most people think that breathing occurs in the chest, and training to breathe diaphragmatically takes time. It may be faster to treat a symptom of GERD with 'acid-reducing' medications compared to the training a client or patient to breathe correctly, which is a more curative albeit time-consuming path to patient health.

When educating clients about 'full-body' breathing that includes engaging both the chest and abdomen, it is useful to review some breathing patterns associated with acid-reflux symptoms. For example, when GERD patients breathe in their chest, they often pull in their abdomen – a pattern associated with fear. To reduce the inter-abdominal pressure on the stomach, the abdomen needs to expand during inhalation. Reducing inter-abdominal pressure includes wearing looser clothing that does not constrict the waist, a phenomenon referred to as *designer jean syndrome.* When clothing around the waist is loosened, then the abdomen has the opportunity to expand in all directions in response to the downward movement of the diaphragm during inhalation.

Most people have experienced the benefits of loosening the waist when eating a large meal. The moment the stomach is allowed to expand, the person may begin to feel more comfortable. If you have experienced this benefit of unrestricted abdominal movement during breathing, ask yourself, "What could the long-term cost be of keeping the waist constricted?" A constricted waist such as from wearing tight clothing, from 'designer jeans' to a corset, may be as harmful to our health as having the emergency brake on while driving for a car. Furthermore, we are usually unaware that shallow, rapid breathing in our chest, especially with constrained abdominal movement, may contribute to symptoms such as anxiety, neck and shoulder tension, heart palpitations, headaches, abdominal discomfort such as heartburn, acid reflux, irritable bowel syndrome, dysmenorrhea and even reduced fertility.

Restrictive clothing, adominal wall tightening, and slouching compress the stomach and push stomach acid into the esophagus.

Assessing Risk of Faulty Breathing

There are some simple behavioral steps for observing less healthy breathing patterns. For example, stand up and observe what happens when you take in what you feel is a 'big' breath and then exhale. Did you feel taller when you inhaled and shorter/smaller when you exhaled?

If the answer is YES, your breathing pattern may compromise your health. When you inhaled you most likely feel the muscles associated with lifting your chest, slightly arching your back, tightening and raising your shoulders, and lifting your head up while slightly pulling the stomach in. When you exhaled, you most likely feel muscles associated with the relaxing and collapsing the torso downward. Even the stomach muscles may have relaxed allowing the abdomen to expand. Unfortunately, expanding the chest while tightening the abdomen during inhalation is a dysfunctional breathing pattern, and the opposite of a breathing pattern that supports health and regeneration.

When you observe the breathing pattern of babies, young children, dogs, and cats, they are peaceful, breathing rhythmically into their belly. The abdomen is the main body area that appears to move during breathing. While breathing in, the abdomen expands in 360 degrees and when breathing out, the abdomen constricts and comes in. Similarly, when dogs or cats are lying on their sides, their stomach goes up during inhalation and goes down during exhalation.

Some people tend to breathe shallowly in their chest, as if they have forgotten to – or cannot – allow their abdomen and lower ribs to widen and extend during inhalation. Some factors contributing that restrict abdominal breathing include the following:

- Constriction by tight clothing such as "Spanx" (a modern form of corset?) to slim the figure, or by wearing tight fitting pants ('designer jeans'). In either case, the abdominal content is pushed upward and interferes with unrestricted healthy breathing.
- Maintaining a slim figure by pulling the abdomen in (i.e. "*I will look fat when my stomach expands; I will suck it in"*).
- Avoiding post-surgical abdominal pain by inhibiting abdominal movement. Numerous patients have unknowingly shifted to shallow breathing in their chest to avoid pain at the site of the incision of the abdominal surgery such as for hernia repair or a Cesarean operation. A 'guarded' breathing pattern – guarding

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against the pain from abdominal surgery – trains a dysfunctional breathing pattern, which becomes the new 'normal' way of breathing unless they actively practiced diaphragmatic breathing to reverse the learned disuse of abdominal breathing muscles during recovery.

- Slouching as we sit to watch digital screens or, look down at our cell phone.

Observe how slouching affects the space in your abdomen**.** When you shift from an upright, erect position to a slouched or protective position, the distance between your pubic bone and the bottom of the sternum (xiphoid process) is significantly reduced. In the slouched/collapsed position, there is less space for the abdomen to expand in the protective collapsed position.

Regardless of why people breathe shallowly in their chest or avoid abdominal and lower rib movement during breathing, re-establishing healthy diaphragmatic breathing addresses a variety of symptoms such as hydraulic movement of acid from the stomach into the esophagus, anxiety, feeling faint, and complaints of various muscle aches associated with the chest and abdomen. Furthermore, students have reported that when they sit erect and shift to diaphragmatic breathing, which means the abdomen and lower ribs expand during inhalation and come in during exhalation, their symptoms such as acid reflux, irritable bowel disease and even menstrual cramping significantly decrease.

Case Example of Diaphragmatic Breathing to Reduce Acid Reflux

Participant: A 21-year-old female student who has suffered acid reflux (GERD-gastroesophageal reflux disease) frequently had to see doctors and has had a very long history of stomach problems since age 6. She was prescribed medications by all of her physicians, but none of them were very effective. Upon entering college, her acid reflux became especially severe. Her acid reflux started affecting her life in more ways than just stomach pain. She would avoid going out with friends with the worry of what they would eat and if it would cause her pain later. She started getting anxious and felt depressed because she felt that her acid reflux restricted her from living a normal life as a young adult. She had taken various over-the-counter antacid medications for a long time, as advised by her doctors, but these over-the-counter antacid treatments were not very effective. The more she took medications, the less effective it would become, and eventually, she completely stopped taking medications altogether.

The following is a typical procedure for assessing and training the participant.

Equipment and Pre-Baseline Stress Assessment: Breathing rate was recorded with respiratory strain gauges around the chest and abdomen (ProComp Infinity version 6.1, Thought Technology, Ltd). The participant sat comfortably for one minute. Respiration monitoring continued while she thought about a stressful memory for one minute, then let go of the stressor and sat comfortably for one minute.

Training: The learning of healthy breathing skills was part of a university class experience learning about biofeedback.

- She was coached in diaphragmatic breathing and instructed to wear looser clothing during the classroom training. During each session, she learned through biofeedback training to associate stressful thoughts with chest or abdominal breathing patterns.
- After several sessions over two weeks, a shift to predominantly diaphragmatic breathing occurred when she became more aware through breathing biofeedback of being stressed or breathing in her chest.
- Sessions also included training her to place her hands on her belly to generalize without the biofeedback devices what it felt like to breathe abdominally without instruments in a classroom.
- She also kept a weekly log during the semester to record severity of acid reflux on a relative scale of zero to ten, with zero being 'not at all severe' and 10 being the 'most severe'.
- She also tallied up each time she was in a stressful event and whether she shifted her attention to her breathing during that time.

Post-Baseline Stress Assessment: Each post-session measurement included sitting comfortably for one minute. Respiration monitoring continued while she thought about a stressful memory for one minute, then let go of the stressor and sat comfortably for one minute.

Results: After training, her breathing pattern shifted from predominantly thoracic breathing (19 breaths/min) to abdominal breathing (7 breaths/min). She also had learned to maintain abdominal breathing during stress, as shown by comparing the pre- to post-stress assessments. Her symptoms decreased within two weeks and she took no more medication.

At the 11-month follow-up, she continued to be symptom free.

Before Training

- She wore tight clothes that added pressure around her abdomen.
- She restricted her diet to avoid foods that triggered symptoms.

After Training

- She wore looser fitting clothes that reduced the pressure on her stomach.
- She started eating foods that previously would have caused irritation and was able to eat spicy or acidic foods and drink alcohol without evoking symptoms.
- Whenever she felt that she was about to have an episode of acid reflux, she calmed down and focused on her breathing while keeping her hands on her stomach, feeling it expand, and making sure she was not tightening her abdomen. Being more mindful of her breathing, she immediately noticed when she held her breath or started breathing thoracically, and she was able to remind herself to take deep breaths from the abdomen.

Discussion

After discovering biofeedback methods that allowed her to monitor her own breathing and learning diaphragmatic breathing techniques, she tried incorporating this knowledge in an effort to mitigate her symptoms of acid reflux. She soon observed that she breathed thoracically, through her chest, rather than allowing her abdomen to expand. When she first started to practice diaphragmatic breathing,

it felt unfamiliar, unnatural and at times uncomfortable because she had unconsciously grown so accustomed to breathing predominantly in her chest.

After she learned to practice slower diaphragmatic breathing by allowing her abdomen to expand naturally during inhalation, her acid-reflux symptoms decreased. She also used imagery to describe what she experienced, stating that her lungs were like a balloon located in her abdomen. To create space for the diaphragm going down, she bought larger size pants so that her abdomen could spread out instead of squeezing her stomach.

In a follow-up one year later, she continued to incorporate diaphragmatic breathing and reported no symptoms of acid reflux.

Before learning abdominal breathing techniques using biofeedback training, she had to restrict her diet by avoiding certain foods. However, after having little to no symptoms of acid reflux, she started eating foods that would previously have caused irritation. Now, she is able to eat spicy or acidic foods, and drink alcohol without having GERD symptoms or affecting her stomach at all.

She had become aware that her tight clothes contributed to adding pressure around her abdomen and shifted wearing looser fitting clothes to alleviate the pressure on her stomach. Whenever she felt that she was about to have an episode of acid reflux, she practiced techniques learned with biofeedback training to calm down and focus on her breathing, keeping her hands on her stomach, feeling it expand, and making sure she's not tightening her abdomen. She reported being more mindful of her breathing, able to immediately notice when she holds her breath or breathe thoracically, and able to remind herself to take deep breaths from the abdomen.

To prevent problematic symptoms from returning, she practiced diaphragmatic breathing many times during the day. In addition, the moment she felt stressed and tightened her abdomen, she interrupted this tightening and re-established abdominal breathing. Practicing this was very challenging since she had to accept that she would still be attractive even if her stomach expanded during inhalation. In addition, each time she slouched, she shifted to an erect position that also allowed her abdomen to expand. (To appreciate the challenges involved and how to integrate breathing and awareness into daily life, watch her interview: https://peperperspective.com/?s=acid+reflux. Also, for a detailed description how this approach successfully cured irritable bowel see: https://peperperspective.com/2017/06/23/healing-irritable-bowel-syndrome-with-diaphragmatic-breathing/.)

Conclusion

A major reason why this case study was successful is that the student integrated the breathing pattern into her daily life. This meant buying looser fitting clothing and shifting to slow diaphragmatic breathing when she became aware of breathing in her chest as a reaction to stress or feeling an increase in abdominal pressure. *What would be necessary for a simple behavioral breathing intervention to be the first strategy in the treatment of acid reflux?* An obvious answer would be training practitioners to incorporate breathing biofeedback techniques into their practice. Participants, patients and clients should be trained to increase diaphragmatic breathing and to interrupt gasping and chest breathing patterns during the day. Using not only diaphragmatic breathing biofeedback training, but also heart rate variability (HRV) training could be a simple intervention for GERD. Slower diaphragmatic breathing with the corresponding abdomen movement at about six breaths per minute helps reduce autonomic dysregulation and increase vagal tone. Healthy breathing regulation has profound self-healing effects that accrue over the lifetime. Whereas breathing biofeedback was found effective for reversing the symptoms of GERD in a college student, the principles of biofeedback training are applicable across a broad range of symptoms, from GERD to autonomic dysregulation. Holistic health treatment techniques that focus on behavioral approaches, including biofeedback training, should be taught as first-line interventions as a complement to all other healing arts. ◆

Erik Peper, PhD, BCB, is an international authority on biofeedback and Professor of Holistic Health Studies / Department of Health Education at San Francisco State University. He is president of the Biofeedback Federation of Europe and past president of the Association for Applied Psychophysiology and Biofeedback (AAPB). He has received numerous awards such as 2013 Biofeedback Distinguished Scientist Award in recognition of outstanding career and scientific contributions from the Association for Applied Psychophysiology. He has a biofeedback practice in Berkeley, California, at BiofeedbackHealth (www.biofeedbackhealth.org). He is an author of numerous scientific articles and books such as *Make Health Happen, Fighting Cancer-A Nontoxic Approach to Treatment,* and *Biofeedback Mastery*. He publishes the blog, *the Peper perspective-ideas on illness, health and well-being* (www.peperperspective.com). He is a recognized expert on holistic health, stress management and workplace health. His research interests focus on self-healing strategies to optimize health, illness prevention, the effects of respiration and posture, and self-mastery with biofeedback.

The Curcumin Conundrum

by Dr. Douglas Lobay, BSc, ND

This article has been abridged from the original. Full article and references available at www.townsendletter.com

"Hi, this is Dr. S from Vancouver. I just wanted to talk to you about a new curcumin compound with 30% bisdemethoxycurcumin that you might be interested in. A lot of new studies say it is better for inflammation and cancer than the old curcumin. I will email you some information and references about this new exciting product. And if you're interested…."

After the phone call I looked at my dispensary and pondered my perplexing dilemma. I realized I had a conundrum on my hands. I have been happily prescribing turmeric and curcumin products mainly for pain and inflammation and for adjunctive cancer treatment. My recommendations were based on what little knowledge I had about curcumin and patient feedback. I concluded that my recommendations were largely based on conjecture and inference on what information the supplement companies were providing about their products. So I decided to research a little further on the medical databases available and to see what I could learn. I remembered that one tenet of naturopathic medicine is that the doctor should be a teacher. I surmised that I should be able to convey accurate, practical, and useful information to my patients so they can make better choices about turmeric and curcumin.

Turmeric (*Curcuma longa*) is a perennial herb that is indigenous to India and Southeast Asia. It grows up to one meter in height. It has small elliptical or oblong green leaves and a deep orange or yellow colored root or rhizome. It is a member of the ginger or Zingiberaceae family and the Curcuma genus, along with over 100 allied species. The brightly colored root and rhizome has been used as a culinary spice in food preparation. As a part of curry powder, it has been mixed with coriander, cumin, black pepper, ginger, and other spices. As a dye it has been used in the clothing and textiles industry. It has also been used in cosmetics and the food and beverage industry. The root and rhizome has been described as pungent, bitter, and earthy and has been used in Ayurvedic medicine for several thousand years.

The chemical constituents of turmeric have been identified as follows: 1% to 6% curcumin, 3% to 7% volatile oils, 2 to 7% fiber, 3 to 7% mineral matter, 6 to 8% protein, 5 to 10% fat, 6 to 13% moisture and 60 to 70% carbohydrate. Other sources have listed curcumin content from 1 to 8%. It should be noted that the total curcumin content of the root is probably better referred to as total curcuminoid content. The curcuminoid content reflects the fact that there are several slightly different but related chemicals in the root and rhizome of turmeric.[1]

Curcumin is the name given to the chemical that is responsible for the bright yellow and orange color of the turmeric plant in the root and rhizome. Curcumin has been identified as the main active ingredient of this plant. However, three main curcuminoid molecules have been identified in the turmeric plant: Curcumin or diferuloylmethane, demethoxycurcumin and bisdemethoxycurcumin. The naturally occurring content of curcumin has been identified to be between 60 to 70% while demethoxycurcumin is between 20 to 27% and bisdemethoxycurcurcumin is between 10% and 15%.[1]

Turmeric and curcumin have demonstrated a wide range of activity including anti-inflammatory, anti-HIV, antibacterial, antifungal, nematocidal, antiparasitic, antimutagenic, antidiabetic, antifibrinogenic, radioprotective, wound healing, lipid lowering, antispasmodic, antioxidant, immunomodulatory, anticarcinogenic, anti-Alzheimer's, and other effects. Another paper explained that the data indicated that curcumin has demonstrated better anti-cancer effects, demethoxycurcumin showed better antilipemic activity and bisdemethoxycurcumin showed better bile and growth inhibition.[1,2]

Curcumin has been described as a pleiotropic molecule with a multiplicity of different and unique biochemical effects. Some effects include down-regulation of nuclear factor kappa-beta (NF-KB), decreased transcription-3 transductase and activator Wn/beta catenin, and increased peroxisome proliferator receptor gamma and Nrt2 cell signaling pathways, which decrease adipokines, including tumor necrosis factor (TNF), interleukin-6, resistin, leptin, and monocyte chemo-tactic protein-1 and increase adiponectin and other gene products. Curcumin modulates cell survival proteins, histone acetylase, histone deacetylase, protein kinases, protein reductases, glyoxalase I, proteasome, human immune deficiency virus I (HIV1), integrase, HIV proteins, Fts Z protofilaments, carrier proteins, DNA, RNA and metal ions. In light of the complex and varied effects, curcumin has been described as a strong cell signaling molecule. Curcumin inhibits several signaling pathways at multiple levels with effects on cellular enzymes, such as cyclooxygenase and glutathione s-transferase, immunomodulation, and on angiogenesis and cell adhesion. Curcumin was further shown to affect gene transcription and induce apoptosis in preclinical studies.[3-5]

Several other non-curcumin chemical constituents of turmeric have

been identified and have exhibited antioxidant, anti-inflammatory and anti-cancer effects. These include turmerin, tumerone, elemene, furanodiene, cardione, biscurarone, cyclocurcumin, calebin A, and germacrone. Other volatile oil fractions include tumerone, altantone, and zingiberone.[6,7]

Curcumin has a notoriously poor absorption profile. Low plasma and tissue levels are due to poor absorption, rapid metabolism, and rapid systemic elimination. Curcumin has been demonstrated to show absorption through active transport mechanism across the small intestine. Curcumin and bisdemethoxycurcumin show concentration-dependent inhibition through active transport, while demethoxycurcumin shows a carrier-mediated saturation pathway.[2,8]

In rats a dose of 1000 mg/kg of curcumin was found to produce a plasma level of an average of 15 ng/ml reflecting a relative absorption rate of approximately 1%. In humans, curcumin levels were measured to be an average of 11.1 nmol/l or 6 ng/ml one hour after consuming between 4 to 8 grams of curcumin. In another study in humans, consumption of 2 grams of curcumin alone made a very low or undetectable measurement in blood levels. Other reviews show a transient detection in plasma not exceeding 10 nanograms/ml after a single dose of varying strengths of curcumin. Another study shows a blood level ranging from 0.42 to 1.75 micromoles/l after one hour of consuming 4 to 8 grams of curcumin, while a level of 0.01 micromoles/l was noted after consuming 3.6 grams of curcumin.[1,3,9,10]

To enhance and improve absorption curcumin has been mixed with a variety of compounds, including liposomes, B-lactoglobulin, phospholipid complex, polymer encapsulation, PEG-PEI encapsulation, oil body encapsulation, soy protein isolate, bovine serum globulin, curcumin polymers, hydrogels, hyaluronic acid, organic gel-based nanoemulsions, casein, nano-particles, gold nano-particles, PHEMA nanoparticles, silica nanoparticles, GMO nanoparticles, chitosan nanoparticles, cyclodextrin nanoparticles and other novel chemicals. Other formulations have mixed curcumin with black pepper or a black pepper extract called piperine.[3,8,11]

One study compared the absorption of curcumin, demethoxycurcumin, and bidemethoxycurcumin and its metabolite tetrahydrocurcumin after oral absorption of three different curcumin formulations. One product of curcumin mixed with cellulose and natural antioxidants enhanced absorption by 45.9 times. A second product of curcumin mixed with volatile oils enhanced absorption by 34.9 times. And a third product of curcumin mixed with a phytosome enhanced absorption by 5.8 times. Bioperine is believed to inhibit intestinal and hepatic degradation of curcumin by decreasing cytochrome activity and inhibiting glucuronidation and sulfation, which has been shown to increase curcumin levels by 20 times. Adding 20 milligrams of piperine increased levels of curcumin by 20 times at one-hour post-consumption. Improved solubility, stability, and low first pass metabolism have dramatically improved curcumin absorption of up to 100 times compared to unformulated curcumin.[3,11-14]

Curcumin modulates numerous molecular targets.

While limited systemic bioavailablity has hindered the use of curcumin as a potential therapeutic agent, thousands of studies have demonstrated therapeutic efficacy of curcumin at low doses. Some researchers contend that in view of the overwhelming body of compelling data, it is very possible that curcumin bioavailability may actually not even be a serious issue. Numerous reports suggest that bioavailability could not be a concern. The dose of curcumin recommended varies from as low as 10 milligrams/day of curcumin powder and 80 milligrams/day of curcumin liquid to as high as 12 grams of curcumin per day. Some researchers have concluded that even relatively low doses of curcumin can have clinical benefits. A commonly recommended dose of curcumin appears to be between 500 to 2000 milligrams per day for general anti-inflammatory effects.[3,13-15]

Curcumin is believed to be safe for human consumption in doses up to 12 grams of curcumin per day. Reported side effects of curcumin consumption include gas, bloating, indigestion, heartburn, upset stomach, diarrhea, headache, and in some cases skin rash. Its use during pregnancy and lactation has not been determined and is not recommended. In vitro studies show that curcumin can inhibit platelet aggregation and its use with patients who are consuming blood thinners and anticoagulant drugs is cautioned. Its concurrent use with cancer patients who are receiving chemotherapeutic drugs is also cautioned. Some preliminary studies show that it can help promote the benefits of chemo drugs while having negligible side effects. However, its use with patients who are receiving chemo drugs should be evaluated and recommended on an individual basis.[1,8,9]

One paper listed the half-life of curcumin as five minutes. Another paper

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has measured detectable curcumin in plasma six to seven hours after oral consumption. Most researchers generally agree that curcumin is rapidly degraded by phase 1 and phase 2 pathways in the liver and small intestine, particularly by glucuronidation and sulfation. Approximately 75% of curcumin and its byproducts is recovered in stool and less than 25% recovered in urine. Metabolic degradation products of curcumin include ferulic acid, vanillin, betahydrocurcumin, tetrahydrocurcumin, hexahydrocurcumin and other dimerized end products and have been detected in plasma samples within 30 minutes after oral consumption of curcumin. Some researchers have suggested that the metabolic byproducts of curcumin are biologically active as well and account for the benefits of curcumin in spite of the fact it has notoriously poor absorption, rapid degradation, and elimination. Curcumin and its byproducts have been detected in fecal material 3 to 12 days after oral consumption.[1,9,15-19]

The Linus Pauling Institute in Oregon has published an overview of the research of the medical benefits of curcumin. The authors point out that the mounting evidence of preclinical studies shows that curcumin modulates numerous molecular targets and exerts antioxidant, anti-inflammatory, anticancer and neuroprotective activities. They further elaborate that while a few preliminary studies show that curcumin has anti-inflammatory activity in humans, larger randomized controlled trials are needed to establish its efficacy in osteoarthritis and radiation-induced dermatitis. They continue to report that no substantial evidence exists so far that curcumin improves cognitive performance in older adults with or without cognitive impairment. Also, its use for depression is very preliminary and long-term clinical trials are recommended. The use of curcumin by patients with diabetes is also preliminary and more long-term trials are needed. And while in vitro testing of curcumin in cancer activity remains encouraging, human trials are very limited particularly in patients with breast, prostate, pancreatic, colorectal, lung, and skin cancer. Other benefits of curcumin have been reported for cardiovascular disease, dermatology, and ophthalmology and while encouraging, the authors conclude that further investigation is warranted.[9,20-23]

The anti-inflammatory benefits of curcumin are particularly encouraging. Curcumin has been observed to down regulate nuclear factor kappa beta, which is an important signaling molecular for multiple pathways that promote inflammation. In one study, 1.2 grams of curcumin was consumed for 5 days after inguinal repair surgery and showed that curcumin was comparable to 300 milligrams/day of phenylbutazone. In another study of 18 patients with rheumatoid arthritis showed that consumption of 1.2 grams of curcumin per day for two weeks significantly improved morning stiffness, walking time, and joint swelling. In yet another study, 45 patients with rheumatoid arthritis who consumed 0.5 grams of curcumin per day for eight weeks showed it to be just as effective as 50 milligrams per day of diclofenac.[3,18,24]

So why the conundrum? Turmeric has been consumed in foods by cultures around the word and used in folk medicine for thousands of years. Reported antioxidant, anti-inflammatory, anticancer effects have been observed in the scientific literature. Curcumin has been identified as the main active ingredient believed to be responsible for its purported medicinal effects. Curcumin has poor absorption, rapid degradation and relatively fast elimination. Novel ways of enhancing curcumin absorption and preventing its breakdown and elimination have been invented. Several other constituents of turmeric have also been identified to have biological activity besides curcumin. The use of turmeric as a functional food in our diet is recommended for its potential health benefits. The use of curcuminoid extracts for its anti-inflammatory effects appears to be reasonable and beneficial. The use of curcuminoid extracts in cancer and other conditions is preliminary at best and more research is needed to substantiate these health benefits. The dose of curcumin varies widely throughout the scientific literature and no standardized recommendation has been firmly established. Daily doses between 10 milligrams to 12 grams per day have been reported on various medical databases. A reasonable recommendation of curcumin can vary from 500 milligrams to 2000 milligrams per day. Higher doses can be consumed if desired or recommended. The development of novel curcumin products such as nanoparticles or mixed with black pepper extracts, phospholipids or other emulsions is exciting. The dosage of these products is variable and best based on the available absorption profile data presented by the research or the manufacturer.

So, in conclusion, I will continue to recommend turmeric and curcumin products in my clinical practice to patients with various health problems, but particularly those with acute and chronic inflammation. I will experiment with different products and formulations and use my clinical experience and listen to patient feedback. I will try to read the medical databases and keep up to date with scientific research as it evolves with this exciting functional food and natural medicine.

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Douglas G. Lobay is a practicing naturopathic physician in Kelowna, British Columbia. Dr. Lobay graduated with a bachelor of science degree from the University of British Columbia in 1987. He then attended Bastyr College of Health Sciences in Seattle, Washington, and graduated with a doctorate of naturopathic medicine in 1991. While attending Bastyr College, he began researching the scientific information on the use of food, nutrition, and natural healing. Dr. Lobay enjoys research, writing, and teaching others about good health and good nutrition. He is the author of four books and numerous articles in magazines. He also enjoys hockey, skiing, hiking, tennis, and playing guitar.

Prevention and Treatment of Chronic Inflammatory Diseases: Sustained-Release Dihydroberberine Protocols for Diabetes, COVID-19, and Other Inflammatory Diseases

by Knox Van Dyke, PhD

Sustained release dihydroberberine (DHB) is a dietary supplement that has therapeutic value for the prevention and treatment of a wide range of diseases associated with chronic inflammation, including pre-diabetes and diabetes, heart diseases, viral infections, chronic neuroinflammatory diseases, lung diseases, kidney diseases, liver diseases, and as adjunctive treatment in a variety of cancers. This article describes the rationale for such use, relevant research, add-on therapies, and suggested treatment protocols.

Prevalence of Diabetes

More than 46% of the US adult population – about 120 million people – have pre-diabetes or diabetes,[1] making this category the proverbial mother of all diseases. Moreover, diabetes is often associated with hypertension, heart disease, cancer, vascular damage, and liver damage.[2] Diabetic retinopathy is the leading cause of blindness.[3]

Moreover, diabetes increases the risk of developing neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease, the latter of which is now referred to as "type 3 diabetes."[4]

Diabetes and Inflammation

Chronic inflammation plays a key role in pre-diabetes and diabetes. The DNA of macrophages and other inflammatory cells is wrapped around spool-like histone proteins. When acute inflammation occurs, these proteins become acetylated by the enzyme histone acetyl transferase (HAT), which eliminates the positive charge of histones. *This is the on-switch for acute inflammation.* The negatively charged DNA then loosens from the histones,

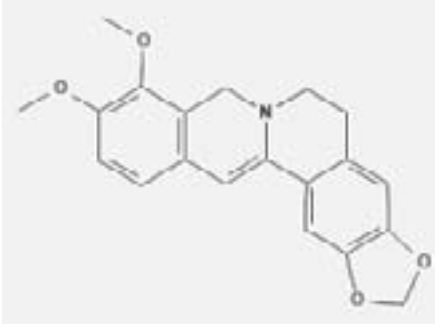

Figure 1
Chemical Structure of Dihydroberberine
https://pubchem.ncbi.nlm.nih.gov/compound/Dihydroberberine

which allows for the transcription of inflammatory genes that produce inflammatory gene products and products of oxidative and nitrosative (O/N) stress.

Macrophages, in particular, become activated and generate peroxynitrite. This highly toxic peroxide can further react with carbon dioxide to produce an even more reactive product called peroxynitrite carbonate, which is a strong nitrating compound. As this inflammatory state continues for weeks to months to years, an increasing number of macrophages produce peroxynitrite in excess. *This damages histone deacetylase 2 (HDAC2) – the "off switch" for acute inflammation – and allows peroxynitrite or its carbonate to continuously signal chronic inflammation.*

Type 1 Diabetes

When acute inflammatory type 1 diabetes begins, T lymphocytes are stimulated and produce interleukins and chemokines that help trigger the chronic inflammatory state in macrophages described above. This state is toxic to pancreatic beta cells that produce and release insulin. The excessive peroxynitrite kills the beta cells, so insulin is not produced. Alpha cells replace the dead beta cells and begin to produce excessive glucagon that, when released, increases glucose in the blood. Without insulin's ability to allow glucose to enter certain organs and tissues like muscle and fat, the high blood glucose becomes very toxic to tissues and blood vessels.

In type 1 diabetes, the proper amount and kinds of insulin must be given at the proper time of day. Insulin must be given to maintain healthy blood glucose levels and sustain life. Most often, treatment is a combination of short- and long-acting insulin to maintain normal blood glucose levels. But nothing is given to control the O/N stress that is toxic to mitochondria, the cellular organelle response for normal glucose and fat metabolism.

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Dihydroberberine

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Type 2 Diabetes

Type 2 diabetes is the most common form of diabetes, accounting for about 90-95% of all diagnosed cases of diabetes. It is associated with insulin resistance, a condition where the insulin released is damaged and fails to be effective.

Dr. Theodore Banting, the co-discoverer of insulin, originally addressed the key question of what causes diabetes. In his 1920s Nobel address he said, "Insulin is not the cure for diabetes." Since insulin helps control glucose and lipid levels in the blood and tissues, a logical inference from his idea is that glucose and fats are also not completely responsible for diabetes since they can be held in check by insulin. In addition, many children who eat considerable amounts of candy and sugary sweets do not develop diabetes. If sugars, which contain glucose, do not cause diabetes, how is it involved in the disease?

O/N Stress and Diabetes

Certainly, multiple metabolic pathways that control carbohydrate and lipid metabolism are involved in diabetes. Almost all the drugs used to treat type 2 diabetes work by controlling the metabolism of carbohydrates or lipids like cholesterol and triglycerides, or they stimulate the production or release of insulin. Some do both. While these antidiabetic drugs may be partially effective to control symptoms, they fail to cure the disease or completely prevent the damage it causes.

We and others have demonstrated that O/N stress is a key cause of diabetes. Since excessive blood glucose and insufficient insulin activity (insulin resistance) increase O/N stress, antidiabetic drugs that control glucose and insulin also reduce some, but not all, of the damage from O/N stress.

Interestingly, people with type 2 diabetes often develop profound insulin resistance that requires large dosages of insulin. We have shown that peroxynitrite can lead to nitration of one or more of the four tyrosine residues on the insulin molecule. Others have shown that peroxynitrite can also damage the insulin receptor as a result of nitration of tyrosine residues in its active site. This causes insulin to be less effective in lowering blood glucose levels.

Table 1. Suggested Prophylactic Regime for Prevention and Treatment of Influenza Caused by Single-Stranded Positive RNA Viruses

Therapy	Route	Dose (Dosage)
SR Dihydroberberine	Oral	300 mg, every 12 hours (600 mg/day)[a]
SR Cannabidiol[b]	Oral	60 mg, every 12 hours (120 mg/day)
Methylprednisolone acetate[c,d]	Injectable	low dose
SR Vitamin C	Oral	2 g, every 12 hours (4 g/day)
SR Inosine[e]	Oral	(3 g/day)
SR Niacinamide	Oral	750 mg, every 12 hours (1.5 g/day)
SR Tetrandrine[f]	Oral	(50-100 mg/day)
Mixed d-Tocotrienols	Oral	Once daily (50 mg/day)
100% Pure Krill Oil	Oral	(500 mg/day)
Coenzyme Q10 + PQQ	Oral	(100 mg/day + 10 mg/day)

SR indicates sustained-release; PQQ, pyrroloquinoline quinone.

[a] Dihydroberberine could possibly be administered in a proper non-toxic solvent as an inhalant. A standard fluid could be used to dissolve DHB so various doses could be tried to ascertain which would be most helpful. Additionally, a steroid could be dissolved with DHB to slow inflammation caused by the virus.

[b] For a period of time to protect against viruses.

[c] Prescription only.

[d] Budesonide and other over-the-counter steroidal inhalers are also available.

[e] Produces sodium urate, one of the body's most important antioxidants.

[f] Calcium channel blocker that inhibits ATP-dependent multidrug resistance pumps from causing the early exit of important supplements from the cells such as dihydroberberine and cannabidiol.

Use of SR Niacinamide

Decades ago, Professor Robert Elliott of the University of Auckland, New Zealand, reported that 500 mg of sustained-release niacinamide (Endurance Products Company; Sherwood, Oregon, USA) taken twice daily may have clinical value in helping to delay the onset of type 1 diabetes in young school-aged children. This is attributed to DNA repair and the need for large amounts of niacinamide. The repair enzyme requires a high level of NAD-dependent, ribose-ADP dependent polymerization. Since NAD is required to make more ATP, its depletion causes cell death. If beta cells fail to produce sufficient insulin, they die and metabolism controlled by insulin is lost. Thus, to live a nearly normal lifespan, a person with type 1 diabetes must continuously replace insulin from external sources and carefully manage their diet and lifestyle. It is crucial that they ingest supplements that produce targets for peroxynitrite. This can control peroxynitrite because the reaction of the two destroys peroxynitrite, which can help control diabetic damage. Dihydroberberine produces many metabolites that destroy peroxynitrite.

Use of Metformin and Berberine

Metformin, the drug most often used in the United States to control type 2 diabetes, is thought to stimulate AMP kinase, which is the "master switch" that controls carbohydrate and lipid metabolism in the mitochondria. The sustained-release form of metformin is considered to be the most effective. However, metformin is not without safety concerns. It is toxic to a fair amount of people, it causes kidney damage to some elderly diabetic patients, and it causes digestive upset in sensitive people.[5]

Over the last five to six years, berberine, a natural plant supplement that has biological activity of a calcium channel inhibitor, has been used by millions of people in the United States and around the world to treat prediabetes and type 2 diabetes. Like metformin, berberine in the form of a hydrochloride salt has been shown to activate AMP kinase. Berberine HCl has

been shown to effectively control blood glucose.[6]

There is no data to suggest that metformin can relieve O/N stress. However, berberine, being a charged cation, is not well absorbed in some people and therefore is not the best form of this compound – i.e., an uncharged form would be better absorbed.

Many people with type 2 diabetes who have difficulty controlling their blood glucose with standard antidiabetic drugs have found berberine HCl treatment to work well without noticeable side effects unless high doses are necessary.[7]

In addition, berberine HCl has been shown to lower cholesterol and triglyceride levels equal to or better than metformin but without the drug's known toxicity, and it is metabolized into effective antioxidants if it can become absorbed.[8]

Berberine HCl should be taken three times per day with a typical dose of 400-500 mg, every eight hours. Patients tend to remember doses to be taken in morning and at night, but forget to take the afternoon dose. Reducing this multiple-dosing frequency does improve patient compliance for correct dosing, which maintains more constant supplement levels.

Berberine and Gut Bacteria

In collaboration with Dr. Nabil Jabbour, we recently investigated the efficacy of berberine HCl in an FDA-approved clinical trial involving approximately 40 older adults with prediabetes or type 2 diabetes with associated eye diseases. The study participants were randomly assigned to take either berberine HCl (400 mg, every 8 hours) or a placebo for 10 weeks. The berberine HCl was 98% pure and prepared to pharmaceutical grade standards (USA).

We assessed fasting blood glucose level, hemoglobin A1C level (a measure of glucose control over a 3-month period), and other physiological parameters (e.g., blood pressure, height, weight and pulse) at baseline and regularly thereafter for several months. Diseases of the eyes were continuously followed.

The two oxygens both need a methyl group -OCH3 to be clear.

Surprisingly, about 40% of the patients in the berberine HCl treatment group failed to respond well. This lack of effect may relate to individual differences in gut microflora or because these patients were elderly with comorbidities. The berberine HCl molecule carries a quaternary nitrogen in one of its four rings, which gives the molecule a formal charge of +1 (see Figure 1). It is well known that charged molecules do not penetrate membranes well.[9]

Human (and animal) studies reveal that some, but not all, people have a gut microflora with bacteria that have nitroreductase.[10] *This enzyme effectively converts the berberine salt into dihydroberberine (DHB) by adding two hydrogen molecules, eliminating the double bond, and neutralizing the positive charge. Since DHB is both lipid soluble and uncharged, it penetrates through cell membranes and is absorbed from the blood much better than berberine compounds.* Once absorbed, DHB reverts back into charged berberine via oxidization and is somewhat trapped via the charge. However, since we know that almost all cells have exit pumps, berberine is likely eventually pumped out of the cell by multidrug resistance (MDR) pumps. Some of the DHB is trapped inside and available to generate multiple metabolites, which occurs in the liver and in bacteria in the gut.[9]

Many DHB metabolites are phenolic compounds and excellent antioxidants that can inhibit O/N stress, the main cause of various types of diabetes. Thus, supplementing with DHB eliminates the need to rely on gut bacteria with nitroreductase to ensure optimal absorption. In addition, lower doses of DHB are needed for efficacy, making it an effective antidiabetic therapy for more people without the side effects associated with berberine HCl.

Dihydroberberine

Interestingly, in our study, we noticed berberine HCl was effective in one patient during only the first six months of treatment. This is likely because the composition of his gut microflora changed and no longer could convert berberine into DHB.

Further, berberine HCl has been shown to be twice as effective in African people than in Chinese people.[11] This difference may be attributed to differences in dietary habits as diet is recognized as the most important factor for modulating the composition and diversity of the gut microbiome, including gut bacteria that produce nitroreductase.

Dihydroberberine crosses cell membranes more readily than other berberine compounds.

Therapeutic Potential of SR Dihydroberberine

Sustained-release DHB has an amazing potential to treat all of the chronic comorbidities even the comorbidities associated with COVID 19 viral infections, including diabetes and hypertension, vascular damage, heart diseases, chronic kidney disease, eye diseases, amputations, and erectile dysfunction, among others. In addition, more than 856 scientific studies regarding the adjunctive use of berberine salts in the treatment of cancers have been published to date. Since DHB does not have to react with bacteria in the intestines to be absorbed, it is a better compound to use. We have studied the effects of sustained-release DHB in an animal model of type 1 diabetes, showing O/N stress is also a major cause of this disease in rats.[12]

Therapeutic Potential of Add-On Therapies

Other supplements, which can be obtained from Endurance Products Company (Sherwood, Oregon), that offer important high quality with solid

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therapeutic continuous value to help control excessive peroxynitrite levels and reduce O/N stress include vitamin C, preferably in a sustained-release form, mixed tocotrienols, and omega-3 fatty acids from krill oil or flaxseed oil. Coenzyme Q10 with its role in the electron transport chain and energy metabolism makes it an especially important supplement for healthy mitochondria.

Cannabidiol (CBD) from hemp oil, preferably in a sustained-release crystalline form to provide uniform dosing, is an important option to help reduce O/N stress. This polyphenol is an excellent target for peroxynitrite. CBD is helpful for all types of diabetes from early to late stages to protect insulin (i.e., lower insulin resistance). Endurance Products Company is experimenting with a sustained-release CBD product that provides 60 mg of crystalline CBD per tablet. This compound is very effective in controlling pain caused by excessive peroxynitrite levels. Therefore, it can help relieve pain associated with damage to joints like knees, hips, ankles, and wrists when in a pure crystalline form packaged in a sustained-release form.

Combined, these therapies not only help reduce O/N stress, but also help control carbohydrate and lipid metabolism. The result is a more complete and effective treatment regime for various forms of diabetes and prediabetes that is safe and less toxic than drugs or supplements presently used. Moreover, the use of highly bioavailable bioactive ingredients in sustained-release tablet delivery helps overcome the challenge of short plasma half-lives and maintains more constant blood and tissue levels for optimal effectiveness.

A growing body of research indicates that both proper control of metabolism (both fats and carbohydrates) and O/N stress are needed to live a normal life. Excellent control of both comprise the most complete method to treat diabetes of any type while helping to maintain the mitochondrial function critical for normal glucose and fat metabolism.

Novel SR Dihydroberberine Tablet

By working with Endurance Products Company, we have been able to develop a novel sustained-release DHB supplement that requires only twice daily doses. This allows for better absorption and continuous maintenance of the blood level of berberine over longer periods of time.

The tablet is made by combining DHB with the company's proprietary vegetable wax tablet matrix. Berberine is extracted from plants of the *Berberis* genus and converted to DHB using sodium borohydride or palladium-catalyzed hydrogenation in solution. (DHB can also be extracted from plants that produce it.) The molecule is purified via extraction and crystallization, resulting in pharmaceutical grade 98% pure crystals. The crystals are then compounded into the tablet matrix, which comprises rice bran and/or carnauba wax, isomalt, stearic acid, magnesium stearate, and silica. All ingredients, except silica, are sourced from plants.

The yellow powder is then compressed using an automated tablet press. Each tablet contains 150 mg of DHB. The usual oral dose for patients with diabetes is two tablets, every 12 hours, for a daily intake of 600 mg of sustained-release DHB. We found this twice daily regime offered better dosing compliance and was easier for patients to remember than immediate-release products. In addition, this non-charged supplement in sustained release form behaves more consistently than standard berberine HCl.

Other Chronic Inflammatory Diseases

Diabetes provides an excellent example of how to control other chronic inflammatory diseases and their associated O/N stress with sustained release, non-toxic polyphenolic compounds and other substances that can act as targets of nitration and oxidation.

O/N Stress and Influenzas

While various types of influenza start with acute inflammation, they can evolve into chronic inflammatory diseases. The most startling example is the 1918 "Spanish flu" – the original H1N1 strain of respiratory influenza – that killed about five percent of the world's population. It was transmitted from human to human in respiratory fluids. Usually, an infected person would sneeze and release tiny virus-laden droplets into the air. Once inhaled by people nearby, the virus would bind to receptors on lung cells, begin to infect, replicate and eventually pass into more people. It is a single-stranded positive RNA envelope virus, a type of virus that exists in a variety of forms, is genetically diverse, and recombines over time to create new viruses. At least two major forms exist: A and B. Presently, the A form predominates, but the B form has occurred more recently.

Interestingly, more people with weak immune systems survived the Spanish flu than those with strong immune systems. This oddity may be attributed to the fact that a strong immune system generates excessive peroxynitrite and other cytokine inflammatory mediators and tremendous O/N stress, which results in extreme edema. In effect,

Table 2. Suggested Prophylactic Regime for Prevention and Treatment of Neuroinflammation (Oral Administration)

Therapy	Dose (Dosage)
SR Dihydroberberine	300 mg every 12 hours (600 mg/day)
SR Cannabidiol	60 mg every 12 hours (120 mg/day)
SR Vitamin C	2 g every 12 hours (4 g/day)
SR L-arginine + IR L-arginine	3 g every 12 hours (6 g/day) + 1 g every 12 hours (2 g/day)
SR Inosine	500-1,000 mg every 12 hours (1-3 g/day)
Krill Oil (100% pure)	350 mg/day
Mixed Tocotrienol	200 mg/day
SR Niacinamide	500-750 mg every 12 hours (1.5 g/day)

SR indicates sustained-release.

healthy people were drowning in their own lung fluid. Cartoonist and Pogo creator Walt Kelly said it best, "We have met the enemy, and he is us."

Many of these single-stranded positive RNA viruses infect humans such as the cold virus, SARS coronavirus (2002), MERS-CoV coronavirus (2012), Marburg virus, dengue virus, rotavirus, HIV virus, and most recently, the SARS-CoV2 coronavirus responsible for the COVID-19 pandemic.

When vaccines are used against these viruses, their success is limited because of the constant genetic recombinations of the viruses. Yet, these viruses can often be inhibited during the early stage of infection if treatment with anti-inflammatory steroids occurs during the acute stage of inflammation.

Combining steroidal anti-inflammatory drugs with multiple antioxidant substances offers more therapeutic value because the combination inhibits the inflammatory system necessary for these viruses to replicate. My patented combination of antioxidants and steroids has been shown to be an effective cure for feline immunodeficiency virus (FIV) and feline leukemia virus and greatly inhibit HIV in humans.

The H1NI virus and its genetic variations are also susceptible to similar supplement and anti-inflammatory drug combinations. These retroviruses are dependent on the transcription factor nf-kappa B, which is greatly inhibited by steroidal anti-inflammatory drugs such as methylprednisolone acetate (Depo-Medrol®), dexamethasone, prednisone, and prednisolone.

Tetrandrine, a bisbenzyisoquinoline alkaloid, has anti-inflammatory actions that inhibit the infection of Ebola virus. A small dose of this calcium channel-blocking compound would be protective particularly with the use of steroids and antioxidants as proposed above. Tetrandrine can help prevent DHB, CBD and other supplements from being pumped out of cells to help maintain correct intracellular concentrations. This helps prevent drug exit and produces primary drug or primary supplement potentiation.

Sustained-release vitamin C, N-acetyl cysteine and other sustained-release antioxidants are particularly effective. Phenolic supplements such as sustained-release DHB, which metabolize to mono-, di- and polyphenols, and sustained-release CBD are also beneficial because they act as targets and neutralize the peroxynitrite radical, the main controller of chronic inflammatory diseases. By targeting the underlying chronic inflammation caused by these deadly lung-acting viruses, these therapies provide a more complete and effective treatment regime. See Table 1 for a suggested prophylactic regime to reduce the risk for or progression of infection by one of these viruses.

Presently, a group in Germany is developing adjuvants that could increase immunity to the SARS-CoV coronavirus. This approach, which stimulates an immune response, is likely the wrong thing to do, based on the 1918 Spanish flu experience in which people with stronger immune systems were more likely to die. I believe this approach will wind up killing people needlessly because of what happened with H1N1 infection in 1918. The people with strong immune systems died quickly, while those with weak immune systems survived. It is a cautionary tale that portends that those who do not learn from history are likely to repeat it. Separately, the present drug combinations proposed to treat COVID-19 fail to adequately treat older people with multiple chronic diseases or comorbidities. The use of sustained-release DHB if given early in the disease state will likely help. For example, the antimalarial drug chloroquine had been approved for treatment with COVID 19 patients. Using sustained-release DHB in conjunction with this drug may help improve drug efficacy. Moreover, using sustained-release DHB with an antimalarial drug would treat comorbidities like hypertension, type 2 diabetes, heart diseases, lung diseases, and cancer. Substantial evidence exists in the literature and complete reviews are available on request.

O/N Stress and Cancer

Chronically activated macrophages and neutrophils underlie all chronic diseases. As described above, the resulting O/N stress can damage many types of cells, including the master molecule DNA. It's a chronic inflammatory system gone astray that can lead to DNA mutation, irreparable cell damage, and ultimately cancer. This happens because chronic inflammatory diseases are caused by excessive peroxynitrite or its bicarbonate. Indeed, chronic inflammation is estimated to cause or stimulate one out of five cancers. Perhaps administering sustained-release DHB in combination ➤

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with various anti-cancer drugs could provide synergistic benefits such that a lower drug dosage provides efficacy with less toxic side effects.

O/N Stress and Neurodegenerative Diseases

Diseases like Alzheimer's and Parkinson's diseases, multiple sclerosis, and Huntington's chorea as well as physical brain damage are linked to chronic inflammatory damage of the brain. Not surprisingly, other chronic diseases like diabetes are very often linked to inflammatory vascular damage.

The blood-brain barrier (BBB) normally acts like a selective filter, allowing needed nutrients to enter the brain while preventing the passage of unwanted materials. Various neurodegenerative diseases, however, can damage the BBB and disrupt its integrity.[13] The resulting "leakiness" of the BBB most often happens as adults enter their later years. Yet, healthy lifestyle and dietary habits, including supplementation, can go a long way to help maintain a person's healthy neurology. For this reason, O/N stress must be controlled throughout the life span, but especially as a person enters older age.

One option that may help prevent damage to the vascular system and the BBB is a combination of antioxidants and substances that generate nitric oxide (NO). NO is generated by two common pathways in the body. The first pathway involves L-arginine and its metabolite L-citrulline. Both provide efficient enzymatic production of NO. The second major pathway involves the nitrate/nitrite pathway, which can be viewed as a non-enzymatic pathway that only requires bacterial enzymes in saliva to convert nitrate into nitrite. Once swallowed, the salivary nitrite generates NO when exposed to stomach acid. Separately, some physicians use sodium nitrate to quickly produce NO in NO deficiency or anaerobic conditions.

To generate significant amounts of NO from L-arginine, it is helpful to use a sustained release form. For example, I use both sustained released L-arginine (3 g) and immediate-release L-arginine (1 g) in the morning and at night for a total daily intake of 8 g. This regimen effectively helps me maintain a normal blood pressure in the range of 100/80 mmHg.

Other therapies offer potential benefits to prevent damage to the vascular system and the BBB. For example, DHB, CBD, tocotrienols, and krill oil components readily penetrate the BBB and may offer therapeutic value in the treatment of chronic neuroinflammatory diseases that damage the BBB and generate excessive peroxynitrite. See Table 2 for a suggested prophylactic regime.

To paraphrase Ben Franklin, an ounce of prevention is worth *much* more than a pound of cure. I have spent most of my adult life studying various diseases. One thing is clear: To live a healthy life, it is paramount that we protect our vascular system from damage. It starts with a healthy lifestyle and dietary habits, including dietary supplementation.

Conclusion

Dietary supplements and other oral therapeutic interventions delivered in sustained-release forms provide a more complete treatment for the prevention and treatment of diabetes and other chronic inflammatory disease. Not only does this delivery form overcome pharmacokinetic limitations, it also provides a steady release of active ingredients over time so they are readily available to combat the continuous production of oxidants and nitrosants and reduce the O/N stress that characterizes chronic inflammatory diseases. Chronic diseases, including chronic inflammatory diseases, generally do not relent. For this reason, regardless of individual's genetic predisposition to a disease, a regular regime of continuous protection would be the best option to help prevent or control chronic inflammatory diseases.

Knox Van Dyke, PhD, is Professor Emeritus of Biochemistry and Molecular Pharmacology at West Virginia University Medical School. During the Vietnam War, he developed the first effective screening for antimalarial drugs by measuring the effects of drugs on synthesis of malarial parasite DNA and RNA. He has also worked on treatments for sickle cell anemia, black lung disease and silicosis, and diabetes. Dr. Van Dyke has been a consultant in the drug industry for Cancer Biologics of America since 1989, and he has co-authored seven books on luminescence biotechnology.

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Cancer Update: New Theories and Advances in Cancer Treatment

by Prof. Serge Jurasunas, MD(Hom), ND

This article has been abridged from the original. Full article and references available at townsendletter.com.

Abstract

Research from past decades has established that the p53 tumor suppressor gene protein provides a major barrier to neoplasic transformation and tumor progression. Its role is not only associated with controlling cell cycle progression and apoptosis, involving other apoptotic genes, but is implicated in several functions, including regulation of glycolysis, promoting oxidative phosphorylation, and repressing overactive telomerase enzymes. Cancer cells first acquire selective advantages by retaining mutant forms of p53 protein that confer new oncogenic functions that upregulate several genes that accelerate tumor progression, metastasis, and chemotherapy resistance.

In this article, we also demonstrate the new role of (Wild Type) WT p53 in controlling telomerase activity since telomerase is overexpressed in most cancers, allowing cancer cells to acquire a stem-cell-like state (CSCs). These cells can continually renew and become almost immortal. Furthermore, they are responsible for cancer recurrence and chemo-resistance. New research demonstrates that mutant p53 cannot repress telomerase enzymatic activity; only WT p53 can. This underscores the critical role that WT p53 plays in cancer therapy. The idea is to establish a new ratio between p53 and telomerase that offers a better dimension and perspective to understand and treat cancer. Several natural compounds have demonstrated efficacy to reactivate p53 function and therefore to inhibit glycolysis and telomerase activity.

Introduction

Have we explored fully the possibilities, new theories, new ways, new treatments to win the battle against cancer, or at least, to have a much better result? Probably not! Today in 2020, cancer has become an epidemic, while in 2005 Andrew Von Eschenbach, director of the NCI, announced there would be an end to deaths caused by cancer by 2015. Would you have believed such a thing back then? Some doctors did believe in this prediction. In one article published in the same year, I read the following: "We are closer than ever from achieving this goal!"

Five years later, this goal continues to be only a dream. Oncology is still in a deadlock since chemotherapy and radiation have yet to bring significant improvement to cancer patient longevity over the past 30-35 years. Cancer metastasis is still responsible for 90% of cancer deaths. Besides, oncologists have absolutely no way to detect cancer recurrence risk or prevent primary tumors, thought to be contained, from metastasizing. How many times have we seen patients undergoing chemotherapy develop more metastasis?

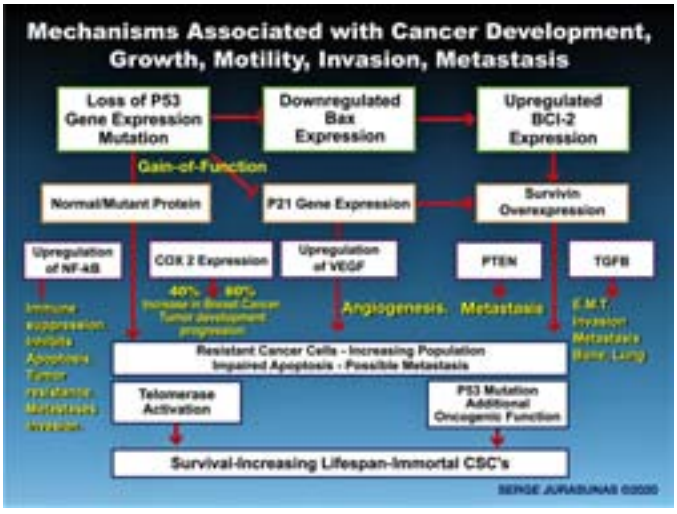
A 2012 study published in *Natural Medicine* strongly suggested that chemotherapy is responsible for disease recurrence. It is supported by Dr. Laurent Schwartz, a well-known professor of oncology at Public Hospitals in Paris, who wrote a new book, *Cancer: A Simple and Non Toxic Treatment*. According to some of its statements, after chemotherapy loses efficacy there follows an increased risk of metastasis. This is also supported by oncologists like Dr. Dominique Belpomme, professor of oncology at Paris-Descartes University, president of the French Association for Research on Treatment Against Cancer (ARTAC), and author of an important book on cancer, *Cure of Cancer and How to Prevent: A Way to Change our Approach to the Disease*. He wrote the following: "Today chemotherapy offers its maximum efficacy where we cannot expect more future progress since it has reached its upper limit. Therefore, the need for new modalities and tools for cancer prevention, cancer recurrence, and treatment with less toxicity, remain the main goal in modern oncology."

There is an urgent need to change the cancer paradigm by searching for new theories and methods to treat cancer with more efficacy, some of which are newly emerging. These include the theories of cellular respiration and the Warburg effect as the prime cause of cancer. Cancer as a metabolic disease is now gaining more interest in the scientific community. More recently, research has shown that the metabolic profile observed in cancer cells includes mitochondrial dysfunction, increased consumption of glucose, increased glycolysis, and increased secretion of lactate, while oncogenes and tumor suppressors have been discovered to have an important role in cancer.

Cancer Cell Resistance

Chemotherapy may kill many cancer cells sensitive to apoptosis; but during the treatment, a small population can acquire apoptosis resistance by the up-regulation of multiple pro-survival factors such as loss of p53 gene function and activated inhibitors of apoptosis (IAPs). In one study, survivin, an IAP, increased the activity of the nuclear factor kappa-B (NF-κβ), inducing lung metastasis of human breast cancer in nude mice treated with Paclitaxel, which was inhibited with curcumin.

A tumor represents a diverse collection of cancer cells. When cancer is detected, the million (or billions) of cells that make up the tumor have become differentiated. Some cancer cells are sensitive to chemotherapy and apoptosis, while others emerging during the late stage of the tumor development – being actuated by the loss of p53 function as undifferentiated cancer stem cells that possess the ability to self-renew – become resistant and can usually originate metastasis. This type of cancer cell harbors mutated p53 that has gained additional oncogenic function, which I will explain in depth as we continue to address the p53 gene function.

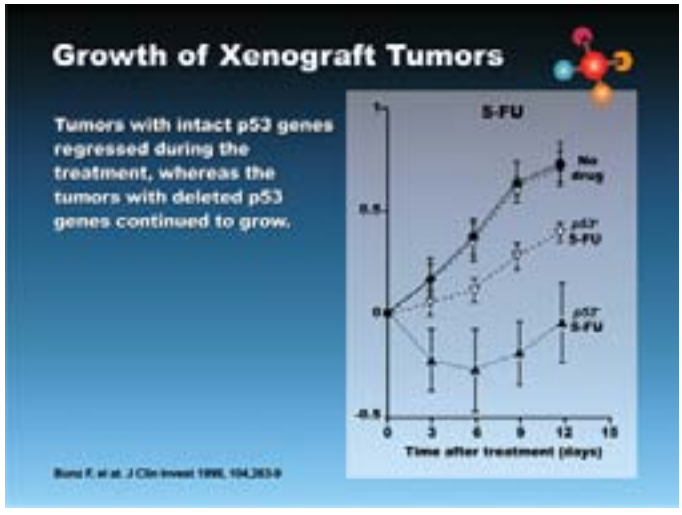


p53 Function

The p53 field has been growing at a rapid pace with more than 2,500 articles published since 1989. However, it's still poorly understood as an important tool in clinical application. Briefly, the p53 gene is a transcriptional factor, a potential master regulator with a broad range of biological functions that include primarily blocking cell cycle progression to induce apoptosis, senescence, DNA metabolism, and angiogenesis. To activate the apoptosis mechanism, p53 transcriptionally regulates other apoptotic genes such as Bax while simultaneously suppressing the BcL2 antagonist. It is a potent anti-apoptotic oncogene that when activated blocks Bax in promoting apoptosis. Both reduced Bax expression and overexpressed BcL2 are associated with poor response to chemotherapy and shorter survival of cancer patients.

Thus, we may better understand the role of WT p53 in the apoptosis process since low p53 gene activity or even loss of p53 has some negative effects by not being able to regulate BcL2 and Bax expression. For instance, Bax is lost in one-third of breast cancers and BcL2 is activated in 60% of breast cancers, which contribute to drug resistance and shorter survival. Both BcL2 and Bax have potential prognostic and predictive significance. Several studies have shown that high Bax expression is associated with improving survival in a number of cancers. Bax and BcL2 are evaluated in a ratio that determines the fate of cells or the level of self-destroyed cancer cells. The Bax/BcL2 ratio may be used as a predictive value for chemotherapy response and offer a better evaluation of what results can be expected. I have been able to observe and follow the Bax/BcL2 ratio with the blood testing we usually do with cancer patients. Thus, we can improve this ratio by using a variety of select natural compounds. Another strong inhibitor of apoptosis protein is survivin, which is highly expressed in cancer tissue, yet undetectable in healthy tissue.

Being only expressed in cancer tissue, survivin is being used as a new cancer marker, a prognostic factor, and a promising therapeutic target in chemotherapy because of the resistance of cancer cells. Survivin expression is observed in virtually all cancers, including breast and prostate cancers. Survivin was found to inhibit three apoptotic enzymes: caspase 3, caspase 7, and caspase 9, thus protecting cells from death. Survivin may act simultaneously with the BcL2 proteins, although differently as I have frequently observed with my cancer patients. Survivin is transcriptionally repressed by wild type p53 but not by mutant p53, which again may explain the crucial role of wild type p53 in apoptosis and against cancer cell resistance during chemotherapy.



p53 Inhibits the Warburg Effect by Reducing Glycolysis and Enhancing Oxidative Phosphorylation

Besides being a tumor suppressor gene associated with apoptosis, which I had previously presented in the *Townsend Letter* (August/September 2015), p53 has other important functions, although these are less known or even ignored. They have not been discussed before, so this is all new for our readers. You have to work with p53 in clinical applications and look behind its normal function as a tumor suppressor. I discovered that WT p53, but not the mutated p53 gene or protein, inhibits glycolysis. Therefore, this offers

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a new approach and way to treat cancer. Furthermore, these functions also provide another approach to one of the main hallmarks of cancer known as the Warburg effect. This is accomplished by regulating glycolysis and shutting down glycolysis transporters as well as other expressions of the glycolysis enzyme promoting oxidative phosphorylation (oxphos) through transcriptional regulation of target genes. p53 can inhibit glycolysis; but when mutated or misfolded, p53 stimulates glycolysis that cancer cells use to generate energy and contributes to cancer progression. Thus, by p53 balancing the use of glycolysis and oxphos, it provides a mechanism blocking tumorigenesis and the Warburg effect.

Glycolysis is the pathway that tumors use as an alternative for generating energy via oxidative phosphorylation or respiration in mitochondria to generate so-called ATP molecules from sugar burned or oxidized in the presence of oxygen and broken down into C02 and H20.

Oxygen reduction in the mitochondria and blockage of the cellular respiratory chain from deficient respiratory enzyme and other electron chain transport damage (or mtDNA mutation observed in a variety of human cancers) may further contribute to respiratory malfunction in cancer cells. The German biochemist Otto Warburg proposed in 1924 that cancer was caused by a defect of oxphos or respiration in the mitochondria forcing cells to switch to the old primitive glycolysis channel when oxygen cannot be used by the mitochondria to generate cellular ATP energy.

Otto Warburg, who was the director of the famous Max Planck Institute for Cell Physiology in Berlin, won his first Nobel Prize for physiology and medicine in 1931 for the oxygen transfer enzyme of cell respiration. His second Nobel Prize in 1944 was for his discovery of hydrogen transferring enzymes. This latter process does not require oxygen because it arose early in the primordial evolution of prokaryotic cells back when the earth's atmosphere had very little oxygen. Warburg analyzed the ratio of oxphos to glycolysis in different cancer cell tissues and found that glycolysis under anaerobic fermentation was particularly high in aggressive tumors when compared with benign tumors and normal tissues. These observations led Warburg to propose a deficiency in oxphos and elevated glycolysis as the primary cause of cancer. Today the Warburg effect is now enjoying a resurrection and has started to be taken very seriously by several researchers and even doctors and oncologists.

Phosphorylation and Aerobic Respiration in Mitochondria

The glycolytic pathway is found in the cytoplasm of each cell that does not require oxygen. However, glycolysis pathways produce ATP less efficiently than aerobic respiration, resulting in the production of only two molecules of ATP per molecule of glucose while 36 molecules of ATP are produced in oxphos; yet cancer cells possess a 20- to 30-fold increased rate of glucose cellular uptake and a more than 30-fold higher glycolytic rate when compared to normal cells. Cancer cells produce ATP from glycolysis a hundred times faster than normal cells in order to support three basic needs of these cells: 1) Maintenance of energy status, 2) Increased biosynthesis of macromolecules such as proteins 3) Maintenance of the cellular redox status, which permits survival and growth. Several studies have already shown that WT p53 plays a crucial role in slowing down or inhibiting glycolysis and at the same time promotes oxphos and cellular respiration through transcriptional regulation of target genes. Mutant protein or even misfolded protein, which has lost its anti-tumor capabilities, triggers glycolysis to favor cancer progression. p53 is mutated in many tumors and thus can influence aspects of both glycolysis and oxphos, thus being significantly important in contributing to the Warburg effect.

Telomerase Activity and p53 Tumor Suppressor Gene in Cancer

A growing number of studies are now showing the implication of telomerase overexpression in the malignant transformation and progression of the human tumor. Telomerase is a large ribonucleoprotein complex in nature, a reverse transcriptase enzyme that carries RNA molecules used as a template to elongate telomeres. The molecules consist minimally and essentially of the protein catalytic subunit coded for human telomerase reverse transcriptase (hTERT) and telomerase associated protein (hTEP1). Its role is to maintain telomere integrity in the sequences of the eukaryotic chromosome ends. This prevents the ends from undergoing DNA damage response, playing a critical role in chromosome replication. This telomerase activity regulates dividing cells maintaining the telomere ends against erosion of their normal length.

As we age, have excess oxidative stress, or are exposed to radiation, telomeres gradually shorten. This shortening leads to cell aging, cell death, or senescence. Some somatic cells lack sufficiently high levels of telomerase to maintain their telomere length for an indefinite number of divisions. Consequently, these telomeres gradually shorten as cells age. This is why telomere activity has been widely studied as an aging factor.

While normal somatic cells show varying telomerase activity, cancer cells express abundantly high telomerase. This may be considered a relevant factor to distinguish cancer cells from normal cells. It's as if cancer cells use telomerase to divide indefinitely. Telomerase up-regulation/reactivation has been observed in 85% of all human tumors. Such tumors may become immortal and play a crucial role during human tumor pathogenesis. Besides being found in primary tumors, telomerase activity is also detected in circulating tumor cells, for example in breast, ovarian, and prostate cancers.

Many cancer cells are considered immortal because telomerase activity allows them to divide virtually forever because they possess the ability to continually regenerate their telomeres. With telomere activation, some types of cells and their offspring become immortal because they bypass the Hayflick limit, thus avoiding all death as long as the conditions

continued on page 62 ➤

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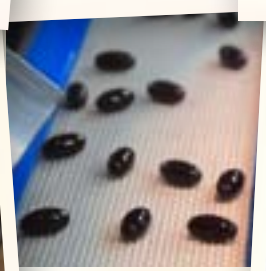
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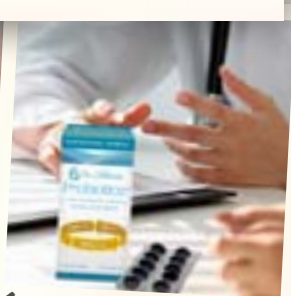
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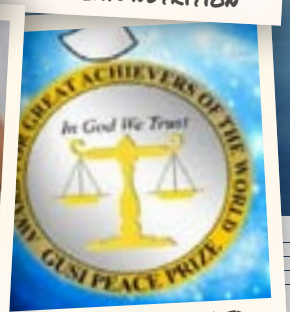

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Cancer Update

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for their duplication are met. Many cancer cells are considered immortal because as mentioned telomere activity allows them to live much longer than any other somatic cells. A good example of immortal cancer cells is HeLa cells, which have been used in laboratories as model cell lines since 1951.

These cancer cells become resistant; and under several circumstances, they acquire some stem cell characteristics known as a cancer stem cell-like state (CSCs). They need to adapt to an ever-changing environment in order to survive. This is accomplished through genetic changes such as oncogene activation, tumor suppressor gene inactivation, epigenetic changes such as hypomethylation/hypermethylation, and metabolic changes with a shift to anaerobic glycolysis. These resistant cancer cells develop a very strong DNA repair mechanism, more rapidly than normal cells. While chemotherapy can damage them, they can repair quickly.

The p53 tumor suppressor gene, independently of inducing cell cycle arrest and apoptosis, seems to also play a crucial role in protecting telomeres from DNA damage by regulating telomerase activity through a crosstalk node employing two important mechanisms. According to a recent discovery led by Paul Lieberman of the Wistar Institute, this is a particularly new function of p53 that had never been described previously. Both telomeres and p53 play an important role in the maintenance of genome integrity and tumor suppression They easily could be regarded as guardians of the genome. The local binding of p53 to the region close to the amino terminus of telomerase associated protein 1 (hTEP1) is one response to DNA damage, protecting the telomere. Wild type p53 further represses telomerase enzymatic activity through downregulation of its protein catalytic subunit, human telomerase reverse transcriptase (hTERT) together with the interaction of the specificity protein 1 (transcription factor Sp1). Wild type p53 protein level prevents telomerase from becoming overactive and proliferating indefinitely. p53 mutation and accumulation of mutant protein correlate with telomerase over-activity in many cancers, such as ovarian cancer, breast cancer, and non-small cell lung cancer (NSCLC). I have also personally observed this during the past few years with other cancers in patients with bladder cancer, sarcoma, and prostate cancer.

With the activation of telomerase, some types of cells and their offspring possess the ability to continually regenerate their telomeres, by dividing continuously. This increases their lifespan and immortality. On the contrary, telomerase shortening provides a barrier to cancer progression where the majority of cancer cells depend on telomerase activation to gain proliferative immortality. If the p53 gene is more activated than telomerase, cancer cells, in all probability, are not yet immortal. They have a limited lifespan and can be destroyed. If telomerase is more highly activated than the p53 gene, cancer cells are out of control and become immortal. p53 gene expression leads to more effective control over the telomerase activity and prevents cancer cells from becoming immortal cells.

Telomerase upregulation/reactivation is observed in 85% of all cancers – and up to 90% in breast cancer – suggesting a crucial role during human tumor pathogenesis. The p53 tumor suppressor gene is mutated in 50% of all cancers. Both p53 mutation and overexpressed telomerase are considered an important event in earlier cancer development and disease progression with metastasis invasion. Over-expression of WT p53 was shown to down-regulate the telomerase enzymatic activity.

The role of the p53 tumor suppressor gene is to kill cancer cells via apoptosis and prevent them from continuously dividing, thus preventing cancer cells from reaching a more aggressive stem-like state.

Mutant p53 and overactive telomerase allow cancer cells within a tumor to turn back time by acquiring a stem-cell-like state (CSCs) by developing survival factors. This type of aggressive cell usually emerges during the later stage of tumor development facilitated by the loss of p53. They possess the ability to self-renew, differentiate by forming resistant phenotypes, and produce metastasis activity, chemo-resistance, failure of treatment, and tumor relapse. These CSCs display high levels of telomerase activity possessing the ability to continually regenerate their telomeres. The WT p53 tumor suppressor gene, indeed, plays a more crucial role than we may have initially learned, such as inducing apoptosis. When activated with the production of normal protein, it prevents established cancer cells from moving toward a more aggressive stem-like state, especially by regulating telomerase activity.

If the tumor suppressor gene is malfunctioning due to a lack of protein production or mutated protein, telomerase can become overactive. This means that along with the transformation of cells by mutated p53 into cancer cells, there is a high probability they also may be able to form a tumor. Fortunately, we can evaluate the presence of cancer cells capable of forming a tumor in the case of a non-cancer (diagnosed) patient, meaning we start at a preventive level. It is important to evaluate the activity of these two genes with the telomerase/p53 ratio for cancer patients under treatment or, even better, before starting treatment.

We have to know if the p53 gene is more activated than the telomerase or vice versa to determine the presence of non-resistant CSCs or, in a case of cancer remission, if there remains a presence of cancer cells somewhere in the body with a high risk of recurrence.

On several occasions, I have seen as a result of testing cancer patients in remission a bad p53/telomerase ratio. This includes the presence of mutated p53 protein. We already know by experience that cancer recurrence is still high in such breast cancers. We have not come across any other technique that permits clinicians to evaluate recurrence risk. p53 mutation by itself together with BcL2 overexpression represents a sign of high-risk for cancer recurrence as I have often observed in several breast cancer patients. New studies have shown that telomerase reverse transcriptase (TERT) overexpression upregulated the expression of BcL2 and downregulated Bax

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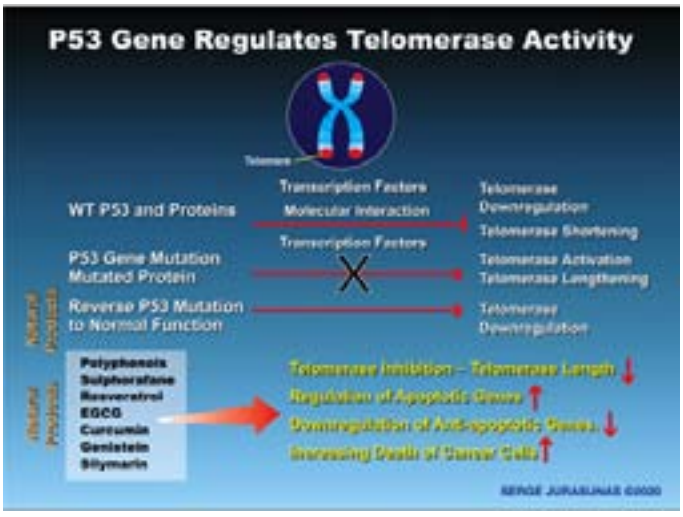
➤ *continued from page 62*

activity reducing the activation of some caspases proteins such as caspase 9. This explains why sometimes, even if p53 is highly expressed, BcL2 expression is also high even if normally activated; BcL2 can be overexpressed because of overexpression of TERT in the telomerase. There is a feedback mechanism between the two that we will develop further in my blog. Thus, a bad p53/telomerase ratio suggests the presence of CSCs with resistance to apoptosis and chemotherapy. Remember that overactive telomerase provides immortality to cancer cells if not regulated by WT p53 and the production of normal protein.



Telomerase activity may be seen as a new marker for cancer. In fact, the levels of telomerase activity (independent of the p53 gene) in the early and late stages of cancer might be used to determine the diagnosis of various human cancers as well as a biomarker for detection.

Ratio: p53/Telomerase Activity – A New Way to Diagnose Cancer

For nearly 15 years I spent considerable time studying and researching molecular markers, especially the p53 gene. I also studied a variety of selected natural compounds that exhibit anti-tumor activity targeting most of the mechanisms used by the tumor to grow and expand. One of the most important biomarkers used with p53 was the telomerase enzyme. An important strategy is to reactivate (restore) mutated p53 to a normal function, such as normal p53 protein production level, together with downregulation of telomerase activity and decreasing glycolysis. For this purpose, we can just perform a blood test with molecular markers. We include p53 gene expression, p53 protein level, BcL2, Bax, survivin, P21 gene expression and proteins, VEGF, MMPs, TNFa, and telomerase activity. As previously explained, telomerase upregulation is observed in 85%-95% of all cancers; and p53 is mutated in more than 50% of all cancers. If not mutated, p53 is often poorly activated. Activated WT p53 downregulates telomerase enzyme activity; therefore. if we have the difference from the activity of a WT p53 gene and the activity of telomerase – or differently from a failure or mutated p53 gene and the high expression of telomerase – surely we can determine a ratio, just as we do for Bax/BcL2.

I believe – first from my study of a number of scientific articles and secondly from my personal clinical experience – that targeting p53/telomerase activity remains today a major challenge in oncology. Theoretically, science has been researching synthesized compounds or drugs that can inhibit telomerase, same as with the reactivation of mutant p53. In the meantime, we already have on hand a range of natural compounds that have demonstrated efficacy to inhibit telomerase activity with no side effects. I am going to explain further.

In order to offer such services, we work with a laboratory specializing in biological assays that is directed by Dr. Olga Galkina Taylor, PhD, a highly reputed Russian scientist who opened a new door in my professional life. I have collaborated with Dr. Galkina's laboratory for over 15 years. We have started working on the p53/telomerase ratio, which she developed; but so far, her work has never been published. In this article, I am presenting for the first time a preliminary introduction with some examples of clinical cases. We conjointly wrote an article in the *Townsend Letter* in August/September 2010 explaining how to reverse p53 mutation with my own therapy protocol, but it probably came out too soon to be well understood at that time. We take a venous blood sample from the patient, before treatment, to determine an exact genetic expression affecting the pro-tumor activity and anti-tumor activity, utilizing the Bax/BcL2 ratio. Since p53 gene expression regulates telomerase activity, we had concluded that we may also define a p53/telomerase ratio and then use it for diagnosis and prognosis. We then prescribe the appropriate treatment according to the results. If WT p53 is overexpressed and it down-regulates telomerase enzyme activity, then the cancer tumor is much less resistant and more sensitized to chemotherapy.

We started testing p53/telomerase activity only a couple of years ago, but so far, we have collected many interesting cases. We then perform a second test (when possible) to verify the effect of our treatment on the expression of the various genes included, and then observe the results. Some patients even after remission continue with regular testing even after several years for purposes of prevention and monitoring recurrence. Often the results have shown a condition of high-risk recurrence where we immediately modify the patient's regimen with appropriate treatment. This is the best way to handle cancer disease and especially prevent any recurrence. Of course, I performed very extensive research and study into the many roles of telomerase in both aging and cancer, especially on the new link between p53 and telomerase and its application in cancer.

I was highly motivated to research which natural compounds had the best efficacy to inhibit telomerase activity while applying the knowledge I gained years ago about restoring mutant p53 to the WT p53 tumor suppressor gene, using selected natural compounds.

In the presence of mutant p53 and highly activated telomerase, we definitively need to first reactivate the gene or the production of normal protein over mutated protein. This is more complicated than only increasing the p53 gene activity. Many natural compounds can stimulate p53 gene activity increasing apoptosis and regulate telomerase, but not all-natural compounds can reverse p53 mutation; yet, I have been able to successfully reverse it. Once again please refer to my previous articles describing in detail the list of the natural agents that have demonstrated efficacy to target both apoptosis and telomerase or interfere with glucose transport. However, this topic is too involved for this article. We will just provide the name of the most important agents with some references but will later offer more details and interesting figures for the reader in my blog along with complete molecular markers clinic case reports with a full explanation. Again, this all requires considerable space; but in summary, it's very important for doctors to understand how to more effectively handle a cancer case and see how applied therapy is currently functioning along with improvement of genetic status.

Today we have ample scientific proof from multiple targeted cancer therapies utilizing curcumin and genistein, which induce apoptosis; activate the immune cells; inhibit NF-κβ, HER-2/Neu, and EGFR; down-regulate BcL2 and survivin; upregulate Bax; decrease COX2 activity; activate caspases; and stimulates the immune system. Most important is to note that both curcumin and genistein have strong properties to inhibit telomerase activity by decreasing the level of TERT. Both curcumin and genistein may kill CSCs more effectively than chemotherapy. This explains why for many years I have included liposomal curcumin and genistein in my cancer protocols together with rice bran arabinoxylan compound (RBAC), a strong biological response modifier that has special properties to activate NK cells. The reader can refer to my last article in the *Townsend Letter* (August/September 2019). Besides being known as a strong immunomodulator, some new studies have shown that RBAC improves the Bax/BcL2 ratio along with radiotherapy. You can use these three compounds together in your cancer protocol and optionally include an anti-angiogenic therapy like C-Statin. This extract is made from a naturally occurring plant (bindweed) that contains a proteoglycan molecule with strong angiogenic properties. You may observe how a tumor can decrease in size and/or eliminate metastasis. (See my *TL* article "How to Approach Cancer Patients, Diagnostic and Treatment." August/Sept 2018;68-73.) Other natural compounds have shown efficacy in repressing telomerase activity as well as targeting other cancer mechanisms such as apoptosis, including resveratrol, green tea polyphenols, epigallocatechin-3-gallate, allicin, sulphoraphane, silymarin, quercetin, and genistein.

Examples with a Ratio of p53 Gene and Telomerase Activity

Here we present three patient case examples. These are incomplete concerning other apoptotic and anti-apoptotic genes (due to space limitations). I plan to show more detailed complete case reports with an in-depth explanation,along with more details about the survivin gene and its relation with p53 and cancer in my blog and on my website.

Clinical Case 1: Female, 66 years old, a medical doctor living and practicing in the US with breast cancer remission after surgery and chemotherapy. A very emotive person, under high stress, who has anxiety. We started her on a better dietary style, and she practices meditation and relaxation. The test was done several months after she started my suggested treatment and diet. The last test was taken in October 2019.

- p53 gene expression: 6116 units/ml of plasma
- p53 normal protein level: 1520 units/ml of plasma. Reference range: 0.1-1.00 unit
- p53 mutated protein level: 28.5 units/ml of plasma. Reference: (N.D. Trace)
- p53 misfolded protein: 500 units/ml of plasma. Reference: (N.D. Trace)
- Telomerase activity: 6816 units. Reference (N.D. Trace)
- The ratio between p53 gene expression and telomerase gene expression: 0.9 (Reference range 1.0)

The p53 gene expression is highly activated together with a very high level of normal p53 protein probably due to the applied therapy; many damaged precancerous cells were destroyed as indicated by the test. However, some cancerous cells started

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to produce mutated protein and a high level of misfolded protein that can trigger glycolysis. It also may compromise the destruction of some populations of cancer cells through apoptosis. The p53/telomerase ratio is a little bit lower but not enough at the moment to create very resistant cancer cells. The apoptosis in process is highly activated. However, with time, if not improved together with the elimination of mutated and misfolded p53 protein, she may develop resistant cancer cells and increase the risk of recurrence. However, through April 2020 the patient remains in remission. (See more details in my blog: NaturopathicOncology.blogspot.com)

Clinical Case 2: Female, a 38-year-old pharmacist living on the Island of Madeira, was diagnosed with lymphoma but has refused chemotherapy. She went to Germany to receive a special dendritic cell vaccine and ozone therapy treatments. Her March 2019 test results follow:

- p53 gene expression: 380 units/ml of plasma
- p53 normal protein level: N.D.
- p53 misfolded protein level: 8.8 units/ml of plasma
- p53 mutated protein: 13.2 units/ml of plasma
- Telomerase activity: 3108 units/ml of plasma
- The ratio between p53 gene expression and telomerase activity: (N.A.)

Here we cannot determine a ratio with these results, since the p53 gene is too low compared to the telomerase activity. Even if it can be calculated as 0.122, the laboratory mentions this result as too low to be meaningful. Also, together with a high expression of BcL2 and survivin gene along with a very low Bax/BcL2 ratio, it shows the presence of cancer cells that are resistant to destruction (see more details in the blog).

Showing p53 gene expression that was too low and producing no WT p53 (normal) protein but only mutated and misfolded protein can trigger glycolysis and inflammation that can stimulate cancer cells. There is an increasing population of cancer cells with active telomerase and only a small fraction had been destroyed. Because of the high activity of the telomerase compared to the p53 gene activity, many cancer cells can turn into CSCs. Here only a small fraction of pre-cancerous/cancerous cells were destroyed through the genes; however many cancer cells may be destroyed via the immune cells, especially by NK cells, which have increased their activity after the treatment in Germany as observed in the report from the clinic. So, the immune system and especially the NK cells are an alternative to destroy cancer cells when tumor suppressor genes alone are not efficient.

Clinical Case 3: Male, 16 years old diagnosed with Ewing sarcoma. This is a very difficult case that I treated for seven years but with very good results so far. Surgery could not remove the total tumor localized on the spine. The boy was subjected to several surgeries, chemotherapy, and radiotherapy yet improved considerably with our treatment. Recently we performed molecular markers testing, including telomerase, to facilitate a better prognostic and possibly prevent any recurrent cancer activity. As of the last scan, the remaining tumor tissue was inactivated.

- p53 gene expression: 5915 units/ml of plasma
- p53 normal protein level: N.D.
- p53 misfolded protein level: N.D.
- p53 mutated protein: 20 units/ml of plasma
- Telomerase activity: 4388 units/ml of plasma
- The ratio between the p53 gene and telomerase activity: 1.3

The patient continued taking my treatment for the past seven years, which is a success. The high p53 gene activity (before: 1134) is probably from the applied treatment, but no normal p53 protein was produced, only mutated protein. However, many cancer cells were destroyed through the highly activated Bax and P21 gene expression. (See my blog) The ratio p53/telomerase is good 1.3; p53 gene expression maintains a lower telomerase activity and an inactivated tumor. However, the result of the test showed the presence of cancer cells somewhere in the body; the patient continues with check-ups and the risk of tumor reactivation still exists (We still closely follow the case).

Discussion

The article has shown that the metabolic cause of cancer is associated with the Warburg effect and mitochondria dysfunction, which allows cancer cells to switch to the glycolysis pathway. The p53 gene plays a key role in inhibiting glycolysis, inducing apoptosis, and as a new function may inhibit the telomerase activity, which today gains considerable interest as a target against immortal cancer cells. Cancer disease is no longer a mystery, but a disease that can be treated differently. Thankfully, at last, some selected natural compounds and other foods have demonstrated properties that target p53 and telomerase, as presented in the article.

More information on cancer can be seen from my last lecture in Europe, "How to Understand and Treat Cancer with Modern Methods" (Zagreb, Croatia; February 28, 2018), on Slideshare: http://www.slideshare.net/sheldonstein.

The reader may also receive an in-depth understanding by viewing my 2019 Medicine Week (Baden-Baden) presentation "A New Modern Way to Approach Cancer" on Slideshare: https://www.slideshare.net/SheldonStein/prof-serge-jurasunas-upcoming-presentation-oct-30-2019-baden-baden

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Serge Jurasunas is an internationally well-known practitioner and researcher in complementary oncology, nutrition, and molecular medicine with 53 years of experience practicing in a private clinic. He is considered as a pioneer in naturopathic medicine and the use of live blood analysis, oxidative dried blood test, and iridology. Dr. Jurasunas received the Silver Medal for Research and Invention by the French Academy. He was a former professor of integrative medicine at Capital University of Integrative Medicine in Washington, DC, and currently is Professor of Naturopathic Oncology at Pan American University of Sciences and Natural Medicine.

He has been a frequent contributor to the *Townsend Letter* for over 21 years and authored a major book in English (3 in French and 4 in Portuguese), *Health and Disease Begin in the Colon* (Amazon); a new book is coming up in the US: *Cancer Treatment Breakthrough – Immuno-Oncology using Rice Bran Arabinoxylan*.

For more information: www sergejurasunas.com; https://naturopathiconcology.blogspot.com (blog)

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Elephant in the Virtual Room

by Rebecca Takemoto, Erica Joseph, LAc, ND, FABNO, and Jacob Schor, ND, FABNO

The conference planning committee of the Oncology Association of Naturopathic Physicians (OncANP) held its first meeting last night (April 14, 2020) to start planning OncANP's tenth annual conference, scheduled for June 11-13, 2021, in Toronto. Was this an act of supreme optimism or one of pure denial? Perhaps it was just habit? Or it was continuing to do what we have been doing for years, just letting the momentum carry us forward.

We used Go-To-Meeting to gather together over dinner rather than Zoom. Does Go-To work better? Not sure I'd go that far, but we've always used it and who wants to break with tradition at a time like this? We spent a good part of our hour together analyzing the detailed evaluations filled out by attendees from this year's annual conference. Our goal has been to make each conference better than the last one, and we've succeeded in part by listening carefully to both our critics and those with the foresight to see what will be useful to learn moving forward. We focused closely on the suggested speakers nominated by attendees and planned on doing some of the routine planning like our call for abstracts via email, in addition to deciding on a timeline for submissions.

It was only in the last few minutes that we dared talk about the elephant in the virtual room; will in-person conferences even be a thing that people do next year? This is the question that many are wondering about these past few weeks. We depend on conferences both for continuing education, for advancing our practices, and for deepening our understanding of the health of our patients. Our state, provincial, and national associations depend on conferences to generate income. Our vendors depend on conferences to meet practitioners in person and promote new products. Seeing our colleagues in person sustains those of us extroverts and those who practice in more isolated settings. Will we have conferences next year? If so, what will they look like?

For help answering these questions we reached out to Rebecca Takemoto of Syncopate Meetings and Events. Rebecca has run the American Association of Naturopathic Physicians annual conferences for twenty-one years since the conference was in its infancy. (https://www.sync-opate.com/meet-the-staff/). She has been the organizing force behind a number of other conferences put on by naturopathic groups, including Hawaii Doc Talks, NHAND, CNPA, ILANP and Integrative Dermatology. After 22 years she knows our profession well.

What Ms. Takemoto Says

Like all meeting planners and hoteliers, I've spent a lot of time lately thinking about what the meetings industry will look like when we all emerge from quarantine. Will we ever gather again in the same way? Will we still have jobs?

I've been a meeting planner for a long time – over 20 years – and seen a lot of ups and downs. As a young planner, I thought 9/11 was surely the end of conferences and I needed to be looking for a new career. In 2011, after working about five years on the incredibly complex application, my company was finally granted a GSA Schedule, necessary for government contractors. Mere months later, 'muffin-gate' was uncovered showing that some government agencies were spending ridiculous amounts of money on conferences, including $18 muffins. I then thought that the government would definitely stop having meetings.

People are social animals. We need each other. Nothing has shown this more fully than those Italians singing from their balconies, or New Yorkers cheering at the change of hospital shifts, (or in Colorado people coming out at night to howl at the moon) or families setting up virtual game nights via Zoom. When it comes to you naturopathic physicians, it is even more than that; if anything, you are tribal. You need each other's company to be who you are.

I don't see meetings coming to a complete halt. All of us have endured conference calls banging our phones against our foreheads as another dog starts barking or baby starts crying or the over-anxious person who interrupts once too often. On the flip side, we are hopefully learning a lot about what really HAS to be done in person and what can just as effectively and more efficiently be done through email or online.

With those thoughts, here are my musings on the future of meetings, and not-meetings, in the age of coronavirus.

Associations will need to diversify revenue. Aside from hotels, the biggest hit directly related to the meetings industry may well be small to midsize

associations: those with a staff and regular salaries to pay; whose members are going to be less likely to pay dues; those who rely on their annual conventions and most particularly their sponsors and exhibitors for a large chunk of their annual operating budget. They are going to be in a challenging situation.

The very first calls I received when things started going downhill fast (which feels like an eternity ago already) were from these kinds of associations. Many were groups I had worked with in the past, who now have full-time planners on staff, but who realized they are going to need some outside help to strategize new or additional revenue. I've had no less than five of these brainstorming sessions in the last week and it all comes down to one thing: associations never should have had all of their revenue eggs in the one basket to begin with. Now is the time to figure out how to diversify. This diversification is going to vary association by association and industry by industry – but with a little old fashioned white board brainstorming (which can absolutely be done via Zoom) the smart and creative people running these organizations, and the less panicked help they might bring in for consultation, will come up with a list of ways to get their sponsors in front of their members.

In industries (like legal and medical) where tightening rules regarding sponsored content were already making even the strongest of us want to quit, this will require a little extra creativity. Do your research on what is and isn't allowed in a virtual setting regarding sponsorship. The old adage that sponsors can support an *activity,* but not *content* gets stickier in a virtual platform. But it's not impossible.

Focus on your goals. Every time I start with a new client, I have a conversation about goals. Sometimes (ok, most of the time) I have this conversation several times through the cycle of a meeting. It's so easy for an organization to lose track of what their primary goals really are. Most organizations are balancing goals of revenue, membership benefit (education, community, gathering), industry information, lobbying, service/charity/goodwill, marketing and PR etc. It is going to be increasingly important to know what those goals are and to plan the event accordingly. If revenue is 99% of the goal and everything else can be accomplished in some other format, then maybe you need to come up with alternative revenue sources and not hold that annual meeting. If giving your members a platform for community engagement and networking is top priority, then you need to meet; but you might need to change the format to lessen your risk with hotels/venues. If lobbying/marketing is one of the big reasons you hold a meeting (to get some attention or to shine light on an issue), are there other ways to do that while still engaging your members? All of these questions need to be the focus of organizational boards and staff in the coming months.

We need to actively steer our way forward. We live in a new world.

Meeting Safety. If meeting planners have learned one thing (aside from how to best negotiate contract cancellations) this month, it is how to write emergency plans, safety protocols and generally, how to try and keep your attendees safe. We will all be buying huge amounts of hand sanitizers for our meetings (good sponsorship opportunity there) and asking venues to do other things to keep things clean. Our exhibitors will be thinking of new ways to safely give out samples. The venues have already implemented more strict sanitation guidelines, and those won't change/lessen when things return to some kind of normal. But how can we encourage and implement new safety measures when 10,000 of our best friends are sitting elbow to elbow for eight hours a day? I've spent some time sketching new seating arrangements, thinking about what kind of sanitary furniture can be used and how to keep people from sharing quite so many germs. I was so excited, years ago, when one of my clients first agreed to move from endless rows of classroom tables to a mix of rounds and standing cocktails. We're going to see new layouts in conference setup. I can't wait to try something new!

Smaller Breakouts. Does your organization host 10,000 people for a city-wide convention? Would it make more sense to rotate those 10,000 people in and out of smaller venues across the city - rather than gather for four solid days in a convention center? Can you find different space so you can have a rotating slate of concurrent instead of general sessions? Do you have pockets of membership in various parts of the country? How about satellite conferences? How can we accomplish our goals of community networking, just in smaller groups of community?

Take it virtual. In the recent weeks I, along with most other planners, have become very familiar with a myriad of virtual platforms out there. We are all going to become more versed in virtual education and smart people much more tech savvy than I will create (or advance) amazing platforms to bring us together virtually when we can't be together personally. It will be important to adapt content, to adapt slides (which already need a full overhaul!) and to adapt speaking styles, should these platforms be utilized. We have the opportunity here to build something new – not merely a video of someone on a stage speaking, with slides in the background – but something more personal. This is going to look different for every conference – but wouldn't it be great if our attendees feel like they are truly in a discussion with (insert big name in your industry here) or being taught the intricacies of some specific practice up close and personal through overhead camera or screen sharing? With the addition of robust discussion groups and chat sessions, virtual learning can be so much more effective than it currently is.

Once again, the small to mid-size organization is going to take the biggest hit here. Many of the robust platforms which offer truly innovative

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virtual conferences come with a price tag well above $100K. Already faced with declining dues, sponsorship dollars and exhibit revenue, most small organizations will not be able to afford this kind of fee. More than ever, now is the time to consult with experts – an experienced planner can help you put together the right system for your event and manage it. Think seamless rather than bells and whistles.

Some organizations may find that virtual education is sufficient, and in some ways superior to in-person. What if the educational parts of the conference continue to happen virtually and groups gather together solely for community building? At Hawaii Doc Talks our motivation has always been to change the paradigm of continuing medical education for attendees, speakers, and exhibitors alike. We encourage exhibitors to recognize that their return on investment is not going to be found during the 20-minute exhibit break, but rather in the long-term relationships built with like-minded attendees. I can imagine forward-thinking associations gathering members for weekend adventures, and companies jumping at the chance to sponsor, in order to network directly with potential customers.

The savings to attendees and organizations alike when meeting in a virtual setting rather than in-person is not insignificant. Can we redistribute that budget in such a way as to host a combination of live and virtual activities and education throughout the year?

A Hybrid Solution. As we come out of quarantine, many of our attendees are going to remain cautious for the foreseeable future. Others may be the first to line up for the next plane out of town. I imagine this contrast will continue through the next year, at least. Some organizations may find that a hybrid model works best. Redesign your in-person education for a smaller group and also provide a well-executed virtual option for those who wish to stay home. A creative meeting planner is going to be able to walk you through which option works best for your group and your meeting.

Combine the virtual with the tangible. I recently spoke with a planner, Patrick Crosson with PC Events and Experiences who, along with Ladidadi XM, has developed At Home Experiences in a Box. He described this as "pairing creative fun experiences with a piece of education/training/messaging from a brand." The idea is to send a physical package to your attendees/staff/customers, which corresponds to some education or training that happens virtually. For example, a t-shirt manufacturer might send some fun samples to customers. Then the customer watches a short educational video about the t-shirts, followed by a social media contest of customers in their new t-shirts. You get the idea.

What tangible item could you send your attendees in advance of their upcoming online training? Maybe we're going to go back to some hardcopy content that can be followed during an online presentation. Maybe we should load everyone up with a conference bag full of goodies that would be useful/fun while watching presentations (thinking fuzzy socks and a coffee mug). Better yet, maybe it's not a bag! The sponsorship possibilities here are endless – and surely sharing photos of "attendees" in a t-shirt or funny socks wearing a sponsor's hat; this would bring some social media community togetherness and build relationships, even virtual ones.

This is where your marketing department (or your meeting planner) can shine! Have fun, be creative. This is a unique opportunity for us to recreate ourselves as organizations and as events. Don't forget to start at the top – identify your goals and stick to them. Everything else should follow that mission.

Whether we are attendees, planners, organizations or all three, we are all going to need to brainstorm, be flexible, and be open to new ideas and change. Meetings will happen, but change will happen as well. It's up to us to decide whether that change is negative or positive. In the meantime, every planner I know will continue to look for ways to make things more efficient, effective and useful, and hotels will continue to find new avenues to make guests more comfortable, even in the unchartered territory we're coming up against.

Conclusion

Without sounding too optimistic, (one of us takes pride in being referred to as a curmudgeon after all), we are excited to see how this landscape evolves and what new opportunities it brings for growth, education, and our ability to adapt to new circumstances. The one thing we are sure of is that sitting back and thinking momentum will carry us forward is not going to work: we need to actively steer our way forward. We live in a new world.

Erica Joseph, LAc, ND, FABNO, practices at Seattle Integrative Oncology (SIO). She received her doctorate in naturopathic medicine (2014), a master's degree in acupuncture (2014), and a bachelor's degree in psychology and biology (2009) from Bastyr University. Dr. Joseph currently sees patients at Providence Regional Cancer System in Olympia and Providence Regional Cancer Partnership in Everett. Seattle Integrative Oncology provides one of the few naturopathic oncology residencies in the Pacific Northwest and Dr. Joseph is passionate about training the next generation of naturopathic oncologists.

Dr. Joseph is a peer reviewer for the *Journal of Alternative and Complimentary Medicine* (JACM), is vice president of the Oncology Association of Naturopathic Physicians (OncANP), and is a member of the group's conference planning committee.

Rebecca Takemoto is the owner and principal planner of Syncopate Meetings & Events, LLC based in Northern Virginia. Rebecca has been a meeting planner for over 20 years, serving a wide range of clients from small associations to large corporations. She has developed a particular love of and focus on medical education.

Over the last several years, Rebecca has broadened her practice to include consulting and training association boards of directors and corporate meetings departments. She recently developed sessions for Learnapalooza, an intensive training seminar for meeting planners, and acts as a mentor for young planners.

Rebecca studied vocal performance and pedagogy at Brigham Young University and Utah State University, where she discovered her love of events and coordination as a member of the student activity board. She has performed in many musical theater and opera productions and currently sings with the Master Singers of Virginia.

Rebecca lives in Leesburg, Virginia, a suburb of Washington, DC, with her husband and four children.

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5G: The End of All Things

by Richard Gale and Gary Null, PhD

Progressive Radio Network

We have become thoroughly accustomed and habituated to endless advertising by drug makers to buy into the promises of pharmaceutical drugs or to consent to the nutritional value of junk food. Yet the drug and food industries are completely indifferent to their products' dangerous adverse effects. They give no thought to what it does to our health. All that matters is the business' bottom line. Fortunately, we have the freedom to make informed choices about most areas that impact our lives, whether it be living a healthy lifestyle or eating nutritious foods. But that is about to change completely due to the brilliant marketing campaigns to make life easier with the arrival of 5G's Internet of Things into our homes, bedrooms, offices and streets and avenues. What we are not being told is that as 5G technology increases, we will eventually be living in a 24-hour cycle that carries threats that are potentially far more dangerous than the occasional hamburger, pizza, or beer.

Nobody seems to be asking whether the introduction of 5G will truly improve the quality of our lives. Is there any redeeming truth to telecom's promises? There are none. But unlike a drug or unhealthy habits that can cause death, the FCC under the Clinton presidency passed legislation through Congress that hands over carte blanch permission to the telecommunications industry to directly violate our democratic freedoms of choice. Privacy will disappear altogether since this new technology increases surveillance capabilities exponentially.

And the average citizen has no choice. You cannot prevent Verizon or any of the other telecom giants from installing 5G transmission antennae in your neighborhoods, grade schools and playgrounds, apartment complexes, hospitals, and parks. And this enormous technological feat will also require a minimum of 50,000 new satellites orbiting the heavens above our heads to beam transmission signals to every habitable place on the planet. This new network will be five times greater than the number of operative satellites in space already.

Under the 5G regimen every American in a suburb or city will be living 100 meters or less from a 5G antenna.

The precautionary principle is intended to avoid inflicting unnecessary harm and injury in order to reduce avoidable health risks, and more importantly death. But this principle is being completely ignored with the full-frontal assault to implement 5G at maximum speed. During a Congressional hearing, Senator Richard Blumenthal asked a very poignant question. Do you have any science confirming that 5G is safe? Is money being spent on studies to determine electromagnetic frequency radiation's safety? At the hearing, every representative of the telecom industry said there were none that they were aware of.

Imagine for a minute that the FDA were to approve and register a drug or vaccine that had never been tested for safety on humans? That would never be permissible; however, the telecom industry is doing just that. And their primary market is the millennial and iGen generations who are also most susceptible to EMF's adverse effects. These are the generations who grew up with social media and chat rooms and who virtually live through the internet. It is their panacea that is fully integrated into their purpose and meaning in life.

This dark and deadly side of EMF-emitting technology, especially 5G, is being hidden by our multimedia system that is being paid to manufacture both consent and doubt: consent that 5G will somehow miraculously improve our lives, and doubt against the 10,000-plus studies that show 5G will be one of the greatest health and environmental risks humanity has ever faced.

Recently *IEEE Access* published a special study out of the Birla Institute of Technology and Science in India as part of its *Special Section on Antenna and Propagation for 5G*. The article, "Electromagnetic Radiation Due to Cellular, Wi-Fi and Bluetooth Technologies: How Safe are We?" is an excellent summary of the state of the science regarding 5G's future threats based upon the confirming evidence at present.[1] To date there are already 15 billion wireless local area network routers connected with the Internet of Things and 9 billion mobile connections. Almost 70% of the world's current population is using mobile phones.

Thousands of studies have been collected that indicate EMF's health risks. The BioInitiative Report (https://bioinitiative.org/) has compiled 1800

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studies alone showing serious impact on both humans' and animals' gene transcriptions, genotoxicity, DNA damage, chromatin condensation, loss of DNA repair capacity, reduction of free-radical scavengers, neurotoxicity, decreased sperm morphology, and impaired development of brain and cranial bone. Worse, Igor Belyaev's research at the Slovak Academy of Sciences has found evidence that some frequencies emitted by this technology damages all cells, including fibroblasts, lymphocytes and stem cells.[2] The Indian scientists breakdown EMF's health risks into seven main headings.[1]

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Cancer

Back in 2011, the World Health Organization's International Agency for Research on Cancer classified radiofrequency electromagnetic fields as possibly carcinogenic to humans.[3] Nine years later, this threat has been confirmed by thousands of medical professionals. No longer are the risks simply possibilities. It is a reality. The US National Toxicology Program's final report on mouse and rat studies in late 2018 confirmed cancerous heart tumors due to the earlier 2G and 3G cell phone technologies.[4] One of the world's leading experts in wireless technology's cancer risks, oncologist Leonard Hardell at the University Hospital in Orebro, Sweden, concludes that "the evidence that RF radiation exposure is a risk factor for cancer is particularly worrying, taking the present deployment of the fifth generation (5G) for wireless communication."[5] Dr. Hardell, along with hundreds of other scientists and medical doctors have demanded a moratorium against 5G until further independent studies are performed to assure the industry's denials of its hazards can be confirmed.

In a study published in the August 2018 issue of *Journal of Medical Imaging and Health Informatics,* after an extensive review and analysis of the medical literature researchers concluded that "incidence of cancer cases was remarkably higher among people who resided 400 meters from mobile antennas, in comparison to those who lived further away. Inhabitants living close to cellular antennas are also at increased risk for developing neuropsychiatric complaints."[6] Under the 5G regimen every American in a suburb or city will be living 100 meters or less from a 5G antenna. In 2016, the Europa EM-EMF guideline found "strong evidence that long-term exposure to certain EMFs is a risk factor for diseases such as certain cancers, Alzheimer's disease, and male infertility…Common EHS (electromagnetic hypersensitivity) symptoms include headaches, concentration difficulties, sleep problems, depression, lack of energy, fatigue, and flu-like symptoms."[7]

Populations living within 350 meters of an 850 MHz, 1500-watt cell phone tower in Netanya, Israel, experienced a 400 percent cancer increase (i.e., carcinoma of the breast, ovary, lung, kidney, bone, and Hodgkin's disease)

Pregnancy and Infertility

The science is conclusive that EMF's erratic pulses from mobile phones induces oxidative stress that damage testicular tissues and decreases sperm quality and motility.[1] EMF exposure results in sperm mutations that have been shown by scientists at the University of Mainz in Germany to contribute to testicular cancer.[8] Prof John Aitken at the University of Newcastle has shown that sperm exposed to mobile phone radiation revealed a 300 percent increase in mitochondrial damage.

We need to take the precautionary principle to heart when animals studies confirm the serious health risks. We are irresponsible when we draw a distinction between alarming animal studies that have yet to be adequately tested in humans and then make assumptions there can be no correlation. Therefore, when research shows that pregnant animals exposed to even low levels of EMF will show uterine congestions, dead and reabsorbed fetuses, hemorrhage, unequal and asymmetrical distribution of fetus implantation, and genetic malformation, we must consider its risks against pregnant women as well.[9] But the FCC and FDA have been horribly negligent in this regard to warn women.

Auditory System Damage

When our phones are linked to the wireless network, our entire auditory system – skin, inner and middle ear, cochlear nerve and our brain's frontal lobe – are absorbing EMF radiation. EMFs are damaging the highly sensitive hair-like cells in the cochlear and likely contributing to the neurological disorder known as tinnitus. Tinnitus is becoming increasingly more common. The high pitch sounds associated with this illness disturb normal sleep patterns and in more serious cases interfere with normal cognitive abilities and have even led to suicides, according to a study conducted by the Medical University of Vienna and published in the *British Medical Journal*. Additional studies have associated long-term mobile use with hearing loss.[10]

Adverse Childhood Development

In addition to EMF's adverse effects on the developing fetus, the younger generations are the most exposed population to EMF radiation through excessive wireless device use. It is well known that children's brain tissue displays much more electrical conductivity when compared to an adult. A child's brain also absorbs EMF radiation more readily. The geometry of a child's head significantly increases mobile phone EMF absorption in the brain, eye, cortex, hippocampus, and hypothalamus. According to a study published in the journal *Physics in Medicine and Biology*, children have especially high bone marrow conductivity, greatly increasing EMF absorption.

Consequently, a study out of the Swiss Tropical and Public Health Institute looking at 7th through 9th graders found that cumulative phone use decreased memory.[11]

Blood-Related Disorders

Even very low intensity EMF frequencies – much lower than what 5G will expose us to – interrupt the blood brain barrier that hinders toxic chemicals from disrupting various tissues, including the brain. EMFs interfere with this protective barrier. Dr. G Salford at Lund University in Sweden, observed that a single two-hour cellular phone session will produce leakage in this barrier and after 50-day use can lead to neuronal damage.[12]

DNA Damage

Medical scientists are quick to warn about the mechanisms by which our cellular DNA interact with EMF radiation. In fact, the DNA's double helix structure "causes it to act like a fractal antenna"[2] whereby it interacts with a wide range of different electromagnetic frequencies. For this reason DNA is highly susceptible to damage across the wide spectrum of wireless frequency ranges. The DNA-EMF interaction creates free radicals that contribute to stress proteins and ultimately gene mutations, including in stem cells.

Mental and Cognitive Risks

The scientific literature increasingly reveals that EMF exposure is contributing to the growing rates in neurodegenerative diseases such as Alzheimer's and Parkinson's. EMF's effects on brain tissue and neurons is an established fact based on epidemiological studies of populations living close to cell towers. 5G will bring these towers into everyone's neighborhoods. An article in *Reviews of Environmental Health* introduces a new observed disorder: "Chronic multi-system illness" (CMSI). CMSI correlates to milder electromagnetic hypersensitivity to 3 MHz-300 GHz, with headaches, concentration difficulties, sleep problems, depression, lack of energy, fatigue, and flu-like symptoms. However, beside these milder effects, long-term exposure to these high output towers are also contributing to severe brain and cognitive disabilities, including paralysis, stroke and psychosis.

In our opinion, the 5G rollout is an irresponsible experiment with potential holocaust-like consequences in the long term. Neither the US nor China have ever felt obliged to follow UNESCO's Precautionary Principle to avoid "morally unacceptable harm" when the science is plausible but still uncertain. In the case of 5G, the harm to human

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life is conclusive, and in the view of Dr. Lennart Hardell, it may be in violation of the Nuremberg Code.[7]

In addition, there is something largely missing from the 5G debate in the US, whereas some European nations are paying attention to it; that is, existing safety standards for wireless technology are obsolete. This conclusion was arrived at independently by Vienna Medical University in Austria and Carl Blackman at the University of North Carolina, published in the journal *Pathophysiology*. The problem herein lies in the failures of federal regulatory agencies to be truthful to the scientific evidence rather than show favoritism to the wireless industry's own junk science and commercial interests. Again, private interests profit and the public is harmed.

Unfortunately, the FCC standards for mobile phones have remained the same since 1996. Since 1997, secondary insurance providers have refused to cover health damages due to wireless radiation. During the past two and a half decades, the technology has changed dramatically, and not for the better. This is not simply the words of independent 5G critics in the medical profession announcing health warnings. The FDA also acknowledges the problem. On its website, we find "the FDA does not review the safety of radiation-emitting consumer products such as cell phones and similar wireless devices before they can be sold, as it does with new drugs or medical devices.... However, the FDA does have the authority to take action if cell phones are shown to emit radiofrequency energy at a level that is hazardous to the use." Unfortunately, the FDA has never taken charge of this mandate and injunction it has been assigned with.

Dr. Devra Davis is the founder of the Environmental Health Trust and a visiting professor of medicine at the Hebrew University Hadassah Medical School and a visiting professor of Medicine at Ondokuz Mayis University, Turkey. For years Dr Davis has served as the director of the Center for Environmental Oncology, which she founded, at the University of Pittsburgh Cancer Institute – the first institute of its kind in the world to examine the environmental factors that contribute to the majority of cases of cancer.

During a recent lecture for the 2020 Expert Forum on 5G and emerging EMF technologies, Dr. Davis outlined many of the gold standard studies that should have us worry about the future ahead as the telecom industry with the blessing of governments roll out 5G.[11] It is not simply EMF exposure from phones and wireless routers that pose dire risks. It is also the accumulative EMF radiation people are exposed to daily – from laptops, cellular phones, towers and antennas, wi-fi routers, and microwave ovens,

In addition to the above risks, Dr. Davis has observed other worrisome EMF effects. Dementia for example has become an epidemic and even adults as young 30 are starting to show signs of this neurodegenerative condition. Recently dementia has been called "diabetes of the brain." Davis has noted that due to EMF exposure brain scans reveal an increase in glucose levels in brain tissue and increased lipid peroxidation that results in cell damage. Mobile phones also significantly reduce glutathione, an essential enzyme necessary for DNA repair.

As we reported in the past, the mainstream media, in particular the *New York Times*, which has a collaborative agreement with the leading 5G provider Verizon, have no intention to warn the public about any of the scientific findings mentioned above. There is a growing consensus in the scientific and medical community that 5G will usher an epidemic of disease never before witnessed in human history. It is too difficult to make forecasts. Nevertheless, if the past and current research on EMF's adverse effects on health and the environment during the past 50 years are any indication, we are entering a new epoch of disease and neurological disorders that humanity is completely unprepared to handle.

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Richard Gale is the executive producer of the Progressive Radio Network and a former senior research analyst in the biotechnology and genomic industries.

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

Raising Your Own Meat

review by Craig Soderberg

Secret Livestock of Survival: How to Raise the Very Best Choices for Retreat and Homestead Livestock by Rick Austin
Ebook and print; ©2016; 210 pp.

Rick Austin is a good writer. I read his earlier book, *Secret Garden of Survival*, and I loved it since it was loaded with practical information. In fact, Austin's previous book became the #1 Best Selling Book in the category of Garden Design within nine months of its release. In his second book, *Secret Livestock of Survival*, Austin not only tells us which livestock he likes to raise and why; he also tells us which livestock is difficult to raise and why it is difficult.

Austin claims that he can raise more food on half an acre than conventional farms do on five times that space! He feeds his family and livestock from this half acre all year long, without tilling, weeding, watering, fertilizer, pesticide, or weed killer. He also gets 1.5 gallons of milk every day from his three small Nigerian Dwarf dairy goats. Austin has also been featured in *Mother Earth News* (3 times), on *National Geographic's* website, in *Newsweek*, on *Doomsday Preppers*, as well as numerous radio shows, TV shows, newspapers, magazines, and internet media.

Austin's *Secret Livestock of Survival* is arranged this way. He puts his livestock recommendations in order of ROI (Return on Investment) as well is in the order of the most discrete animals to raise. For example, the first livestock animal that he discusses is the rabbit because the rabbit is the easiest animal to care for, requires the least effort, the least amount of space and resources, and still gives the owner the most return in food produced.

The rabbit advantage. Chickens take almost half a year (over 5 months) to get 8.5 pounds whereas rabbits take only 2 months to get to 12 pounds. Or to put it another way, in the same amount of time it takes to produce 8.5 pounds of chicken meat, Austin can get 30 pounds of rabbit meat (12 pounds/2 months + 12 pounds/2 months + 6 pounds/1 month = 30 pounds in 5 months). This is one reason that Austin likes rabbits. Secondly, rabbits are quiet, and you can keep them in your barn, basement, or garage, so that no one would know that you had them. Thirdly, rabbits only need about 10 minutes per day of human care (in feeding and watering). Fourthly, rabbits are small enough for a family to consume in one meal, so there is no need for leftovers or for food preservation. Fifthly, rabbit pelts can be used to make various sorts of clothing, from mittens and gloves, to slippers and moccasins. These provide warmth and can be used for barter or sale. Sixth, rabbit bones can be used to make a broth or soup stock. Finally, rabbit feces are a great natural fertilizer. Put solid dropping boards under each rabbit cage; the poop and pee fall from gravity and flow downhill into a bucket.

In the rabbit chapter, Austin gave a great overview of how he converts one pound of barley seed into 13 pounds of livestock feed in just 8 days.

The beekeeping advantage. Honeybees not only provide honey as food, beekeeping provides you with medicine, preservatives, sweeteners, wax products, and even a line of defense for your homestead. Throughout the rest of this chapter, Austin discusses the necessary beekeeping equipment, ways of extracting honey, how to catch swarms of wild bees, how to protect your bees from their enemies, and 10 interesting facts about honeybees that most of us probably did not know.

The duck advantage. Austin likes ducks because they eat bad bugs, slugs, and snails out of his garden and provide a natural substitute to pesticides and chemical fertilizers. Ducks don't scratch up roots like chickens. Ducks are also less susceptible to disease, than most other domestic fowl. Austin created a backyard pond for his ducks; and he raises Pekin ducks for meat and Khaki Campbell ducks for eggs because they produce 320 eggs per duck per year. The rest of his chapter discusses feeding, housing, and incubation of the duck eggs.

The goat advantage. Austin prefers dairy goats over meat goats since dairy goats can provide him with milk every day (and various dairy products from that milk). His favorite dairy goat is the Nigerian Dwarf goat because the Nigerians don't require a lot of outdoor space or indoor space, they are quiet, and they don't consume as much feed as other goat species. The rest of the chapter covered goat housing, goat vitamins, goat feed, watering methods, dairy products, fencing, breeding, and raising kids (baby goats).

The fish advantage. I was enlightened by Austin's comparison of establishing a fish pond on the property vs building an aquaponics system. The whole problem with man-made aquaponics ecosystems is that they are not sustainable. First, you have to add food for the fish. So you can either collect bugs, grow bugs, or buy commercial fish food to feed the fish. Second, you need pumps and electricity to move the water, or the whole system doesn't work. In a grid down situation, you won't have power to heat the water or move the water through the pumps. Granted you could use solar power to do this, but that could take a lot of solar energy and the mechanical parts will eventually clog and fail.

So why would someone want to do all this work, create all this infrastructure and make all this investment, when you can just dig a hole in your back yard, and fill it with water and fish? It is far cheaper to dig a hole in your backyard and buy a cheap

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Raising Your Own Meat

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pond or pool liner and use that pond to house fish that will survive on their own, without any other investment or input on your part. Austin uses edible Koi and edible Goldfish in his pond. But one can also grow other native fish, like catfish. The other advantage of a pond is that Austin's pond holds 11,000 gallons of emergency water storage.

Chickens. Austin does not like chickens. They scratch the roots of plants until the area you keep them in becomes nothing but a desert. Compared to ducks, chickens are bad for garden plants – not good for them. Chickens dig holes everywhere, and roosters make a lot of noise. Also, hens sound like they are having their feathers pulled out every time they lay an egg. Austin only raises chickens because his wife has a rare allergy to duck eggs. The rest of this chapter discusses feed and water for chickens, chicken breeds, preserving eggs, incubating eggs, fencing and butchering.

Pigs. Austin does not really like pigs. The biggest problem with pigs is the amount of time and number of people it takes to butcher and preserve the meat of just one pig. Unless you have a walk-in commercial freezer, processing a 700-800 pound pig is not something that you and your wife can do over a long period of time.

Austin's conclusions. I liked the fact that Austin told us specifically which animals he would not want to raise. He doesn't recommend cows because of the amount of space and feed required to raise cows. He doesn't recommend turkeys because they are more susceptible to diseases than chickens. He doesn't recommend geese because they are loud and are known to even attack their owners. He doesn't recommend horses because they are not raised for meat, and they require a lot of time and expense to raise them. He doesn't recommend sheep because he does not like the taste of mutton.

Strong points in Austin's book. Throughout his book, Austin provided great color photos and helpful YouTube links. He also provided color photos of other related books that he recommends to his readers. Austin provided a good example to his readers by placing his barn and greenhouse near his home to save time and energy. Austin wisely advised his readers to learn more about trapping wild animals.

Suggested improvements. Austin states that some people have double fencing around their livestock paddocks. But he doesn't state whether or not he follows that practice (p.26.) Austin had some great color photos throughout his book. In the chapter on beekeeping, Austin notes that he produces the retail equivalent of over $2537.00 yearly revenue on a one-time investment of $700 in beehives. But he did not mention the annual costs of feeding and caring for the bees. There were a few spelling errors in the goat chapter (pp.104, 105). But despite these few minor issues, I recommend this book to anyone interested in the topics mentioned above. ◆

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Cancer and the New Biology of Water

by Thomas Cowan, MD

The following excerpt is from Dr. Cowan's book *Cancer and the New Biology of Water: Why the War on Cancer Has Failed and What That Means for More Effective Prevention and Treatment* (Chelsea Green Publishing, September 2019) and is reprinted with permission from the publisher.

We are erroneously taught early in life that matter can only exist in one of three "states": solid, liquid, or gaseous. For example, copper can exist as solid copper (often mixed with other elements), molten or liquid copper, or, when exposed to extreme heat, gaseous copper. There is no other state possible; the transition is from one state to the next with no intermediate steps. The transformation occurs mainly under the influence of heat, but influences such as pressure may also play a role.

If we apply this concept to water, then we can conclude that water can only exist as ice (solid), water (liquid), or steam (gas). We were all taught this in elementary school science class. The problem, like so many "truths" in science (and frankly in our culture in general), is that it doesn't stand up to even a cursory examination. In this case, we have all seen and probably eaten Jell-O, which is composed of over 90 percent water yet clearly is in none of the above three states. In fact, the state of matter that a substance assumes is not a vague concept; it can be clearly demonstrated with apparatuses that measure the bond angle between the individual molecules. Ice has a distinct bond angle between each molecule, water has a different bond angle, and in steam the molecules are mostly unattached to the other molecules. The gel that makes up Jell-O has none of these bond angles. Instead it has an intermediate bond angle that is characteristic of the gel state. Dr. Gerald Pollock, in his seminal book *The Fourth Phase of Water*, describes in detail the formation and characteristics of this fourth phase. That it exists is not in dispute. The issue is that it is not recognized for the importance that it has to the entire field of biology.

Water is the only "substance" that can exist in this fourth state, at least as far as I know. This fourth phase of water, also called structured water, is the basis of biological life.

I first started questioning the three-states-of-matter dogma when I started working as an ER doctor. We, of course, had been taught that every cell contains about 70 percent water. This was easily proven, and then no further mention was made of the water. In other words, after this cursory mention, the role and state of water were completely ignored. We just assumed it must be liquid water. But in the ER I saw hundreds of people with traumatic injuries – bullet wounds, stabbings, and other terrible wounds – but I never once saw any water squirting out of a wounded person, nor any puddle of water lying on the floor next to the injured patient. Where was the water? Blood, yes, but I had just spent years being told that humans are basically a bag of water with stuff dissolved in it, yet clearly there is no water in any cell in our bodies.

Reading the work of Dr. Pollack and of cell physiologist and biochemist Dr. Gilbert Ling years later finally cleared up this mystery. All of the "water" in our cells is in the fourth, or structured, phase. As with Jell-O, you can poke holes in it or squish it and you will never see "water" squirt out because the water is held together in a gel matrix. Jell-O is formed through the interaction of a hydrophilic surface (in this case the gelatin proteins), water, and then a heat source. The role of heat in producing Jell-O is to unfold the proteins so that they can attach to the water molecules. Without the heat the proteins remain tightly folded and can't bond to water and no gel forms. Upon cooling, the characteristic gel forms. The water inside of our cells is similar. You start with water and add protein (some evidence exists that the protein is actin, one of

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the main structural proteins in the body), which then together form the characteristic fourth-state gel.

What about the heat? Obviously we can't add direct heat to this system to unfold the proteins.

What Ling discovered is that ATP, the so-called energy molecule, does not produce energy at all but rather plays the role of heat in biological systems. Specifically, ATP binds to the end of the intracellular structural proteins, unfolding them, therefore allowing them to bind with the water in the cells to form gels. Without ATP, no gel forms and the function of the cell collapses. This vital but misunderstood role of ATP in biological systems will become crucial in our understanding of the cancer process.

The integrity of the intracellular gel has a role in every important function carried out by the cell. It is the foundation of life itself and the manifestation or embodiment of what I will be calling the life force of the organism. For example, when it is formed properly in a clear, crystalline, correct bond angle "structure," the intracellular mesh, because of its specific size, inherently binds to potassium inside the cell and excludes the sodium. As I explained in my 2018 book *Vaccines, Autoimmunity, and the Changing Nature of Childhood Illness*, this is the real sodium-potassium pump – not the mostly irrelevant pump that exists in the cell membrane. Nature has been so organized that the gel itself, with no energy needed, creates and supports this important distribution of potassium inside and sodium outside the cell. As a result, the cell becomes charged, is able to "do work," and, because it then carries a charged "halo" at its exterior, is able to assume proper spatial orientation with other cells. In other words, without the healthy sodium-potassium gradient, a cell loses its charge and, like a battery, becomes a dead cell. A dead cell loses its "halo," clumps together with other cells, and forms the characteristic tumor that is one of the hallmarks of cancer.

Another function of the intracellular gels is to provide spatial orientation to the protein or DNA structures in our cells. In other words, proteins and DNA function because they assume a particular and functional three-dimensional shape inside the cell. This shaping is a direct result of the cell's interaction with water. For example, through the Human Genome Project, we learned that DNA contains about 30,000 functional genes. As the action sites of the DNA, genes are the unit that codes for the individual protein. We once thought that each gene coded for one and only one specific protein, but then we found out that there are at least 200,000 proteins in our cells. The question was, how do 30,000 genes code for 200,000 proteins? It's like a game of scrabble. A gene is like the letters *T*, *E*, and *A*. This makes the word (or protein) *tea*. But it can also make *eat* or even *ate*; it depends on the "consciousness" of the player. Now we know there are cutting and splicing proteins that actually determine the order of the letters in our genes, but the determining factor in how a gene will be expressed lies in the structured gel within which the DNA resides, not in the DNA itself. In other words, the gel structure of the water is the consciousness of the player in the Scrabble game. *This means that the expression of our DNA, the very thing modern oncology is so focused on, is nothing more than a result of a properly formed and functioning gel structure in the cell.* [emphasis added]

The "reason" nature chose water to play this fundamental role in our biology is that structured water has two unique and fundamental properties. The first is that it has infinite binding sites, and the second is that when anything binds with this intracellular crystalline gel structure, it can produce instantaneous effects throughout the entire cell. The way to picture this is to imagine a window blind that can exist in either an open (lets light in) or closed (darkness) state. One simple turn of the lever or pull on the string and the entire blind changes state. The intracellular gel binds to hormones, chemicals, emotions, thoughts, and on and on; each creates subtle changes in its configuration, which is then translated into a specific action by the cell. For example, if you put estrogen in the cell, it binds with intracellular gel, subtly changing it; this then creates the unfolding of the DNA so that it facilitates the expression of the part of the DNA that codes for proteins that produce breast tissue. In this way, exposure to estrogen creates the effect desired by the cell. Humans interact with and are impacted by an infinite number of stimuli. Our ability to accept these stimuli and turn them into action is a function of our intracellular gels. This is the case whether we're talking about chemicals or deep spiritual impulses. Nothing turns into action without impacting our intracellular gels.

This understanding then allows a working definition of health and disease. Health is the state of perfect intracellular gels. Disease is when this gel state deteriorates. It is then no wonder that good food, healthy water, sunshine, interaction with the earth, love, and acceptance – all of which produce healthier, more robust intracellular gel – improve our health. In contrast, interaction with glyphosate, electromagnetic fields, and toxic chemicals deteriorates our gels and makes us sick. My latest book *Cancer and the New Biology of Water* is fundamentally an exploration of how things affect our intracellular gels and, in the end, can either result in or heal us from the disease state called cancer.

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

The New Science of Signaling Exercise

by Denis Wilson, MD

The following excerpt is from Dr. Denis Wilson's book *The Power of Fastercise: Using the New Science of Signaling Exercise to Get Surprisingly Fit in Just a Few Minutes a Day* (Chelsea Green Publishing, October 2019) and is reprinted with permission from the publisher.

Do you have a cell phone? If you do, chances are that you interact with your phone many times a day – to tell it to make a call, send a text or a tweet, or check the weather or see what your friends have posted. Your phone interacts with you by making sounds, vibrating, and displaying information on the screen for you to see. You interact with your phone by touching the screen and pressing buttons. In other words, your phone sends you signals, and you respond by sending your phone signals. Your interaction with your body is very similar. Your body definitely sends you signals, and you can respond by sending signals to your body. One of the most basic signals that the body sends is hunger. Hunger is the signal the body sends to let you know that the fuel it's currently burning is running low. If you eat, your body will burn the food you consume to provide the energy it needs. But if you don't eat, your body will begin to burn stored glycogen and fat and also muscle tissue. That's not a good thing because we want to preserve our muscle. What if we could direct the body to burn only stored fat instead of muscle? The remarkable fact is that you *can* direct your body to burn stored fat and to build muscle, simply by doing a very short burst (three to sixty seconds) of specialized signaling exercise I call fastercise. As you fastercise, your body increases its burning of stored fat and your hunger goes away in moments. It's as simple as that. Seriously? Seriously.

Diet and exercise send powerful signals to our bodies and can promote optimal health. However, when we think of diet and exercise as being only about our intake and expenditure of calories, we can get some very confusing results: "Why am I gaining weight even though I'm eating less and exercising more?" It's important to take a broader view of the signals we send the body with diet and exercise. In my opinion, the human body is the most advanced technology on earth and given the right signals, circumstances, and resources, our bodies can do incredible things automatically.

What Is Fastercise?

Fastercising between meals is a super convenient, natural, and effective way to fit in a healthy, sustainable, and enjoyable lifestyle. Fastercise is a form of high-intensity exercise that is usually done for anywhere from a matter of seconds up to about a minute or two. Fastercise is based on two body movements that are so natural our bodies do them automatically – the "morning stretch" (which is actually a period of tightening up various muscle groups) and shivering (what we do when we are stuck in a cold place for too long). I call the two variations of fastercise that are based on these two movements *tightercise* and *shivercise* because they are good descriptions that are easy to remember.

Tightercise and shivercise are not difficult to do. You may feel a little awkward the first couple of times you try them since they are so unconventional; but before you know it, they will become so natural that you may even find yourself doing them automatically.

Tightercise

Tightercise is simply the act of voluntarily contracting your muscles as hard as you can for three to eight seconds (or longer), the way you do when you wake up and stretch in the morning. Why do we do that every morning? I believe that one of the most important reasons is that our bodies are low on fuel when we first wake up because we haven't eaten for hours. Contracting our muscles really hard for a few seconds mobilizes our energy stores to push off our hunger and give us the energy we need to get up, hunt for breakfast, and start our day. As it turns out, contracting our muscles this way is useful whenever we are low on fuel, not just when we wake up. For example, later in the morning when we get hungry for a snack, we can tightercise for several seconds to instantly push off our hunger for a time. And we can repeat that a number of times if we wish. Tightercising can also help mobilize fuel for other purposes, too, such as when we are about to expend a lot of energy in an athletic event.

In technical terms, tightercise is an isometric resistance exercise. You can contract several muscles at a time for three to eight seconds and can run through all of your big muscle groups in about a minute. Or you can tighten up all of your muscles at once and be done in eight or ten seconds.

First thing in the morning is a good time to tightercise because the body is naturally inclined to contract muscles automatically upon waking. A good sign that you have tightened enough of your muscles hard enough for long enough is that you become winded enough to catch a deep breath. Breathing is one mechanism that the body uses to get rid of acid that can build up in muscle tissue with exercise. The faster you exercise, the more acid can build up, which signals your body to increase respiration. You'll find it's not difficult to catch a deep breath after tightercising because there's a natural tendency to breathe less while you contract your muscles. You may experience a deep, full inhalation and exhalation within ninety seconds after you tightercise. This deep breath is similar to a full-fledged yawn. The muscle contractions and deep breaths we experience by tightercising enable our bodies to mobilize and

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burn energy stores to generate the energy we need to get a great start on the day.

Shivercise

Shivercise is the act of intentionally rapidly shifting between contracting (tightening) and relaxing your muscles, causing them to shiver, shake, or shudder. These small-amplitude movements (less than a couple of inches) are performed as fast as possible. Picture shivering or running in place while moving your arms and legs only a couple of inches in either direction, lifting only your heels off the ground. The purpose is to maximize the number of muscle contractions and relaxations per minute. Speed is the key. Though we can shivercise when we feel cold and want to feel warm, we can also use it to become winded enough to catch a deep breath.

There are similarities and differences in the signals that tightercise and shivercise send your body. Both signal the body to mobilize stored energy (in the form of glycogen and fat) in order to provide the body with instant energy, but shivercise does this more aggressively. Both techniques can also stimulate muscle growth, but tightercise more so than shivercise. Does being able to lose fat and preserve muscle without much discomfort, time, money, or slowing of the metabolism seem too good to be true? Actually, canceling hunger with fastercise often does deliver these benefits.

It can be very difficult to motivate ourselves to get up, get dressed, and drive across town for a strenuous workout. But with fastercise, we just get started, contract our muscles for a minute or so, catch a deep breath, and we're done. By the time it starts getting difficult, we're done. Fastercise is exercise that almost anyone can do; after all, almost anyone can shiver or tighten some muscles, right? This includes older people, people with arthritis, and postpartum women.

Through the fastercise techniques of tightercise and shivercise, we can send more powerful signals to our bodies in just a couple of minutes than we might otherwise accomplish in an entire day. To get the most benefit from fastercise, I also recommend that people drink plenty of water. Taking supplements of vitamins, electrolytes, and branched-chain amino acids (BCAA) can also be helpful.

The timing of signaling exercise in relation to eating is also a key to success. By choosing the right timing of fastercise in relationship to eating, we send powerful signals to the body that direct it to work with our efforts rather than against them.

Denis Wilson, MD, is the author of *Wilson's Temperature Syndrome, Doctor's Manual for Wilson's Temperature Syndrome*, and *Evidence-Based Approach to Restoring Thyroid Health*. Dr. Wilson speaks at medical conventions and medical schools both nationally and internationally and trains physicians on the use of herbs and nutrients. His latest book is *The Power of Fastercise* (Chelsea Green Publishing, October 2019).

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911 Tyler Street
Pt. Townsend, Washington 98368-6541 USA
http://www.townsendletter.com | info@townsendletter.com

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Publisher Jonathan Collin, MD
Editor Jule Klotter
Contributing Medical Editor Alan Gaby, MD
Managing Editor Barbara Smith
Circulation Manager Joy Reuther-Costa
Managing Assistants Julie Reuther; Jill Tomasi
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Jonathan Collin
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Barbara Smith

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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.

Healing with Homeopathy

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

Two Different Approaches to the Homeopathic Treatment of Cancer: The Banerji Protocol Compared to a Constitutional Remedy

A Non-Classical Homeopathic Approach

Bob and I, and now just me, have written a column for the *Townsend Letter* for nearly 30 years. Those of you who have followed these columns know that I am unequivocally (and quite vocally) a *classical* homeopath. Classical means one remedy at a time prescribed for the whole person. For *all* of her symptoms – mind, body, and emotions. And, using Rajan Sankaran's *Sensation Method*, the remedy (*simillum)* should fit the totality of the patient's case as far as Kingdom/Subkingdom, Family, and Miasm. I have long been skeptical of combination homeopathic remedies, figuring that, since only one remedy is the best match, they must work simply because they include the simillimum, among others.

In 2005 we did write a column on Dr. A.U. Ramakrishnan, an Indian homeopath specializing in the treatment of cancer. But it was never a protocol that I used myself – primarily because I did not feel comfortable regarding liability in treating cancer patients – and, secondarily, because that type of rote prescribing never really made sense to me.

On Samuel Hahnemann's birthday this year, April 9th, ten or so prominent homeopaths throughout the world, gave excellent case presentations of cured cases. One of these was presented by a homeopathic teacher and colleague from Mumbai, Dr. Sujit Chatterjee, whom I first met there in 1993. His case, which he has kindly given me permission to present in this article, was quite impressive. Around the same time, I watched the recently released film created by a Canadian homeopath, Ananda Moore: www.magicpillsmoviecom. One segment of her film takes place in India at the Banerji clinic in India. Those two synchronous events occurred within weeks of the deadline of this issue, for which Jonathan requested that I write about cancer.

Who Are the Banerjis and What Are Their Protocols?

The late Dr. Prasanta (1933-2018) and Dr. Pratip Banerji are the founders of The Prasanta Banerji Homeopathic Research Foundation in Kolkata, India. As with many doctors in India, the daytime is spent treating large numbers (100 or more) of patients in a public hospital or clinic, and the evening is spent in a private clinic setting. Dr. Prasanta treated, tirelessly, the rich and poor alike with love and compassion, and his work is now being carried on by his son, Dr, Pratip. The Banerjis questioned the practicality of spending up to two hours with an individual patient (my first office visit lasts 90 minutes, and occasionally more), and the corresponding fees needed to justify that long an appointment, as well as the difficulty of scientifically validating homeopathy using clinical trials based on the prescription of a single remedy.

The Banerjis, admittedly and unapologetically, do *not* practice classical homeopathy. Their goal was to develop homeopathic protocols using state-of-the-art scientific methods to prescribe specific remedies, in combination, for specific diseases. Drs. Banerji feared that the true healing potential of homeopathy could be denied by, and eventually lost to, mainstream medicine because of the difficulty of conducting persuasive clinical trials. They have streamlined their treatment protocols utilizing the most modern of diagnostic tools, including ultrasonography, MRI, cancer biomarkers, and other procedures. They often combine two potentized remedies, based on their clinical observations and experience with thousands of patients. Clinicians check carefully for aggravations, adjusting the remedies accordingly. They have quite an impressive track record of recovery, often astoundingly rapid, compared to anything I have seen using conventional chemotherapeutic treatments.

So, what *would* Dr. Samuel Hahnemann say about the Banerji protocol and success? Would he roll over in his grave, crusty

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old fellow that he was, yelling, "This is *not* true homeopathy?" Or would he, foreseeing the current threat to homeopathy internationally and, at this very time by the FDA, find the Banerji approach brilliant and necessary? That we will never know, unless Dr. H somehow figures out a way to come back as a ghost and let us know! In the meantime, the Bannerjis have collaborated with American researchers at the M.D. Anderson Cancer Center at the University of Texas to demonstrate plausible biological mechanisms for the antitumor effects of the homeopathic medicines tested. In one report, fifteen patients diagnosed with documented intracranial brain tumors were treated exclusively with homeopathic *Ruta graveolens* 6C and *Calcarea phosphorica* 3X without additional chemotherapy or radiation. Of these 15 patients, six of the seven who had glioma showed complete regression of the tumors. In their clinic in Kolkata, India, physicians see 1000-1200 patients a day, including about 120-200 cancer cases. Patients come from over 70 countries to receive their care. The clinic has submitted several cases to the National Cancer Institute, where they indeed passed scrutiny, and were presented before the Cancer Advisory Panel. One of the reasons that I felt compelled to present this information is the growing incidence of glioblastoma among our friends and close community within a small radius of our home in Langley, Washington, on Whidbey Island. There is speculation of EMFs as a causative factor, which prompted us to make significant changes in our EMF use over the past year.

As I mentioned, I do not treat patients with cancer, so I do not have any clinical results of my own. If you are intrigued and wish to pursue further study of this protocol, I refer you to their book and their foundation: Prasanta Banerji Homeopathic Research Foundation in India: https://www.pbhrfindia.org/contact-us.html

Dr. Sujit Chatterjee: A Case of Stage IV Lung Cancer in a Young Man

This case was shown last month in a video case presentation for an International National Homeopathy Day webinar. Though some will find it controversial, if not unbelievable, I think you will understand why I want to share it with you in this issue of the *Townsend Letter*. Dr. Sujit Chatterjee was one of the original instructors in Dr. Rajan Sankaran's training program, which we first attended in January of 1994. A brilliant and dedicated homeopath, he treats a number of cancer patients in his practice. I prefer to have long-term follow-up of at least two years when I present my own cases. This young Indian man was first seen six months ago, and this case presented one month ago. However, it is a remarkable case, the opportunity arose for me to write this article now, and this journal reaches many individuals who are open to alternative therapies. If even one life could be saved as a result of either Dr. Chatterjee's case or the Banerji Foundation protocols, then this article will have served its purpose; and the lack of long-term follow up in the following case might be excused.

First visit: This 31-year-old Indian young man consulted Dr. Chatterjee in Mumbai on November 1, 2019. The PET scan finding from October 16, 2020:

- Multiple cervical and bilateral supraclavicular lymphadenopathy, the largest being 2.6 x 5.9 x 8.9cm.
- A spiculated lesion in the right lung measuring 3.2 x 3.1 x 2.6 cm.
- Multiple pulmonary and pleural nodules in both lungs, the largest in the left upper lobe: 13 mm.
- Linear and nodular septal thickening radiation from the primary lesion and the pulmonary hila onto the lungs (lymphangitis carcinomatosis).
- Mild right pleural effusion and subtle left pleural effusion.
- Multiple mediastinal and hilar/paraesophageal nodes. Multiple retrocrural and left paraaortic nodes, the largest measuring 20x35 mm.
- Multiple lytic lesions in multiple ribs, vertebrae, and pelvic bones.

Symptoms:

- Dry cough past two months not responding to any treatments
- Cough is aggravated by talking, lying down, and cold drafts
- Sleep disturbs the cough, causing the patient to sleep in a sitting position most of the time
- Breathlessness on slight exertion
- Right upper back pain during the cough
- General weakness
- Chilly
- Weight is 87 kg.

Stressors, mental/emotional state, family history: This young man has three small daughters and is responsible for his sisters. He is the only son in the family. He has sole responsibility for the finances, home, and extended family. He feels very depressed and does not want to seek treatment; he has given up. The patient's father suffered from depression and died after taking out a huge loan which he had to repay. It was up to the son to be responsible for the defaulted loan, as well as to assume responsibility of finding grooms for his sisters. The patient's nature was silent, quiet, and he kept his feelings inside. His reason for not wanting treatment for his cancer was that it would deplete the money needed for the future of his family.

The initial prescription: *Saussurea lappa* mother tincture 5 drops three times a day and a homeopathic remedy from the Actinides group with an affinity for lungs, bones, and lymph nodes, plussed three times a day for three days. Dr. Chatterjee learned about *Saussurea* from a colleague, Dr. Sunirmal Sarkar in West Bengal, because it is indicated for advanced lung cancer with a severe, constant cough and dyspnea. The *Actinides*, considered a new frontier of remedies in homeopathy, are elements near the bottom of the periodic table, prescribed for patients who exert strong efforts to hold their lives together in order to prevent them from falling apart and being out of control.

The patient's lung symptoms were 60% improved, but Dr. Chatterjee was not satisfied that the mental state of the patient was covered. His analysis: The patient is extremely responsible

for his family and feels that life is a burden. Even in Stage IV cancer, his main preoccupation was for his family, rather than of his own mortality. He used the following rubrics in the *Reference Works* program: Lung cancer; Delusions, alone, always being; Delusions: being alone on an island; Delusions, being in the world alone; too much sense of duty; forsaken, sense of isolation; Mind; undertaken things opposed to his intentions; and Grief, silent. Dr. Chatterjee recommended continuing the *Saussurea*, but changed the homeopathic remedy to *Disopyros Kaki* 1M twice a day for two days.,

Diospyros Kaki is a homeopathic remedy that was proved in October of 2000 by the Dutch homeopath, Marijke Creveld. The Nagasaki *Kaki* tree growing close to the impact site of the plutonium atomic bomb on August 9, 1945, miraculously survived the explosion and aftermath. Seedlings of the tree have been planted in the US, Brazil, Japan, and, in the summer of 2000, at the botanical garden at Leiden University in The Netherlands. Also used in Chinese herbal medicine for tumors, as well as for other conditions, it was hypothesized that it might be a fascinating homeopathic remedy. The name, *Diospyros*, from the Greek, translates as "God Fruit," and some consider it to be a symbol of the World Tree, possibly playing a role in the survival of the earth.

Follow-up Visit After One Month:

- The cough has reduced by 70%.
- Breathlessness is significantly improved. The patient can walk for two kilometers a day.
- Weakness is much less.
- Sleep is improved.
- Attitude is much more positive. Weight has increased by two kilograms.

He began palliative oral chemo-therapy as prescribed by his oncologist.

Three and a half-month follow-up:

- Cough nearly gone
- 90% overall improvement in symptoms.
- Weakness nearly gone
- Much more hopeful

Repeat CT scan of the neck and chest results March 5, 2020 (four and a half months after the previous scan):

- Multiple enlarged and discrete, conglomerate, bilateral cervical and supraclavicular metastatic lymph nodes are mildly regressed in size and number.

Healing with Homeopathy

- Small soft tissue density lesion of right upper lobe regressed in size.
- Mild septal thickening in both upper lobe and right middle lobe are significantly regressed since previous scan. Multiple other nodular lesions in both lungs previously seen are also regressed.
- A residual, mildly prominent right paratracheal lymph node is regressed in size. There is regression in the size and number of mediastinal lymph nodes.

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Conclusion by Dr. Chatterjee at this point of treatment: "The patient is clearly improving." In advanced cancer cases, only one remedy is not enough to bring significant changes, A nosode or an Actinide remedy with deep pathology, and an organ-specific remedy (in this case, *Saussuria lappa*) is needed. If you wish to contact Dr. Chatterjee about this case, he can be reached at drsujitc@gmail.com.

I found this case compelling, due to the fascinating *materia medica* of the Kaki tree and the rapid response of the patient to the combination of *Kaki* and *Saussurea Lappa* mother tincture. *Saussurea*, also known as Kuth root, is an endangered plant from the Himalayas. It is commonly known as castus, saw-wort, and snow lotus, and is a member of the *Asteraceae* family. It is also a famous Ayurvedic herb used to treat respiratory disorder, skin diseases, and gout.

This case clearly needs to be followed over time to make sure that the tumor regression and improvement continues. I wanted to present this case as a counterpoint to the Banerji method. As a classical homeopath for nearly four decades, I am steeped in the tradition and belief of the constitutional prescription. It is through finding the one remedy to treat the whole person that Hahnemann postulated deep and permanent healing could occur. There is a highly respected, experienced Indian physician who does work at a distance treating patients with cancer using the classical approach. His name is Dr. Farokh Master, email: drfarokhmaster@gmail.com and his website is www.farokhmaster.com. You can watch a YouTube interview concerning his work with cancer at https://www.youtube.com/watch?v=JmEiPfq1gYY.

Resources

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Judyth Reichenberg-Ullman is a licensed naturopathic physician, board certified in homeopathy. She previously received her Master's in Psychiatric Social Work from the University of Washington. Dr. Reichenberg sees patients in person at Serene Natural Health in Edmonds, Washington, as well as by phone consultation internationally. Fluent in Spanish and French, Dr. Reichenberg is passionate about homeopathy and uses the Sensation Method of Dr. Rajan Sankaran. Drs. Reichenberg-Ullman and Dr. Robert Ullman have been together over 35 years and live on Whidbey Island, Washington, and in Pucón, Chile. Avid adventure travelers, they have visited nearly 50 countries, including hiking two Caminos in Spain and Portugal. Dr. Ullman retired from homeopathic practice as of April 1, 2020.

Dr. Reichenberg is the author of *Whole Woman Homeopathy* and co-author with Dr. Ullman of eight books on homeopathy: *Ritalin-Free Kids, Homeopathic Self Care* (with companion kit), *The Savvy Traveler's Guide to Homeopathy and Natural Medicine, Whole Woman Homeopathy, A Drug-Free Approach to Asperger Syndrome and Autism, The Homeopathic Treatment of Depression, Anxiety, and Bipolar Disorder,* and *Rage-Free Kids* as well as *Mystics, Masters, Saints and Sages – Stories of Enlightenment.* Pioneers in their field, they have been columnists for the *Townsend Letter* since the early 90s. They taught originally at Bastyr University, then offered seminars internationally, most recently in Prague in 2018.

Please visit their website at www.healthyhomeopathy.com (which contains a wealth of articles, blogs, and more) and Facebook at Healthy Homeopathy. She can be reached by phone at (425) 774-5599 or through email at drreichenberg@gmail.com. Dr. Reichenberg-Ullman was recently honored by the American Holistic Health Association in their anniversary ebook: https://ahha.org/30th-anniversary .

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AUGUST 20-23: 11th ANNUAL INTEGRATIVE MEDICINE FOR MENTAL HEALTH (IMMH) CONFERENCE live streaming online. CONTACT: https://www.immh2020.com/

AUGUST 21-22: 28th ANNUAL A4M/MMI SPRING CONFERENCE online. CONTACT: 561-997-0112; https://www.a4m.com/

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AUGUST 22-23: 6 STEPS TO WELLNESS SEMINAR – Muscle Testing and More with John W. Brimhall, DC, in Philadelphia, Pennsylvania. CONTACT: 800-890-4547

AUGUST 27-30: ACUPUNCTURE MERIDIAN ASSESSMENT (AMA) TRAINING For Doctors, Dentists & Health Professionals: Detecting Parasites, Dental & Fungal in St. Louis, Missouri. Simon Yu, MD, CONTACT: www.preventionandhealing.com. 314-432-7802**.**

SEPTEMBER 9-11: FREQUENCY SPECIFIC MICROCURRENT MASTER CLASS in London, United Kingdom. Also, **OCTOBER 30-NOVEMBER 1 (Master Class)** in Taiwan. CONTACT: 360-695-7500; https://frequencyspecific.com/

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OCTOBER 15-18: MISTLETOE & INTEGRATIVE ONCOLOGY COURSE in Denver, Colorado. CONTACT: https://anthroposophicmedicine.org/event-3678093

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OCTOBER 23-25: GENETIC METHYLATION SERIES 1 with Marc Harris, MD, ND, in Chicago, Illinois. Also, **DECEMBER 4-6** in Las Vegas, Nevada. CONTACT: 800-890-4547.

OCTOBER 31-NOVEMBER 1: ARIZONA NATUROPATHIC MEDICAL ASSOCIATION CONFERENCE – Neurological and Musculoskeletal Issues in Scottsdale, Arizona. CONTACT: https://www.aznma.org/

NOVEMBER 6-8: FREQUENCY SPECIFIC MICROCURRENT CORE MODULE 2 – NEURO & VISCERAL in Chicago, Illinois. Also, **DECEMBER 3-5** in San Francisco, California. CONTACT: 360-695-7500; https://frequencyspecific.com/

NOVEMBER 7-8: 2nd EPIC FUNCTIONAL MEDICINE CONFERENCE in Charlotte, North Carolina. CONTACT: https://epicfmconference.com

NOVEMBER 13-15: 21st ANNUAL CONFERENCE OF THE WESTON A. PRICE FOUNDATION – Staying Healthy in a Toxic World in Atlanta, Georgia. CONTACT: https://www.wisetraditions.org/

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Ask Dr. J

by Jim Cross, ND, LAc
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Does the Answer Just Lie Within?

My son was born with a condition called prune belly syndrome, with an extremely large, dystonic bladder as one of its sequalae. My son always has a large amount of residual urine left in his bladder as a result, which leads to cystitis unless he continuously takes a low dose antibiotic. This seems like a pretty clear-cut example of the germ theory where bacteria aren't consistently cleared from the urinary bladder and can eventually lead to a UTI.

On the other side of the spectrum, I just inhaled deeply and brought in a large quantity of microbes that occupied the inrushing flow of air. A study in *Proceedings of the National Academy of Science* showed the air you breathe in is teeming with approximately 1,800 different species of bacteria, including harmless relations associated with bioterrorist attacks.[1] Now the conundrum: why am I not becoming violently ill?

Cancer is another topic where we can look at treating from without (radiation, chemo, surgery) or within (for e.g. the late, great Nicholas Gonzalez's sympathetic, parasympathetic balancing system). Gonzalez claimed hard cancers tended to be sympathetic dominant. According to Gonzalez, this condition resulted in cellular membranes that were locked up tighter than a drum, which prevented chemotherapeutic drugs or functional medicines from penetrating the cancer cells and destroying them. By rebalancing the autonomic nervous system, this allowed membranes to become less stiff and functional again, which allowed substances into the cancer cells to neutralize them.

This leads me into my topic for the day: pleomorphism versus monomorphism. Louis Pasteur and other scientists developed the to-this-day dominant paradigm, monomorphism, which believes microorganisms are locked into only one possible form and cannot transform into other types of microbes. This theory segues nicely into the germ theory where one type of microorganism is responsible for a specific infection and by killing that microbe you resolve the infection.

Contrary to Pasteur, Antoine Bechamp and Gunther Enderlein advanced the theory of polymorphism, which proposes that microorganisms aren't locked into one possible form but can progress through various stages of development and life cycles that are completely dependent on the host organism's internal microenvironment or milieu.

Bechamp was an interesting fellow with multiple advanced degrees and was refining his polymorphism theory in the same time frame as Pasteur was developing his germ theory. Much experimentation led Bechamp to theorize that tiny bits of matter observed in the cells of plants and animals might actually be living entities that he termed microzymas and led to his formulating the theory of microzymas.[2] Bechamp had come to the conclusion that all living beings have free form, living, independent micro-entities occupying space in their bodies.

Bechamp also believed that these microzymas helped to maintain a healthy internal milieu in the bodies they inhabited. The microzymas were very sensitive to internal biological signals, especially the pH, and would evolve into other microscopic forms if the terrain became negatively compromised. Bechamp theorized that the change in terrain signaled to the microzymas that the body was either mortally sick and dying or already dead. These signals stimulated them to change into other forms that would be able to help restore internal homeostasis or recycle the organism upon death.[2]

So, Pasteur thinks disease comes from without. However, Bechamp's microzyma theory considers the internal milieu as the most important contributing factor. One corollary is that Bechamp did not deny the existence of microbes outside the body. He just didn't agree that they were the primary source of internal diseases. Rudolph Virchow made an excellent analogy stating that mosquitoes seek stagnant water but do not cause the pool to become stagnant.[3]

So, is it the chicken or the egg? Should we be wearing masks and social distancing or attempting to make our internal milieu impenetrable and, if penetrated, so well organized and protected that no prisoners are taken? Pasteur's side is very thoroughly represented already, so I will focus on some of the history and professionals who have furthered Bechamp's side.

First off, are there any articles documenting the existence of pleomorphic microorganisms in the human body? An article from the *Journal of Clinical Microbiology* identified, using dark-field microscopy, a wide variety of microorganisms in the blood and body while searching for spirochetes in Alzheimer's disease.[4,5] By using PCR amplification and sequencing of the 16S ribosomal RNA, researchers in another study were able to characterize the breadth of bacterial diversity within the human subgingival crevice.[6] Two other reports by Nikkari et al and by Tedeshi et al detected blood-associated bacterial sequences and the presence of pleomorphic bacteria as intraerythrocytic parasites in clinically healthy human subjects.[7,8]

Next, are there any studies linking human cancers with pleomorphic bacteria? At a symposium of the Annals of the New York Academy of Science in 1970, a paper by Wuetherle-Caspe Livingston and Alexander-Jackson documented isolating a highly pleomorphic microbe that was found consistently in human and animal cancers. This microbe could resemble cocci, bacilli, fungi, and viruses. Here is a direct quote: "The virus-like bodies present in tumor and culture filtrates can evolve after one or more months into larger mycoplasma-like L-forms, and thence to frankly bacterial rods and filaments."[9]

Finally, are there any other prominent scientists/doctors who scientifically furthered Bechamp's work? One such person was the German microbiologist Guenther Enderlein who was considered by many the father of pleomorphism. He also used a darkfield microscope that allowed him to look at live blood and bodily fluids. He saw Bechamp's small microzymas, which he termed protits, and claimed to find them extensively throughout the human body in its cells, blood, and other fluids. He also found them after the death of an organism, ostensibly performing the function of decomposition.[10]

He found that the protits appeared to be working with the various systems of the body in a synergistic relationship that established a natural bioregulatory process where the protits assisted in maintaining a healthy internal milieu. However, should the internal environment become destabilized biochemically or metabolically, these protits could evolve into more complex forms, including bacteria and fungi, that would attempt to restore this synergistic equilibrium. He also classified these new forms' level of development according to the state of degeneration that the terrain had devolved into.[10]

Enderlein then basically viewed disease as an imbalance of the internal environment or soil out of which virulent forms of his protits could develop to help restore internal homeostasis by returning virulent forms to their harmless, functional forms. Out of this research he developed his isopathic Sanum remedies, which can stimulate at a deep constitutional level the return of the protits back to their avirulent form to return the overall constitution to health and vitality.[10]

What can we as practitioners and patients make out of this? Modern microbiological medicine will doubtless view this "pleomorphism theory" as merely a wild mixture of speculation and contaminated cultures. However, it seems worthwhile to reappraise the basic tenets of pleomorphism as we may be ignoring medical concepts of fundamental importance.

So, does the answer just lie within? For me, the wise person considers both sides. Sure, a virus could penetrate our defenses and cause serious disease. Nature, on the other hand, is always richer in untapped healing modalities than we think it is. Utilizing a wide variety of those healing modalities can strengthen the wall and moat around the fort (body) and can prevent any invaders (microbes) from breaching the fort. Basically, your body is the only place that you have to live in at this present moment. If you take most excellent care of your body, you will have a much better chance of engaging a viral foe and coming out the other end as healthy as you did upon entering into that viral tussle.

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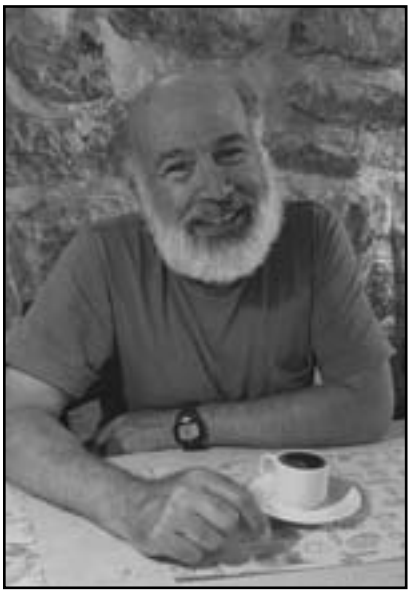

Curmudgeon's Corner

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

New Way to Target Cancer Stem Cells: Doxycycline, Vitamin C, and Berberine

There's a recent study on women with breast cancer that has me thinking. Researchers in the United Kingdom led by Michael Lisanti have over the last five years been investigating the effect of various antibiotic drugs on cancer stem cells and their findings have been both methodical and exciting.

Their 2018 human trial showed doxycycline has significant effect against breast cancer stem cells.[1] Before we go further into this study, we need to back up and talk about Lisanti's earlier work. Even before that, we probably should talk about cancer stem cells.

No one likes to admit when they are wrong. The generally accepted theories about cancer are being amended, yet we don't hear much about this shift in thinking. We used to believe that healthy cells would be damaged over subsequent generations acquiring genetic mutations that led to the shifts in phenotype that we define as malignancy. Current theory is that these genetic shifts occur at a pre-tissue level, in undifferentiated stem cells. Pluripotent stem cells become cancer stem cells and give rise to cell lines that form cancer tumors.

This shift in theory is important for many reasons but two stand out. First, the standard cancer treatments, chemotherapy and radiotherapy, do not affect stem cells. These cells are left unscathed. Radiation and chemotherapy target only fast dividing cells but cancer stem cells are the opposite; these cells are slow growing. The second reason is that cancer stem cells are now given credit for the recurrence of cancers where there was 'no evidence of disease' post treatment. Finding ways to get rid of these cancer stem cells is pretty much on the top of every oncologist's wish list.

A 2014 paper sums up the situation succinctly:

> Cancer stem cells have been identified in a number of solid tumors, including breast cancer, brain tumors, lung cancer, colon cancer, and melanoma. Cancer stem cells have the capacity to self-renew, to give rise to progeny that are different from them, and to utilize common signaling pathways. Cancer stem cells may be the source of all the tumor cells present in a malignant tumor, the reason for the resistance to the chemotherapeutic agent used to treat the malignant tumor, and the source of cells that give rise to distant metastases.[2]

In 2015, Michael Lisanti's team reported that they had studied cancer stem cells from a variety of cancers using some sophisticated genome sequencing tests that we won't detail here. What they were seeking was a common denominator, an Achilles heel that these many cancers shared. They had assessed cancer stem cells from multiple tumor types and, "… identified a conserved phenotypic weak point – a strict dependence on mitochondrial biogenesis for the clonal expansion and survival of cancer stem cells." Their analysis revealed that the mitochondria in stem cells are the weak link in cancer stem cell survival. Mitochondrial biogenesis, the process by which mitochondrial mass is increased within cells, is how cells adapt to increased energy demand.

Lisanti demonstrated that antibiotics that target mitochondria by inhibiting mitochondrial biogenesis, could eradicate cancer stem cells in multiple types of cancer; it is possible, in his words, "to treat cancer like an infectious disease." Lisanti's group published a list of drugs that could "eradicate cancer stem cells, in 12 different cancer cell lines, across 8 different tumor types (breast, DCIS, ovarian, prostate, lung, pancreatic, melanoma, and glioblastoma)."[3] (We may need to remind readers that in an evolutionary sense, mitochondria are descendants of bacteria and remain acutely sensitive to the antibiotics more often employed to inhibit bacterial growth.[4])

That same year these same researchers identified doxycycline as the preferred drug to use in targeting cancer stem cell mitochondria.[5] This is not a new drug; the FDA first approved it as a broad-spectrum antibiotic in 1967. The standard dose is 200 mg/day. It is now a cheap generic.

Doxycycline is sometimes used for infections in cancer patients and there are case reports of unexpected remissions, particularly with lymphoma, that are associated with doxycycline use.[6,7]

In April 2017 Zhang et al delineated doxycycline's action as inhibiting the transitional steps of stem cell phenotypes into breast cancer.[8]

It was in light of this knowledge that *in vitro* doxycycline can eradicate breast cancer stem cells that Lisanti's group performed a human pilot study that was published in 2018. They recruited

15 female patients with early breast cancer. Nine of these patients received doxycycline (200 mg per day, the standard dose for treating infection) for a 14-day period between initial breast biopsy and their eventual lumpectomy. Both groups were well-matched for age and other clinical characteristics.

Immuno-histochemical analysis of the tissue samples obtained during biopsy and post lumpectomy were performed on samples from each of the 15 patients, measuring biomarkers of "stemness" (CD44, ALDH1), mitochondria (TOMM20), cell proliferation (Ki67, p27), apoptosis (cleaved caspase-3), and neo-angiogenesis (CD31).

The lumpectomy tumor samples in those treated with doxycycline had a statistically significant decrease in the stemness marker CD44 (p-value < 0.005), compared to their pre-doxycycline tumor samples. More specifically, CD44 levels were reduced between 17.65 and 66.67%, in eight out of nine of the doxycycline treated patients. Overall, this represents a nearly 90% positive response rate. Similar significant results were seen with ALDH1, another marker of stemness.

In June 2017 this research took a turn that is of further interest to us: Lisanti's group reported, that *in vitro* research showed the impact of doxycycline is optimized by combining it with vitamin C and berberine. The breast cancer patients in their trial had received doxycycline alone. Vitamin C and berberine were not included. Doxycycline is so effective at suppressing cancer stem cell populations that it quickly selects and then synchronizes the surviving cancer cell populations to a "predominantly glycolytic phenotype, resulting in metabolic inflexibility." They identified, "… two natural products (vitamin C and berberine) and six clinically-approved drugs [atovaquone, irinotecan, sorafenib, niclosamide, chloroquine, and stiripentol] for metabolically targeting the doxycycline-resistant CSC population." This combination strategy eliminates surviving cancer stem cells providing, "a simple pragmatic solution to the possible development of doxycycline-resistance in cancer cells." Doxycycline not only works but does so better with the addition of vitamin C and berberine. [9]

These results suggest but they do not prove efficacy. The significant decrease in "stemness" observed is not proof that doxycycline will reduce risk of cancer recurrence or slow progression of advanced cancer. Yet, given the safety profile of doxycycline, it is tempting to jump to employ this treatment strategy before definitive evidence is published. We should note that an April 2019 publication suggests that adding azithromycin to the mix might further enhance the effectiveness of this combination.[10]

There are some obvious thoughts these publications suggest. Patients will, on occasion, "need" to take a course of doxycycline to treat infection. This 'habit' might be useful in that it eradicates developing cancer stem cells and could lower risk of recurrence. Obviously at this time, this idea is unproven. No one seems to have data on doxycycline use and eventual cancer occurrence. But if we assume that this might be helpful, simply adding vitamin C and berberine during their course of doxycycline might enhance any preventative effects. This is a stretch of course, but what would it hurt, especially if they are sick and already taking doxycycline? Since there is a reasonable argument that both vitamin C and berberine help fight infection, some might argue that the patient wouldn't even have to know why you suggest it. (That isn't how I think, but ….)

For patients at high risk for cancer, either primary or recurrence who are looking for ways to lower their risk, might we consider occasional prophylactic doxycycline? Down the road perhaps, once we have more evidence.

For those cancers we suspect are driven by cancer stem cells – glioblastoma and ovarian cancer come to mind – might taking these antibiotics when there is no evidence of disease, decrease cancer stem cell activity enough to change their risk of recurrence?

The fact that Lisanti's approach targets the mitochondria of cancer stem cells raises another question. In recent years some supplement vendors have promoted a treatment strategy that is the direct opposite of Lisanti's. Their thinking is that mitochondrial injury is responsible for cancer progression, and they have decided it is a good idea to prescribe a smorgasbord of supplements selected to repair mitochondrial injury and inhibit oxidative phosphorylation. One online advertisement from a well-known vendor states: "Studies on the nutraceuticals [sic] present…suggest various beneficial effects including enhancement of mitochondrial biogenesis…."

These two approaches, the one being researched by Lisanti and the one advertised in promoting these supplements, are in such direct opposition to one another that one might be justified in wondering how both theories can be true. We should think twice before we promote mitochondrial biogenesis in cancer patients, if doing so protects cancer stem cells and this is what Lisanti's research suggests. My thought is to take a pause and stall until we understand this better, ideally until clinical trials suggest whether either approach makes an appreciable difference in humans.

In an August 2019 paper, oxidative phosphorylation itself is identified as a potential therapeutic target for cancer therapy.[11] The idea to supply mitochondria with a buffet of nutrients that promote their activity sounds good in a general sense; but the more closely I consider this, the more nervous I find myself with the idea. Cancer often seems to have a malicious intelligence to it that defies our ability to predict its behavior; our assumptions have too often been proven wrong in clinical trials.

There is an urgency in working with cancer patients, a life or death immediacy to their disease, that inspires some practitioners to think and work outside normal standards of care. They and their patients will justify this by saying "We've got nothing to lose."

This is, in effect, experimenting with the patient. I will not find fault in that. I have had my own moments of desperation with patients. My concern is that in our eagerness to help, we may neglect the basics steps of experimentation that we were introduced to in basic science classes as undergraduates: the notebook, hypothesis, the tracking of results, the analysis and most importantly, reporting our findings to others.

Somehow as medicine has split into clinical and research tracks, many of us have forgotten that as naturopathic physicians we remain as much scientists as clinicians. When we experiment with patients (and much of what we do is experimental), we should be gathering data to see if what we did helped. Sadly,

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Curmudgeon's Corner

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our patient charts have been transformed into legal documents that justify insurance billing and provide protection against malpractice claims rather than effective tools to document and gather data on efficacy of treatments. Perhaps it is time that we reinvent ourselves and our charting habits. If we are going to experiment with patients, we should keep records, report and gather outcomes in a manner that allows meta-analysis that may further our knowledge. Is there a way to turn our electronic record keeping into laboratory records? Could each patient treatment be part of an experiment? If I choose a particular treatment for a specific condition, could the patient's outcome electronically be added to a virtual cohort? Surely, we can make this happen. One can name endless websites and apps that seem to do far more complicated things than following patients who might take some vitamin C and doxycycline and then track how long they remain cancer free.

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Women's Health Update

by Tori Hudson, ND
womanstime@aol.com

Additional Strategies to Reduce Cancer Risks

More Ways to Reduce Breast Cancer Risk

There are two recent studies that I want to call attention to, that are relevant for our continued efforts to reduce the risk of breast cancer. The first, by Teras et al, addresses the issue of weight loss. In post-menopausal middle-aged women who lose weight and actually are successful in keeping it off, their risk of breast cancer is lower. Researchers studied over 180,000 women who were 50 years old or older and had their weight recorded three times over about 10 years. (Wow, only 3 times!!!) The follow-up period for assessing invasive breast cancer started after the last weight measurement.

Over a period of eight years, more than 6,900 invasive breast cancers occurred. After the researchers adjusted for baseline body mass index, the use of hormone therapy or not, and other select issues, women who had lost 2.0-4.5 kg and were successful in keeping the pounds off, had a 13% lower risk for breast cancer compared to women who had no weight loss and had stable weight. Those who kept off 9 kg or more had even better results with a 26% reduction in risk (1 kg = 2.2 pounds). These benefits of weight loss and maintaining weight loss were strongest among overweight and obese women, meaning a body mass index of less than 25, and also among women with no history of using postmenopausal systemic hormone therapy.

Bottom line: If you are overweight and 50 or older, make every effort to lose weight a minimum of 4.5-10 lbs. and maintain that weight loss. Even better risk reduction occurs if you achieve 20 lb. weight loss and maintain that.

The second study, by Eberle et al, is likely more controversial as is common with environmental exposures and disease risk and incidence. In an observational study of approximately 47,000 women in the US, questionnaires about their use of hair care products was used to assess breast cancer risk. These women were followed over eight years. At entrance to the study, women did not have a history of breast cancer but did have at least one sister who had a breast cancer diagnosis. Over the course of follow-up, 2,800 breast cancers were reported; and after analysis, any use of permanent hair dye in the prior year was associated with a 9% increase in breast cancer risk, which is considered statistically significant. The risk was even greater for black women in the US, with an increased risk of 45%. Hair straighteners were less risky but did have an increased risk if they were used at least every five-to-eight weeks.

We know from other research that the chemicals found in human hair dye have been shown to cause mammary gland tumors in rats when those animals are exposed to those same chemicals. We also know that some hair straighteners contain formaldehyde, which is a known carcinogen.

These results on hair dye and hair straighteners are a part of a larger study called the Sister Study. The Sister Study is attempting to look at the causes of breast cancer and other health issues in women, including factors that affect quality of life and outcomes after a diagnosis of breast cancer.

These results on hair dye and hair straighteners are part of a larger study, called the Sister Study. The Sister Study is an ongoing study by scientists at the US National Institute of Environmental Health Sciences (NIEHS) that includes 50,884 women living in the United States and Puerto Rico. The women joined the study between 2003 and 2009. The women were between the ages of 35 and 74 when they joined the study, and none of the women had been diagnosed with breast cancer, but all had at least one sister who had been diagnosed. The Sister Study is looking at the causes of breast cancer and other health issues in women, as well as factors that influence quality of life and outcomes after a breast cancer diagnosis.

Bottom Line: Go au natural on the hair color and hair structure. Mother Nature is a beautiful thing!!!

Eberle CE, et al. . Hair dye and chemical straightener use and breast cancer risk in a large U.S. population of black and white women. *Int J Cancer*. [Online 4 December 2019].

Teras L, et al. Sustained weight loss and risk of breast cancer in women ≥50 years: a pooled analysis of prospective data. *JNCI.* 2019. (early release online)

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Breastfeeding and Endometrial Cancer

Breastfeeding exclusively decreases overall estrogen secretion, and this mechanism is one that may contribute to the lowered risk of ovarian and breast cancer. This relationship may also link to lowering the risk of endometrial cancer. To investigate this, researchers pooled data from 17 studies (3 cohort and 14 case-controlled), that totaled 8981 parous women with endometrial cancer and compared them to 17,241 controls. For women in both groups, about two-thirds of them reported histories of breastfeeding.

Having ever breastfed at all was associated with 11% lower risk for endometrial cancer. The lifetime cumulative breastfeeding of three months or less and the average breastfeeding duration per newborn of three or less months was not associated with this lower risk for endometrial cancer. However, an average duration of breastfeeding that was up to nine months was associated with a consistently decreasing risk.

Commentary: There is a robust list of the benefits of breastfeeding, including a lower risk for the child of gastroenteritis, respiratory illness, asthma, allergies, otitis media, and urinary tract infections. For women, breastfeeding lowers the risk of diabetes mellitus, breast, and ovarian cancer. We can now add to this list, that breastfeeding for greater than three months and at least up to nine months has a likely beneficial effect, although small, of lowering the risk of endometrial cancer.

Despite the increasing toxin load found in breast milk of women in the US, which is hugely bothersome, breast milk is still an optimal food because it contains unique oligosaccharides that promote healthy gut bacterial flora, including the proliferation of *Bifidobacterium infantis* species, as well as the antimicrobial agents lactoferrin and secretory IgA.

Jordan S, et al. Breastfeeding and endometrial cancer risk: An analysis from the Epidemiology of Endometrial Cancer Consortium. *Obstet Gynecol*. June 2017; 129:1059

Safety of Phytoestrogens on Breast or Endometrial Tissue in Menopause

Consumers, patients, and clinicians have long wrestled with the safety issues of phytoestrogens regarding the breast and uterine endometrium in particular. Phytoestrogens are used for both prevention and treatment strategies in areas of bone health, cardiovascular issues, bone density, hot flashes and more. Research has been debated regarding their effects on endometrial or breast tissues. The authors performed a systematic review (SR) and meta-analysis (MA) of existing published evidence.

An extensive search of electronic databases and literature sources identified 1070 records; 543 publications were removed due to duplicate titles and abstracts. Other articles were removed from the review and analysis due to screening criteria, which left 33 systematic reviews and meta-analysis publications. These 33 were randomized, placebo-controlled clinical trials (RCTs) in which peri- and/or postmenopausal women received phytoestrogens vs. placebo or phytoestrogens vs. hormone replacement therapy. These studies also included changes in endometrial thickness as measured by transvaginal ultrasound and/or breast density as measured by mammogram.

Within these 33 RCTs, there was a total of 4047 participants. Thirty reported on endometrial thickness (ET) and four on breast density (BD) and one study reported both. Of the endometrial thickness studies, 25 compared phytoestrogens with placebo; two studies compared phytoestrogens with hormone replacement therapy (HRT); and three with both. In three studies, the phytoestrogen metabolite equol was the active intervention. In one, white *kwao krua* (*Pueraria candollei* var. *mirifica*,) was the phytoestrogen source. Three studies used red clover (*Trifolium pratense*,). Two used lignans and 19 used isoflavones. In six of the latter, the soy isoflavones genistein and/or daidzein were used. All studies of breast density compared isoflavones to placebo. Doses ranged from 10 mg/d (equol) to 270 mg/d (lignans). Duration was from eight to 156 weeks. Of the endometrial thickness studies, five included peri- and postmenopausal women; the rest included postmenopausal women only. All of the breast density studies were in postmenopausal women.

In the meta-analysis of endometrial thickness studies that used placebo (n = 31), the effect of phytoestrogens was nonexistent or negligible when comparing to placebo. In one of the studies, ET increased with phytoestrogens; in three, it decreased; but in the others, there was no difference. When compared with HRT in five RCTs, phytoestrogens did not affect endometrial thickness. Body mass index (BMI) was a potential confounder of phytoestrogens' effect on ET; age and study duration were not confounders. The lower the BMI, the greater the increase in ET in the phytoestrogen groups. In four RCTs from the meta-analysis, phytoestrogens did not affect breast density compared to placebo in postmenopausal women or perimenopausal women.

Commentary: The results of this systematic review and meta-analysis should be reassuring to all, about the safety of phytoestrogens on endometrial thickness and breast density in peri- and postmenopausal women, at least in use for up to three years. There was a previous meta-analysis with different findings, but the difference is likely due to the inclusion of newer studies and correction of classification errors. There have been only a few RCTs that have assessed ET and BD with phytoestrogen supplementation, compared to many studies on their effectiveness and safety in treating menopause symptoms, especially hot flashes and night sweats. These studies vary greatly in the plants and formulations used, as well as the daily dose and duration of use. In addition, many had missing data. To further understand the safety and efficacy of phytoestrogens, there is a need for more RCTs and of longer duration.

Mareti E, et al. Effect of oral phytoestrogens on endometrial thickness and breast density in perimenopausal and postmenopausal women: a systematic review and meta-analysis. *Maturitas*. June 2019;124:81-88.

Do Oral Contraceptives Affect Risk for Breast Cancer?

The issue of whether or not oral birth control pills increase the risk of breast cancer has been confusing and contradictory for at least the last 20 years. It is certainly an ongoing concern in the minds of many women and clinicians. This recent prospective cohort study from the Denmark national data base attempted to determine if there was any association between use of hormonal contraception and risk for invasive breast cancer in women aged 15-49. Approximately 1.8 million women were followed for an average of 10.9 years from 1995-2012. In that period of time, 11,517 breast cancers were diagnosed. Most of the hormonal contraceptives were oral formulations and then secondarily, progestin IUDs. The relative risk for breast cancer in current or recent users of these products was compared to those women who never used hormonal contraception and found to be 1.20 with an absolute risk of 13 additional cases of breast cancer per 100,000 person years. Current or recent use of the progestin IUD was associated with a similar, 1.21 relative risk. Breast cancer was uncommon in women who used contraceptive implants or injections.

Commentary: The authors of this study adjusted the findings for many things, including duration of hormonal contraceptive use, age, education, parity, polycystic ovary syndrome, endometriosis and a family history of breast or ovarian cancer. What they did not adjust for was clinical breast examinations, screening mammograms and lactation history, all of which are considered potential issues that confound the results. In addition, it must be factored in that >80% of breast cancers are in women older than 49; and in the current analysis, they limited their age group to women between 15 and 49.

Researchers consider that a relative risk of less than 2 or 3 should not be interpreted as an indication of causation; so in this study, with the results of 1.21, it could not be concluded that current or recent use of hormonal contraception was the cause of their breast cancer.

In one of the definitive studies on this topic, conducted by the Centers for Disease Control and published in the *New England Journal of Medicine* in 2002, there was no suggestion of an excess risk for breast cancer with use of oral contraceptives.

The current study does indicate the possibility of a very small increase in risk; the best available data on this topic does shows that they do not have an impact on the risk of breast cancer. With increased understanding of numerous genes on breast cancer risk, not just BRCA genes, and an increased attention to the effect of environmental pollutants, it is likely that this is where we should be putting our attention. However, it may also be true that in women who take in particular oral contraceptives, these medications may provide some kind of fertile environment for an added negative influence from the genetic issues as well as environmental exposures, two areas that currently leave us asking more questions. In the meantime, there are numerous non-hormonal options for contraception, and pregnancy is a risky enterprise in and of itself, with medical risks that outpace the *possible*, very small increased relative risk of breast cancer from birth control pills.

And don't forget…there is good published scientific evidence that the following reduce our risk of breast cancer: exercise at least 3.5 hours per week; less alcohol – not more than seven drinks/week (some data says 0-3/week); avoiding excess weight/obesity. While the research is not as robust, there is also evidence that we can reduce our risk of breast cancer by eating a Mediterranean diet, getting more sunshine (adequate vitamin D levels), fish and/or fish oil supplements, higher fiber diets, olive oil, and green tea.

Morch L, et al. Contemporary hormonal contraception and the risk of breast cancer. *NEJM*. December 7, 2017; 377:2228
Hunter D. Oral contraceptives and the small increased risk of breast cancer. *NEJM*. December 7, 2017;377:2276

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the protocol, because of evidence that HCQ exerts its antiviral effect in part by stimulating the uptake of zinc into cells.

Negative Results in the US Veterans' Study

After the French study appeared, a retrospective chart review was conducted on US veterans who had been hospitalized with COVID-19. In those patients, the death rate was higher among those given HCQ than among those not given the drug. This study has frequently been cited to support the view that HCQ is ineffective and unsafe. However, it was not a randomized trial, and HCQ was only given to patients who were at the highest risk of having a poor outcome.[4] Furthermore, the findings from this study may not be relevant to the use of HCQ early in the course of the disease. Because it is an antiviral agent, HCQ may be most effective when used before complications have occurred. In the more advanced stages of COVID-19, treatments that suppress the cytokine storm may be more important than treatments that inhibit viral replication.

The *Lancet* Study and the Retraction

On May 22, *Lancet*, one of the most respected medical journals in the world, published an observational study of 96,032 patients who had been hospitalized with COVID-19 in 671 hospitals on six continents. Compared with the control group, patients treated with HCQ (with or without a macrolide) had a higher in-hospital mortality rate and a higher incidence of new-onset cardiac arrhythmias.[5] By the time this paper was published, HCQ was being widely used around the world for early treatment of COVID-19 and for prophylaxis in healthcare workers and others with high risk of exposure to the virus. The *Lancet* paper created great confusion because it stood in stark contrast to the positive results many clinicians were seeing.

It soon became apparent that the *Lancet* paper was plagued with serious problems. In an open letter to the authors of the study and to the editor of *Lance*t, 146 international researchers raised 10 different concerns about the study. For example, the data from Australia showed an implausibly large number of cases from just five hospitals, and the number of COVID-19 deaths reported from those hospitals was greater than the total number of COVID-19 deaths in all of Australia during the study period.[6] Another major concern was that the authors refused to identify any of the hospitals that contributed to the data set.

Further examination of the company that compiled the database of over 96,000 patients (Surgisphere; Chicago, IL) raised concerns that the research may be fraudulent. It seemed impossible that a company that no one had ever heard of and which had only a handful of employees (most of whom had no experience in data analysis) could have accomplished the task of coordinating complex data from hundreds of hospitals around the world in a very short time. An investigation of Surgisphere by the British newspaper, *The Guardian*, revealed a number of disturbing issues.[7] For example, *The Guardian* contacted seven hospitals in Australia whose cooperation would have been necessary for the database to have included the reported number of Australian COVID-19 patients. All of the hospitals stated that they had no involvement with such a database, and none of them had heard of Surgisphere. In addition, Surgisphere had almost no online presence. Until June 1, the "get in touch" link on Surgisphere's website redirected the reader to a WordPress template for a cryptocurrency website. This raised questions about how hospitals could have contacted the company to join its database.

Four authors were listed in the *Lancet* paper. One was Sapan Desai, the founder of Surgisphere, who was solely responsible for generating the data used in the study. After concerns were raised about the legitimacy of the data, the other three authors initiated an independent third-party peer review to examine the integrity of the research. The independent peer reviewers informed the three authors that Surgisphere would not provide the data that was needed to conduct the review, so the peer reviewers withdrew from the process. On June 4, just two weeks after the paper was published, the three authors asked *Lancet* to retract the paper, because they "can no longer vouch for the veracity of the primary data sources."[8]

Are Hydroxychloroquine and Azithromycin Effective?

At present, it is not possible to provide a definitive answer to that question. Several randomized controlled trials are in progress, and when these trials are completed we should have a better idea whether this treatment is effective for treating uncomplicated COVID-19 cases or preventing infection in people at high risk of exposure to the virus. Based on my review of the available data regarding safety and efficacy, I would strongly consider taking HCQ and azithromycin if the situation warranted.

Questions Raised by the Hydroxychloroquine Saga

There are a number of questions raised by the events surrounding the research on HCQ for COVID-19.

1. Why did *Lancet* to do such a poor vetting job on a paper that had such important implications for public health? Of note, the *New England Journal of Medicine* was also apparently scammed by Sapan Desai and Surgisphere. On June 4, that journal was forced to retract another paper on COVID-19, for which Surgisphere had supplied the data.
2. What has caused some portions of the media to become so biased that they allow political considerations to guide their views on a scientific issue? Early in the course of the pandemic, President Trump mentioned HCQ

as a potential "game changer" in the fight against COVID-19. Trump later announced that he was taking HCQ prophylactically after a few White House staff members had tested positive for the virus. What followed was a barrage of dueling narratives in the media, in which opinions about HCQ appeared to become a surrogate for opinions about the President. Media outlets that habitually opposed Trump tended to emphasize evidence that HCQ is ineffective and dangerous, whereas media outlets that typically supported the President tended to emphasize evidence that HCQ is effective and (if used properly) quite safe. A June 4 editorial in the *Wall Street Journal* rightly stated that HCQ "should rise or fall as a treatment on its medical merits, not whether people think it vindicates or repudiates Donald J. Trump."

3. What motivated Sapan Desai to perpetrate what appears to be a major fraud upon the world?
4. Why were official agencies so quick to interfere with clinical trials of HCQ and with the use of this medication by practicing physicians? After the *Lancet* paper was published, the World Health Organization halted their randomized controlled trial of HCQ, although they did resume the trial after the paper was retracted. France's public health agency warned against the use of HCQ outside of clinical trials, while around the same time French authorities suspended those clinical trials. Even before the *Lancet* paper was published, the US Food and Drug Administration (FDA) recommended that HCQ should only be taken in the hospital or as part of a formal study. That same recommendation appeared in the COVID-19 Treatment Guidelines of the National Institutes of Health (NIH). The advice against out-of-hospital use of HCQ is difficult to understand, considering that HCQ appears to be most effective when used before the disease has become severe enough to require hospitalization.

   Because of the negative press, the warnings against HCQ by government agencies, and the apparently fraudulent *Lancet* paper, many people are afraid to take HCQ. This has made it more difficult to enroll subjects in randomized controlled trials.
5. Is there a money trail to follow? The COVID-19 pandemic has presented an opportunity for the pharmaceutical industry to make enormous amounts of money on vaccines and patented drugs. Widespread acceptance of a regimen such as HCQ plus azithromycin (which costs a total of less than $20 for a course of treatment) could threaten the financial success of these other treatments. One drug currently being investigated is remdesivir. This intravenously administered drug, which is manufactured by Gilead Sciences, is likely to be very expensive if it gains FDA approval. According to one report, at least seven experts on the NIH panel that developed the COVID-19 Treatment Guidelines (which recommended against the use of HCQ) had financial ties to Gilead Sciences. The drug industry has a long history of using its financial clout to try to influence politicians, the FDA, the press, and medical researchers. While there is currently no evidence of a clandestine industry-sponsored campaign to discredit HCQ, one might be forgiven for wondering whether such a campaign exists.

Conclusion

The results of randomized controlled trials are eagerly awaited. If the results turn out to be as good or nearly as good as those observed by practitioners in Marseilles and elsewhere, an important advance will have been made and the need for lockdowns will be greatly diminished.

Note: Since this editorial was written, the National Institutes of Health has withdrawn funding for HCQ/COVID-19 studies. However, other randomized controlled trials are still in progress. Also, the FDA has revoked emergency approval to use HCQ for COVID-19, although FDA approval is not required for a physician to prescribe HCQ for "off label" use. Based on my evaluation of the current evidence, I believe the actions of the NIH and FDA are unwise.

Alan R. Gaby, MD

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COVID-19 and the Hydroxychloroquine Caper

As the United States and the world endured the trauma of a pandemic in the spring of 2020, a major controversy developed over whether hydroxychloroquine (HCQ) is useful for the prevention and treatment of COVID-19. HCQ has been widely used for more than 60 years to prevent and treat malaria and to treat several autoimmune conditions, including rheumatoid arthritis and systemic lupus erythematosus. This drug has also demonstrated an antiviral effect against COVID-19 *in vitro*.[1] Around 5.7 million prescriptions were written for HCQ in the US in the year 2017.[2] HCQ is manufactured by many generic-drug companies and it is very inexpensive, with a retail price of $10 or less for a full course of treatment against COVID-19.

HCQ can cause a number of side effects, the most serious of which include potentially life-threatening cardiac arrhythmias and rare cases of retinal toxicity. The risk of developing serious side effects appears to be related both to the dosage and to the duration of treatment. HCQ has a half-life of more than 40 days, which means that with prolonged daily use, the drug continues to build up in the body for many weeks before reaching a steady-state concentration. The short duration of treatment that is currently being recommended for COVID-19 (typically 5-10 days) results in a relatively low peak serum concentration and would therefore be expected to have a low incidence of side effects. Physicians who have been prescribing HCQ for COVID-19 (patients with contraindications are generally not offered the drug) have reported that serious side effects are essentially nonexistent.

The Positive French Study

Interest in the potential value of HCQ was sparked initially by an uncontrolled trial[3] conducted in Marseilles, France. The study included 1,061 individuals who had a positive polymerase chain reaction (PCR) test for COVID-19. These cases were identified from a massive PCR-screening program and included both symptomatic patients (n = 1,005) and asymptomatic contacts of confirmed cases (n = 56). Forty-four percent of the patients had radiological evidence of pneumonia at the time of presentation. All patients were prescribed the combination of HCQ (200 mg three times per day for 10 days) and azithromycin (a macrolide antibiotic; 500 mg on day 1 followed by 250 mg per day for 4 days). Azithromycin was included because of empirical evidence that HCQ is much more effective against COVID-19 if it is used in combination with this antibiotic. The median time between symptom onset and the start of treatment was six days. Patients who had contraindications (such as electrocardiographic evidence of a prolonged QT interval, which is a risk factor for HCQ-induced serious arrhythmias) were not given the treatment and were not included in the study. During the treatment period, drugs that can prolong the QT interval and potassium-depleting drugs used to treat hypertension were stopped. Good clinical outcomes and virological cures were seen within 10 days in 973 patients (91.7%). Eight patients (0.75%) died, all of whom were 74 years of age or older. Two additional patients (ages not specified) died after the paper was written. No arrhythmias attributable to the treatment were seen, and no patient had a prolongation of the QT interval beyond the threshold that would contraindicate treatment. The authors concluded that the administration of HCQ and azithromycin before complications occur is safe and is associated with a very low mortality rate in patients with COVID-19.

Other clinics that are using similar protocols have reported positive results similar to those in the French study. In some clinics, zinc is being added to

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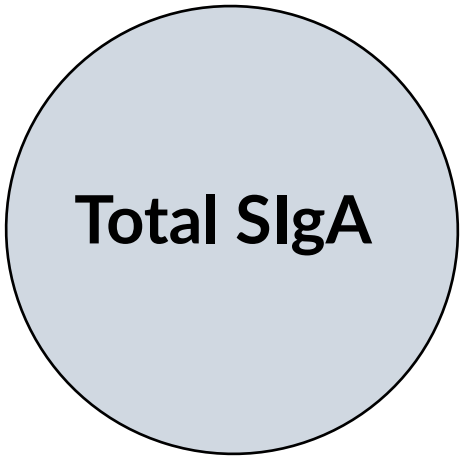

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TruGen3® continues the Lioon family legacy of three generations and more than a half-century of nutraceutical experience, with products produced under the highest ethical standards, available exclusively through Health Professionals. Contact us to find out how you can put our highly innovative products to work for your patients, and your practice, today.

Contact us today for FREE SAMPLES and to find out how you can put our innovative, one-of-a-kind products to work for your patients, and your practice, today.

† For a complete copy of the TruEase® Clinical Trial Study, visit trugen3.com/truease.

Get More with TruGen3®

Direct access to **Chief Clinical Advisor Dr. Chris D. Meletis** for answers to all your CBD questions

- **VESIsorb® Technology for up to 440% more** bioavailability than ordinary CBD products†. Many Turmeric components' (including curcuminoids) fat-soluble nature can make gastronomical absorption a challenge. The VESIsorb® delivery system minimizes these challenges, better supporting the body's natural inflammatory response, as well as joint, brain and immune health.*
- **Proprietary Super Critical CO^2 extraction process** eliminates solvents and impurities with non-detectible THC content at < 10pm.†
- Cannabinoid profile confirmed by 3rd party Certificate of Analysis

TruGen3®

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