

**FUNCTIONAL MEDICINE UPDATE**  
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**Clinical Trials on Nutrients: A Subject of Debate and Controversy**

Vitamin supplementation has broad public health implications. Studies have been conducted with the objective of evaluating long-term effects of supplementation on a range of diseases. In many cases, the results of these clinical studies indicate either neutral or no effect on health outcome. This trend has caused disillusionment among proponents of giving nutrients for the treatment or prevention of disease. Dr. Bland discusses two large-scale studies as examples. The first study by Slatore, Littman, Au, *et al*, and published in the *American Journal of Respiratory and Critical Medicine* in 2008, explored the association of supplemental multivitamins, vitamin C, vitamin E, and folate with incident lung cancer. This study involved a prospective cohort of 77,721 men and women aged 50-76 years from Washington State in the VITAL (VITamins And Lifestyle) study. At the conclusion of this study the researchers found that supplemental multivitamins, vitamin C, vitamin E, and folate were not associated with a decreased risk of lung cancer. Supplemental vitamin E was associated with a small increased risk, and it was advised that patients should be counseled against using these supplements to prevent lung cancer. The second study—also published in 2008—appeared in the *Journal of the American Medical Association* and was an evaluation of data from the Physicians' Health Study II randomized controlled trial. The objective of this study was to evaluate whether long-term vitamin E or vitamin C supplementation decreases the risk of major cardiovascular effects among men. Here again, the data provided no support for the prevention of cardiovascular disease. Dr. Bland acknowledges the strength of the data yielded by such large-scale trials, but also poses the question: are we sure there are not, buried within these large data sets, cohorts of individuals with genetic uniquenesses for whom the data has not been stratified? He suggests a bit if a conundrum exists as we start to study the responsiveness of specific nutrients in human populations with double-blind placebo-controlled randomized trials for all genotypes. REF #1-2

**A Conversation with Abram Hoffer, PhD, MD**

Dr. Bland discusses a recent visit with Dr. Abram Hoffer, the renowned psychiatrist who has also been called the father of orthomolecular medicine. Dr. Hoffer's 2005 book, *Adventures in Psychiatry*, recounts his journey from his Saskatchewan farm childhood, to his subsequent training in biochemistry and agricultural science, and his insights into the central importance to human and animal health of soil and plant food quality. Dr. Hoffer is perhaps best known for his pioneering work in the treatment of schizophrenia, which included the application and study of vitamin therapy. REF #3

Dr. Hoffer was a contemporary of Dr. Linus Pauling, who published a landmark paper on mental disease in *Science* magazine in 1968 that resulted in controversy about high-dose vitamin therapy. In the years following Dr. Pauling's article, a number of researchers challenged his hypotheses. Dr. Bland uses this history as a starting point for a discussion of recent publications, including a comprehensive 2008 review article authored by Dr.

Leonard John Hoffer titled “Vitamin Therapy in Schizophrenia.” In this article, Dr. LJ Hoffer advocates for “small, carefully conducted clinical trials of nutrient combinations in appropriately selected patients.” Dr. Balz Frei and Dr. Stephen Lawson, both of the Linus Pauling Institute at Oregon State University, also published a 2008 review article, this one titled “Vitamin C and Cancer Revisited.” Finally, Chen, et al, have—in recent years—published a series of studies on intravenous use of vitamin C therapy for cancer, all of which seem to indicate that continued assessment is justified. REF #4-14

### **A Study on Nutritional Supplementation in Stroke Rehabilitation**

Rounding out his discussion of clinical trials on nutrients, Dr. Bland focuses on a December 2008 paper published in *Neurology*. This study conducted by a group of researchers from the VA Medical Center in Oklahoma tested whether intensive nutritional supplements given to undernourished patients from the time of their admission to a specialized stroke rehabilitation service would improve patient outcomes. The analysis included the 90% of patients who completed the study (e.g., were not lost to follow-up due to acute or subacute hospitalization). These researchers concluded that intensive nutritional supplementation, using readily available commercial preparations, improves motor recovery in previously undernourished patients receiving intensive in-patient rehabilitation after stroke. REF #15

### **Therapeutic Lifestyle Changes: A Functional Strategy**

The concept of Therapeutic Lifestyle Changes (TLC) suggests that even modest behavioral lifestyle change reduces risk and improves quality of life. Change in dietary patterns is a central element of TLC. Some studies have shown that use of accessory types of nutritional support agents, such as the use of pre- and probiotics, has been found to have a favorable effect on gut immune function. Dr. Bland discusses a recent article that appeared in the *Journal of Clinical Gastroenterology* titled “Probiotics: Use in Allergic Disorders.” This group of researchers at the University of Finland is focusing on identification of specific strains with immunomodulatory potential, and on the question of how the food matrix and dietary content interact with the most efficacious probiotic strains or specific strain combinations. REF #16-17

### **Clinician/Researcher of the Month**

**Brian Berman, MD**  
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Dr. Brian Berman is Professor of Family Medicine and the founder and director of the University of Maryland Center for Integrative Medicine, the first center for research, education, and clinical care in complementary and integrative medicine based in a US academic health center. A family physician and pain management specialist, Dr. Berman’s practice of medicine includes a broad, integrative approach that encompasses complementary therapies and mind/body approaches.

Currently, Dr. Berman is principal investigator of two NIH-funded centers studying traditional Chinese medicine, one of which is an international center with colleagues in Hong Kong. He is the author of more than 200 peer-reviewed publications and seven books. On the national and international front, Dr. Berman has taken a leadership role in promoting integrative medicine, based on a firm evidence-based approach. He chaired the ad-hoc advisory committee to the NIH Office of Alternative Medicine when it opened in 1992, and he was first chair of the Consortium of Academic Health Centers for Integrative Medicine. Dr. Berman also co-founded and coordinates the complementary medicine field within the Cochrane Collaboration, and international organization dedicated to evaluating all medical practices through systematic reviews of the research literature. In 2005, Dr. Berman was the recipient of the Bravewell Leadership Award.

Dr. Bland and Dr. Berman discuss his distinguished career, publications, and insights. They also discuss the potential future of integrative medicine as the United States enters a new era of politics in which a focus on health care will play a central role. REF #18

### **Lead, Follow, or Get Out of the Way**

Dr. Bland concludes this issue with a discussion of an impactful article written by Dr. Ralph Snyderman (chancellor emeritus, Duke University) and Dr. Ziggy Yoediono (also of Duke University). This article is titled “Prospective Health Care and the Role of Academic Medicine: Lead, Follow, or Get Out of the Way.” The authors of this article contend that “the crisis facing the US health care system is in large part a consequence of that system’s disease-oriented, reactive, and sporadic approach to care.” And further, “...personalized, predictive, preventive, and participatory medicine—that is, prospective care—has been receiving increasing attention as a solution to the US health care crisis.” They believe that academic medicine has the opportunity and responsibility to play a role in the conception and development of better models to deliver health care. REF #19-20

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