Integrative Medicine: Agriculture's New Opportunity

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In 1998, at the national meeting of the American Heart Association, former United States Surgeon General David Satcher, MD, noted that in the previous year our nation spent 425 billion medical-care dollars to treat chronic disease. However, the *per-capita* expenditure for chronic disease prevention was only $1.21 (SoRelle, 1998). A political realist, Satcher's proposed response for prevention then is our challenge now: Partnerships.

Who is included in those partnerships? Then-president of the American Heart Association Martha Hill, RN, PhD, noted that AHA partnerships working toward reduction of cardiovascular disease included the Centers for Disease Control, the Health Care Finance Administration, the Health Employers Data Information Set, the National Committee for Quality Assurance, the National Heart, Lung and Blood Institute as well as corporate partners in the pharmaceutical and medical device industry (SoRelle, 1998). Missing from this list was agriculture and the prepared-food industry, which is both surprising and tragic for many reasons.

I will address two surprisingly new understandings from the emerging field of integrative medicine that deserve to be highlighted. First, food is pharmacologically active. Second, food's pharmacologic activity is of significant public concern. I will use the documented pharmacologic activities of omega-3 polyunsaturated fatty acids to draw the conclusion that now is the time for medicine and agriculture to partner to positively affect public health.

Food as Medicine

There is no question that Hippocrates's injunction to consider food as medicine is supported by modern science. Cross-cultural epidemiologic studies of disease prevalence have revealed that risk factors for disease are, for the most part, culturally rather than genetically determined. For example, studies of Japanese

living outside of Japan demonstrated a two- to three-fold higher incidence of diabetes compared to age, sex and body-mass-index matched Japanese. (Hara *et al.*, 1994; Huang *et al.*, 1996; Robinson *et al.,* 1995). Likewise, the adoption of westernized diets appears to play a very significant role in the development of diabetes in Pima Indians (Williams *et al.*, 2001; Ravussin *et al.*, 1994).

There is no question that food fortification has played an important role in promoting public health. Agriculture and the prepared-food industry deserve much praise for their delivery of medically important therapies to the broad public. Successes include prevention of goiter with iodized salt; rickets with vitamin-D-fortified milk; beriberi, pellagra and anemia with B-vitamins and Fe-enriched cereals; and neural-tube defects with folic acid. (Darnton-Hill *et al.*, 2002)

Although the culture of medicine tends to dismiss the importance of dietary interventions in disease management and prevention, medical research has identified the potent role that dietary elements play, both in regulating gene expression and in modifying inflammatory responses. These major activities represent just some of the pharmacologic activities of foods. For this reason, dietary supplements and foods can be considered drug therapies. As noted by Rick Kingston of the University of Minnesota College of Pharmacy, drug therapies are "regulated and non-regulated substances or modalities that exert a pharmacologic or physiologic effect in the human body."

Insights on the positive pharmacologic properties of food have not been lost on practitioners of integrative medicine who prescribe dietary supplements responsibly both for disease prevention and for treatment. Nor have insights on the negative pharmacologic activities of food been lost on lawyers who are now equating "Big Food" with "Big Tobacco." This has garnered much media attention including a front-page article in the *New York Times* during this conference. *Newsweek* magazine's August 2002 article "Fighting 'Big Fat'" described the growing coalition of professionals targeting agriculture and the processed-food industry (Tyre, 2002). The impetus appears to be the skyrocketing rates of childhood obesity, hyperlipidemia, and type-2 diabetes mellitus.

These reports in the media reflect what might be called "the stick." However, there is a carrot. The positive spin is that agriculture and the prepared-food industry have an important window of opportunity to positively affect public health. There has been no better time in which to partner with medicine, and in particular with the integrative medicine community. The evidence base is strong enough to take a more proactive stance in partnering for the public's health. I will use the deficiency of omega-3 polyunsaturated fatty acids in the diets of North Americans and Europeans as an example.

Omega Fatty Acids

Fatty acids of the omega-3 and the omega-6 series are crucial components of cell membranes and are considered essential: humans cannot synthesize them,

only plants can. Neither can we interconvert them—our intake and the ratio of our intake of omega-3 and omega-6 fatty acids determines their content in our bodies. Truly, we are what we eat.

Their presence and the ratio of their presence in our cell membranes directs three functions important to health: gene expression, inflammatory responses, and intercellular communication. An imbalance in intake results in imbalanced physiologic functioning and markedly increased risk of disease.

In the past 30 years, North American and European diets have seen increased intake of omega-6 fatty acids. Vegetable oils rich in these include corn, grapeseed, safflower and sunflower at 60 to 70%, and soy, cottonseed and sesame at 45 to 50%. Increased use of cereal-based livestock production means that meats and many fish are now rich in omega-6 fatty acids. Processed foods rich in omega-6 include: infant formula, margarine, mayonnaise, salad dressings, crackers, cookies, prepared-dough products, snack foods, as well as meats and seafoods.

As meats and fish were traditionally our sources of omega-3 fatty acids, we have experienced an unprecedented shift in the balance of these two essential fatty acids. Omega-6 intake has skyrocketed and omega-3 intake has plummeted. What used to be a 2–4:1 balance has shifted to 10–25:1, as documented in breast milk and in serum (Sanders, 2000; Simopoulos, 2001). The scientific literature documents or supports that omega-3 deficiency, and the imbalance of omega-6 and omega-3 fatty acids, have important negative effects in:

- coronary artery disease,
- breast and other cancers,
- post-partum depression,
- major depression and bipolar disease,
- attention-deficit disorder,
- osteoporosis,
- inflammatory arthritis, and
- inflammatory bowel disease.

The mean current intake of omega-3 fatty acids in a typical North American diet is approximately 130 mg/day or about 0.15% of total dietary fat intake (Kris-Etherton *et al.*, 2000). The American Heart Association's 2000 guidelines recommended an omega-3 fatty acid intake of 900 mg/day based on the results of large intervention trials that demonstrated significant benefit at that level (Krauss *et al.*, 2000). This means that current intake of 130 mg/day is just 14% of the recommendation. Of note, the dietary intake of omega-3 fatty acids is about 14 g/day in Eskimos (Feskens *et al.*, 1993).

In this paper, I will share evidential data regarding the power of omega-3 fatty acids in cardiovascular disease. Given the interest of the American Heart Association and others in partnering for improved cardiovascular health, there clearly exist new opportunities for agriculture.

Omega-3 and Cardiovascular Disease

Mechanisms for cardioprotection from the omega-3 fatty acids include:

- reduction in malignant ventricular arythmias,
- inhibition of atherosclerosis,
- improved endothelial relaxation,
- lipid lowering, including reduction of both fasting and postprandial triglycerides, and
- antithrombotic effects, including reduced platelet reactivity.

The positive consequences of these actions have been reflected in a large number of studies from basic science to randomized controlled trials. Two significant articles were published just before this conference. Albert *et al*. (2002) used a nested, case-control analysis of apparently healthy men followed for 17 years in the Physicians Health Study. The fatty-acid composition of blood for 94 men in whom sudden cardiac death occurred as the first manifestation of cardiovascular disease was compared with that of 184 matched controls for age and smoking status. The authors documented that the base-line blood levels of omega-3 fatty acids were inversely related to the risk for sudden cardiac death both before and after adjustment for potential confounders. Compared to those in the lowest quartile of omega-3 blood levels, those in the highest had an adjusted relative risk of just 0.19 (95% CI: 0.05–0.71); the *P* for trend was 0.007. This is considered a very strong association with great statistical strength. This finding is consistent with the large volume of basic scientific research, and is also supported by other epidemiologic studies of primary prevention both in men and in women (Hu *et al*., 2002).

Critics will point out that even with a well established mechanism of action and supporting studies, correlation does not equal causality. Therefore, Bucher *et al*. (2002) reviewed all of the randomized controlled intervention trials that compared intake of omega-3 fatty acids with a control diet or placebo in patients with established coronary disease (secondary prevention): was there a positive causal effect? They identified eleven trials that included 7,951 patients in the intervention arm and 7,855 patients in the control groups. They documented that the risk ratio of a fatal myocardial infarction was significantly reduced at 0.7 (95% CI: 0.6–0.8, $P < 0.001$). In five trials, sudden cardiac death was associated with a risk ratio of just 0.7 (95% CI: 0.6–0.9, $P < 0.01$). Consistent with the multiple effects in other disease states noted above, including cancer, the risk ratio for overall mortality was also significantly reduced at 0.8 (95% CI: 0.7–0.9, $P < 0.01$) (Bucher *et al*., 2002).

In essence, omega-3 fatty acids appear to be both important and absent in our diet. And this represents just one natural product known and used by integrative medicine practitioners to positively effect health states. There are literally dozens more that should be of interest to agriculture and to the prepared-food industry.

Responsibility and Opportunity

In regard to the public's health, agriculture and the prepared-food industry have both a significant responsibility and a significant opportunity regarding the public's health. Sticks and carrots exist to promote innovations in health-promoting foods; I believe in carrots. And I believe in new partnerships to identify the best business- and best health-promoting opportunities. And, clearly, partnerships are also needed to transform public-opinion and consumer-purchasing patterns.

In summary, I hope I have conveyed two points: food is pharmacologically active, and this pharmacologic activity is of great public concern. I also hope that I have conveyed the importance of looking to the integrative medicine community for partnerships in new-product as well as market development. The University of Minnesota's Center for Spirituality and Healing plus the Center for Plants and Human Health represent two such potential partners with expertise and interest in effecting positive change in our nation's food supply.

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