July 1999 Issue | William Grant, PhD

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Welcome to *Functional Medicine Update*™ for July 1999. This month's focus is on understanding the relationships among diet, lifestyle, and disease, and whether those relationships are of clinical importance. We will focus on clinical specifics in the ecological approach to epidemiology. Our Clinician/Researcher of the Month, Dr. William Grant, will share his insights into this topic.

The Sixth International Symposium on Functional Medicine in May took place in Tucson, Arizona, with more than 500 professionals in attendance. The Symposium theme was "Disorders of Intercellular Mediators and Messengers: Their Relationship to Functional Illness." Assessing and intervening in health problems of dysfunctional intercellular communication will remain a leading-edge topic in medicine of the 21st century.

How do heart disease, cancer, arthritis, maturity-onset diabetes, and digestive disorders originate in the body? Throughout the past 70 years of medical education, practitioners—and through them their patients—have been taught that people are well until they are proven sick. This concept underlies the pathophysiological model of medical education and the practice of looking for the disease. The ICD9 codes were built on the supposition that one is well until proven sick.

In placing the emphasis on the diagnosis of disease, this model amplifies the importance of medical taxonomy. Even if you don't know where it came from or what it might mean, if you can define the disease and name it, the suggestion is that you know it. By this model mechanisms of the origin of a disease are less important than classification of the disease. Doctors are reinforced for memorization and recitation rather than for understanding how symptoms originate.

Practitioners who follow the prevailing philosophy often consider a patient's chronic illness and prescribe specific medication to treat the symptoms, as if monitoring, measuring, and managing symptoms is, in fact, managing the disease. Medications typically work by clocking specific biochemical/physiological processes associated with intercellular communication. Uncoupling (i.e., blocking) the intercellular message with a medication may in some cases be like "shooting the messenger." Uncoupling the message may relieve the symptoms while the underlying dysfunctional process continues, perhaps more severely. The result might be that the disorder "goes underground," resulting in disease progression and pathophysiology of greater proportion. An examples is pain medications that may manage the symptoms of arthritis but whose continued use may actually create their own dysfunction. The continued use of antibiotics to treat recurrent middle-ear infections in children may create other immunological sequelae that later produce their own dysfunctions. In the use of H2-blocking drugs to manage symptoms of *H. pylori* infection, the stealth organism may

One historical reason for this emphasis on diagnosis and pathophysiology is the lack of an acceptable mechanistic explanation for the origin or prevention of chronic disease. During the past decade, however, a rational, mechanistic formalism for both the origin and treatment of chronic disease has been emerging. This mechanism is rooted in understanding alterations in intercellular communication related to the onset of chronic symptoms that precede end-organ pathology. In addition to infection and trauma, lifestyle, diet, and environmental influences can modify genetic expression and alter intercellular messengers.

This understanding is the basis of my new consumer book, titled *Genetic Nutritioneering*, in which I describe the concept using specific examples. Research in this area has led to a new explanation for the origin of disease. By focusing on functional changes in health that occur as a consequence of altered intercellular communication, this process forms an information paradigm for the origin of chronic disease. That term originated in a landmark paper by Drs. Candice Pert and Michael Ruff, who discussed the nature of endorphin-binding sites and the immune and nervous systems cross-communicating through this informational paradigm concept.[1]

INTERVIEW TRANSCRIPT

Clinician of the Month:
William Grant, PhD

JB: This month's COM, Dr. William Grant, comes to us with a different background from that of many of our visiting clinicians. Dr. Grant earned a PhD in physics in the early 1970s at the University of California at Berkeley. He has been involved with laser remote sensing and atmospheric science, working with NASA/Langley. Thus he has a variety of skills in mathematics, computer modeling, and physics.

He also has a very deep interest in the environment, working in advocacy positions with the Sierra Club, and he has transferred his expertise recently into advocacy in the area of diet and chronic disease. To me, this approach signals where we're going in looking at data—applying ecological approaches to analyzing epidemiological information, leading to new insights and perspectives we may lose if we don't cut across disciplines. Dr. Grant, with his background and approach to problem-solving, gives us that cross-disciplinary perspective.

Dr. Grant, welcome to *FMU*. Tell us how the application of ecological analysis to epidemiological data can benefit clinicians.

WG: The ecological approach takes the disease condition or health condition of total populations and looks at what the total population is exposed to in terms of air pollution, diet, or environmental factors. While I originally applied this work to the study of air pollution effect on forests, I found the same approach was applicable to studying the effects of diet and chronic disease. I take mortality, incidence, or prevalence data by country, along with national dietary supply data. I try to match the statistics and find the dietary component or components that have the greatest statistical influence, or greatest correlation, with the disease I'm trying to explain.

JB: Let's take a specific example, the apoE genotype. As we have discussed in past issues of *FMU*, three

common apoE polymorphisms are found in human populations—apoE2, apoE3, and apoE4. We carry two alleles, one from our mother and one from our father, so we could be an apoE2/2, apoE2/3, apoE3/3, apo E3/4, or apoE4/4. In the association between apoE genotype and disease, statistically there have been suggestions that apoE4 genotypes, either single or double allele, are associated with increased incidence and risk of both Alzheimer's and heart disease.

Last year, in the *Journal of the American Medical Association* (1998;279(10):751-5), a paper by Tang et al. talked about the apoE4 allele and risk of Alzheimer's disease among African Americans, whites, and Hispanics. You wrote an insightful editorial in response to that paper. In it you explained that beyond the genetic factor of apoE genotype there are other environmental modifiers. In fact, Tang pointed out in his article, maybe the combination of a genotype with environmental modifiers gives rise to the expression of a disease. It's not just the determinism of the gene itself. Would you describe, using this apoE genotype example, how your model can provide different insight into reducing the risk of disease?

WG: My work on Alzheimer's disease was sparked by reading a paper by Ron White et al. reporting in 1996 that Japanese Americans in Hawaii had two-and-one-half times the Alzheimer's disease prevalence of native Japanese. Right away I thought that if genetics play a part, it's not really reflected in those data. Subsequently, I found that African Americans in Indianapolis have four times the Alzheimer's disease rate of Nigeria, again showing an environmental factor. And the primary environmental factor for most people is diet. I got the prevalence data from 11 countries and looked at the diet components about four years in advance of the study. I found amount of total fat had the highest correlation, closely followed by the total amount of calories.

When I used only the seven Western countries, I found that dietary fat, with monthly intervention with fish, gave the best set of all, but it was fish that reduced the prevalence of Alzheimer's disease, and fat that was the risk factor. This led to a hypothesis that the primary cause (if we can use the word "cause" in this context) of Alzheimer's disease is diet late in life. Diet causes inflammation because fat gives rise to a lot of the prostaglandin 2s, which cause inflammation. Fish oils, on the other hand, are known to give rise to prostaglandin 1 and/or 3, which reduce the amount of inflammation.

This conclusion was consistent with the other finding that people with rheumatoid arthritis, who were taking antiinflammatory drugs all the time, have much less risk of getting Alzheimer's disease. The apoE4 gene regulates, in part, the body's ability to handle serum lipids, and certainly those with more E4 will be more affected by dietary fat than those with E3 and E2. I think that's how the two are put together.

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