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RESEARCH ARTICLE

Prevention and Treatment of Heart Disease with the Same Nutrition Protocol

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ABSTRACT

Addressing the effect of nutrition on heart disease requires a dialogue somewhat different from contemporary practice.

Heart disease is used here as a generic name for at least a dozen or more cardiovascular disease subtypes. Each subtype has its own identity, its own causes, its own pathology, its own biochemistry, and its own treatment protocols. Although disease specification certainly has advantages, it also has a shortcoming that is commonly overlooked. The more detailed this information is, the more difficult it is to comprehend prevention and treatment protocols that may benefit all heart disease subtypes.

Questions arise, for example, whether information specific for one disease subtype applies to other subtypes. This likely requires additional research, regulatory development, and health claims oversight. However effective this information may be, increasing disease fragmentation and specification nonetheless increases opportunities for confusion, both for the public and the practitioner.

Relying on specialized information, however, presents a serious dilemma for understanding nutrition, unless it is characterized by specific nutrients in food, specific mechanisms of action for each nutrient, and specific heart disease subtypes. This is reductionism, which is the popular but incorrect perspective on nutrition.

In contrast, wholist interpretation of nutrition refers to the combined biologic activities of countless nutrients when consumed as food, and countless metabolic activities for each nutrient, working in unison when the proper food is consumed. At the tissue level during metabolism, this dynamic is highly sensitive to change, and it does so very rapidly. Change simultaneously occurs with changing supply of nutrient substrate and changing demand of the tissues. The default position for nutrition, by definition, is that which optimizes health, prevents, and even reverses (treats) disease development. Numerous enzymatic and hormonal mechanisms, acting like transistor switches, are available to manage this extraordinary dynamic.

Oft cited evidence shows that nutrition, when properly understood and used, can control as much as 70-85% of the premature mortality caused by cardiovascular disease. This nutrition is ideally powered by whole foods from the plant kingdom, with nutrients acting wholistically in the body in a way to benefit all disease subtypes, even though effect size and outcome responses for each heart disease subtype may differ.

Introduction

The *aim* of this commentary is to describe the role of nutrition in heart disease. In doing so, it will consider nutrition as having a broad *scope* that applies 1) to disease prevention and treatment and 2) to varied subtypes of cardiovascular disease as well as to related chronic, degenerative diseases in general. Considering a common effect of nutrition requires transitioning from an assumption of reductionism to an assumption of wholism. This commentary extends an earlier paper(*1*) which proposed that dietary fat is not the main cause of heart disease that has been widely assumed but our virtually unquestioned belief in the nutritional necessity of consuming high quality animal protein that is the primary cause.

For background, I should note that I am neither a heart disease specialist nor a medical practitioner, but a biomedical researcher conducting studies (for well over six decades) on chronic degenerative diseases within the formal conventions of a) pharmacology, b) toxicology, c) chemical carcinogenesis, and d) nutrition. It is through these lenses that this commentary arises.

Pharmacology and toxicology associate with very specific cause-and-effect relationships that rely on qualitative and quantitative properties of individual chemicals and events, presumably acting independently. Chemical carcinogenesis relies on this same assumption but is specific for cancer, of course. This overriding assumption of reductionism is in sharp contrast to nutrition, which operates via an assumption of wholism ('w' intended), even though most investigators of nutrition assume otherwise, unfortunately. There are many ways to question nutritional reductionism, but one of the most informative is the observation that the biologic effects of nutrients consumed in food are not same as when consumed independently.

Cardiovascular disease is commonly described as a group of individual diseases. But for this discussion, they will be referred to collectively as 'heart disease'. Even though these diseases are understandably considered to have different etiologies and treatment modalities, nutrition, as I define it, is a generalizable effector for all these diseases. I know of no evidence, for example, that optimal nutrition for one disease subtype will differ in its direction of response for other subtypes, although effect sizes and symptoms vary.

The economic cost of heart disease, the leading cause of death in the U.S., is virtually incalculable, now said to be $320 billion annually in health care costs and worker productivity, as of 2017.(2) A number this large, however, tends to lose meaning and significance for the average person, especially when estimated costs determined by different studies will depend on the particulars of the populations studied. For this commentary, however, it is simply enough to know that this disease is a monumental problem urgently needing a solution.

On another perspective, this disease has caused tens, if not hundreds of millions of premature deaths during the past century, conservatively speaking. Furthermore, evidence shows that nutrition, when properly used, could have prevented a very large proportion of these premature deaths. A rough approximation of the number of avoidable deaths can be estimated by comparing the difference between highest and lowest disease mortality rates among countries, then estimating the proportion of these deaths attributed to nutritional practices. Similarly, this might be done by comparing populations over time as nutrition practices change. In both scenarios, evidence shows that a very large proportion of these diseases is controllable by nutritional practices, ranging from 70% to 85%, perhaps even higher.(3)

Let's set aside for the moment, however, whether it is 50%, 75%, or even higher, and simply agree that this proportion is unacceptably huge and that its solution is urgent. It is also important that this heart disease problem is only part of a still larger problem because the nutrition discussed here is similar for related diseases (cancers, diabetes, many autoimmune diseases), all of which contribute to an even more serious problem concerning the environmental crisis.

Heart Disease and Dietary Fat

My earlier commentary,(*1*) which questioned dietary fat as the main cause of degenerative diseases like cancer and heart disease, suggested that this focus on fat distracted us away from our long-held fascination with animal protein that could not be challenged. The emphasis on dietary fat included specific roles for cholesterol, total fat, saturated fat, polyunsaturated fat, and monosaturated fat, and circulating levels of fat-derived markers of disease risk (e.g., beta-lipoproteins, low density lipoproteins, high density lipoproteins, apolipoprotein, phospholipids, triglycerides, troponin proteins and various types of fatty acids).

Ancel Keys is one of the most memorable researchers on heart disease during the last century.(*4*) He was chiefly responsible for the initial interest in the Mediterranean diet during the 1950s and was generally accountable for our focus on fats, especially saturated fats, and their main source, animal-based foods.(*5*) However, rather than subsequent research investigating the disease-promoting effect of animal-based foods on heart disease, most research focused specifically on dietary fat. Saturated fat in the marketplace fell out of favor, and sales of its chief food sources of lard and butter plummeted. Polyunsaturated fats (as liquid oils), mostly found in plants and said to be healthy, were extracted and used as cooking oils and salad dressings. More recently called 'added fat', there is little or no evidence that this practice has improved heart health. In fact, polyunsaturated fats are more, not less, biochemically reactive than saturated fats because they generate reactive oxygen species (ROS) that promote aging, cancer, and other pathologies.(*6*) Good is bad and bad is good, thus creating serious confusion in the marketplace. Such confusion unquestionably has set back an understanding of the nutritional benefits of whole foods that contain these fats and oils, along with companion antioxidants to control their otherwise production of disease-producing ROS. Incidentally, Keys' research reputation may have been tarnished somewhat because late in his career, he pointed out that his original interest in the Mediterranean countries was their "mainly vegetarian" tendencies, obviously including whole foods. He also recommended use of "diet before resorting to drugs".(*7*)

Dilemma Of Partitioning Heart Disease

There are said to be 16 heart disease sub-types which are mainly considered as independent diseases (coronary heart disease, myocardial infarction, heart arrhythmia, rheumatic heart disease, congenital heart disease, valvular heart disease, aortic aneurysms, venous thrombosis, angina pectoris, stroke, atrial fibrillation, hypertensive heart disease, ischemic heart disease, peripheral heart disease, atherosclerosis, and arteriosclerosis). Sub-dividing a complex disease like heart disease into ever more refined subtypes is meant to refine and improve disease management, but it also increases the risk of "becoming too narrowly focused, too reductionist, less relevant and more confusing",(*1*) with each sub-type potentially involving 12 independent causes, and each cause independently acting via countless biological mechanisms.

Suddenly, this presents a maze of possible cause-and-effect relationships. Which fat does what to which heart disease subtype? Or, perhaps, which protein does what to which heart disease subtype? A maze like this minimizes and even obscures the possibility that there may be a comprehensive cause of disease like nutrition. But once again, this poses the same dilemma of knowing which nutrient does what to which heart disease subtype.

This now describes a complex, virtually hopeless environment for understanding food and health, making it very difficult to identify single causes (nutrients?) and single mechanisms that participate in disease causation and/or treatment with minimal side effects. Obviously, this is a source of unresolvable confusion that represses our understanding not only of heart disease but also of other diseases as well, especially chronic degenerative diseases like cancer, diabetes, and other metabolic related diseases

Reconstructing A Reality For Heart Disease

It seems safe to assume that most people want authentic and practical information on this very common disease, such as 1) what causes heart disease, and 2) how can this information be used to good effect? In popular conversation, the 'causes' of heart disease are high blood pressure, high serum cholesterol, smoking, inadequate exercise, diabetes, arterial plaque buildup, excess body weight, stress, lack of sleep, inadequate hydration, polluted air, and poor 'diet', yet again finding it necessary to partition our thoughts. Although correction of each of these causes can help prevent disease, it will almost always be a combination of causes that work best. No single cause will accomplish all. Investigating each cause in detail can, of course be helpful, but this generally comes at the expense of failing to see the whole.

Aside from partitioning heart disease into subtypes, most discussions also assume that the best evidence is that which is quantitatively and qualitatively specific, as if this is the best of science. This understanding of science relies on forming specific hypotheses, designing experiments to investigate very specific information while controlling for confounding, interpretating data using discriminating statistics having sharp boundaries for significance, then applying this information at the table and in the clinic in specific and quantitatively discreet ways.

Oversimplifying complexity by exclusively focusing on its parts runs a risk of not seeing the whole while

simultaneously leading to unexpected and undesirable consequences. It offers endless opportunities to focus on single agents such as considering nutrients as disease causes and pharmaceuticals as disease treatments. Commercializing these observations is made possible by intellectual property instruments (patents, trademarks, copyrights, licensing) that are further enhanced by minimally regulated public health claims.

Borrowing from a different literature, consider the case of beta-carotene and lung cancer. Initially, among heavy smokers, at high risk for heart disease, as beta carotene consumption increased, lung cancer decreased in a dose-response manner.(*8*) This finding led to an interest in testing beta-carotene, as a supplement, on smokers. In this second study, lung cancer again decreased as food beta-carotene increased, but on the contrary, lung cancer increased with supplement beta-carotene.(*9*) Since then, many studies have shown that a nutrient consumed in isolation may not behave like it does in food. Again, confusion is fostered. Good is bad, and bad is good.

Focusing on parts of the whole, that is, believing in the concept of reductionism, is widely accepted as the 'best of science'. This is a serious problem for understanding nutrition. Nutrition, in reality, is not the arithmetic sum of individual nutrient activities, but is a biologically integrated effect of countless nutrients and nutrient-like substances in whole food—all from the plant kingdom.(*10*)

Because this assertion is provocative for many, what is its evidence? In my laboratory, it came as an unusual revelation, albeit a companion degenerative disease. Initially, a series of experimental animal studies (rats, mice) had shown that modestly increased intake of animal protein quickly and substantially increased development of experimental liver cancer (hepatocarcinogenesis).(*10*) Disease development also could be rapidly reversed simply by decreasing animal protein intake. After replicating this finding several times, it became essential to determine its biological plausibility, especially in reference to its applicability for humans. Seeking a specific biochemical mechanism such as, for example, an enzyme-catalyzed reaction, is demanded within the reductionist perspective of pharmacologic dialogue.

In a series of experiments conducted over about a dozen years, increased protein intake altered the activities of ten candidate causal mechanisms, eight increasing and two decreasing their activities.(*10*) The increased activities represented innate mechanisms naturally favoring cancer development whereas the decreased activities were those naturally preventing cancer. Regardless of these differing directional changes, all led to the same outcome, with no exceptions, thus suggesting a remarkably unified response. It suggested the presence of a 'master control' mechanism, likely being hormonal, although it seemed difficult to visualize a control mechanism responding to a variety of factors, like nutrients. This phenomenon of apparent unity suggested a fundamental biological response existing throughout the body, becoming even more substantial if it describes mechanistic properties of countless other nutrients.(*10*) I call it 'wholism'. A network of complexity like this could help explain why nutrition provided by a diet of health promoting whole foods acts so comprehensively, having similar effects on different diseases and different stages of disease development, from prevention to treatment.

There is little doubt that the effect of nutrition on heart disease, conceptually speaking, is any different. Why would such an infinitely complex nutrition function like this not exist elsewhere in the body? If cholesterol and saturated fat are independently causing heart disease, consider the practical question how this disease could be controlled? Should consuming animal foods containing these nutrients be avoided? If so, this would mean consuming less 'high quality' protein, which has long been considered a vital nutrient for good health. For more than a century, researchers who dared to question this nutrient were ignored or chastised, however reliable their evidence may have been. Or should procedures be found to selectively remove the cholesterol and fat from this food? This would be impossible without destroying the reality of this food. Or should the cholesterol-containing food be eaten, then rely on using pharmaceuticals (statins and their side effects?) to treat the health problems that occur? Each of these choices arose from the hypothesis that cholesterol and saturated fat independently cause heart disease. In retrospect, this dilemma made little or no sense, if human health is the desired result.

In Defense of Nutrition

On a more positive note, what if the protein is not high quality as claimed for so long, thus refuting the justification for consuming this food? Consuming less animal-based food also means consuming more plant-based food containing countless nutrients widely known to decrease disease risk. In doing so,

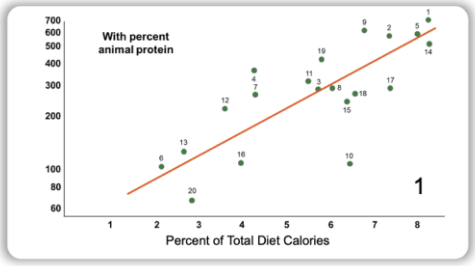
the wholist concept of nutrition would then apply to both food groups, simultaneously working to produce the same outcomes, namely, less disease.

The futility of this decades-long journey consuming large amounts of high quality protein is readily apparent when it now has been convincingly shown that consuming whole plant food reverses heart disease via wholist nutrition.(*11, 12*) These results were unusually impressive when, 10 years prior, laboratory animal studies had shown the same nutrition-induced disease reversal for experimental cancer.(*13*) Yet, ironically, the long-time belief that animal protein is 'high quality' is still very much part of normal conversation.

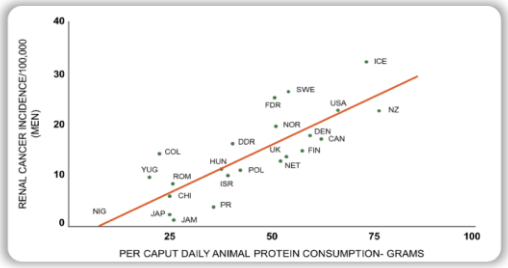
The following evidence therefore speaks more specifically to this tenacious belief.

First, as mentioned above, animal protein dramatically promotes chemical carcinogenesis, and it is biologically plausible, as demonstrated by the unified activities of multiple mechanisms.

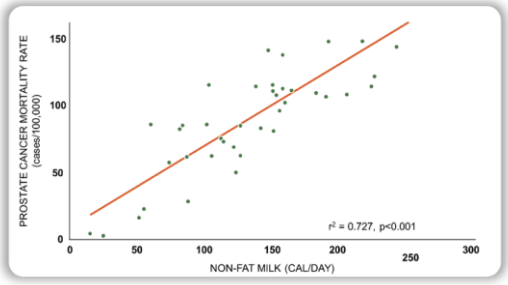
Second (Fig 1), when comparing countries, animal protein consumption is linearly correlated with coronary heart disease incidence and mortality.(*14*) In addition, the same linear correlations exist for other degenerative diseases, including renal cancer and animal protein intake,(*15*) prostate cancer and non-fat milk intake,(*16*) breast cancer and saturated fat intake,(*17*) heart disease and cholesterol intake,(*18*) colon cancer and meat intake,(*15*) and uterine cancer and total fat intake,(*15*) bone fracture and animal protein intake,(*19*) and bone fracture and calcium intake,(*20*) all intercepting at or very near the X,Y origin, suggesting that almost any amount of animal-based foods increase risk for multiple degenerative diseases. Note that heart disease mortality is listed twice, once for animal protein intake(*14*) and once for cholesterol intake(*18*) both exclusively present in animal food. Also note that bone fracture is listed twice, once with animal protein(*19*) and once with calcium intake(*20*) both provided by dairy. These decades-old findings by different research groups (1959-1999), have been undoubtedly ignored because of the then existing belief that individual diseases have individual causes, a concept that easily promotes confusion. These findings show a remarkably comprehensive animal protein/food effect on diseases, which are more common to economically affluent countries. Importantly, these various foods and nutrients are surrogate markers for animal protein effects.



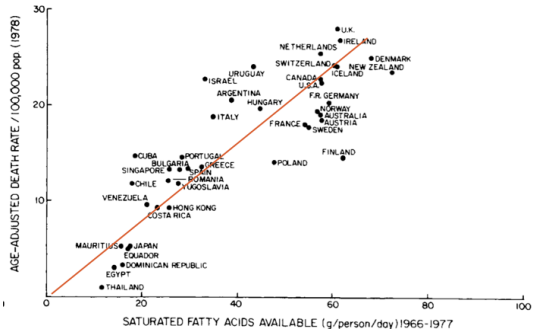
CHD Mortality(Y)—Animal Protein(X)



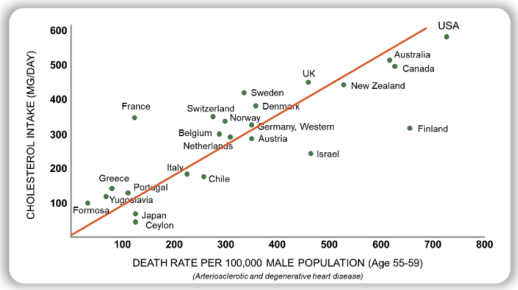
Kidney Cancer Incidence—Animal Protein



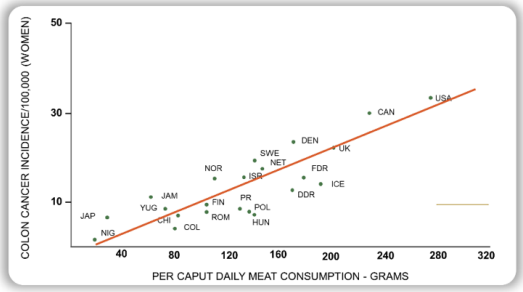
Prostate Cancer Mortality—Non-Fat Milk



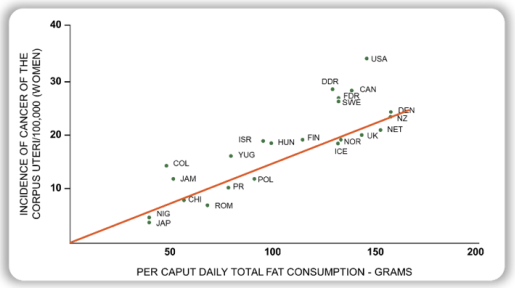
Breast Cancer Mortality—Saturated Fat



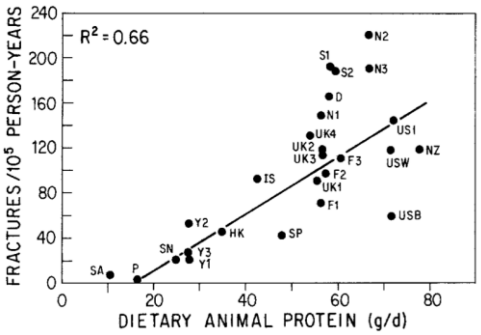
CHD Mortality(X)—Cholesterol Intake(Y)



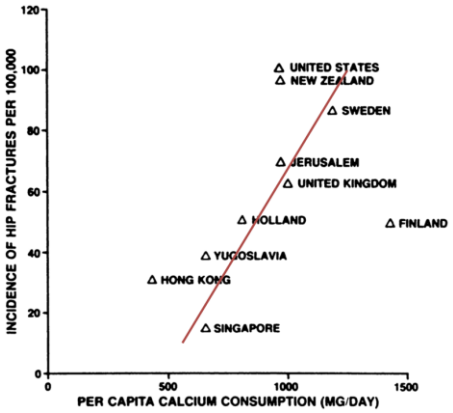
Colon Cancer Incidence—Meat Intake



Uterine Cancer—Total Fat Intake



Bone Fracture—Animal Protein (Women Over 50 yrs)



Bone Fracture—Calcium Intake

Figure 1. Diet and Disease Correlations. Screenshots of publications (1959-1999), reflecting associations of multiple chronic diseases with animal protein-based foods. Except for bone fracture and animal protein,(*19*) the regression lines were drawn simply to position them between an equal number of data points. No inference on linear or curvilinear associations can be determined, although there is little doubt that all are simply linear regressions.

For the more discriminating researchers, the common criticism that correlation does not infer causality does not have the same meaning here. This criticism is fair when a single causal agent is hypothesized. But in these studies (by different research groups), animal protein is not acting as a single agent. It indicates a diet high in animal foods and low in plant foods, whereby countless agents in both food groups cooperate to cause disease.

Third, in an unusually comprehensive observational study on diet, lifestyle, and disease mortality among 65 rural Chinese counties in 1983,(*21*) Western ' diseases of affluence' (cardiovascular, neoplastic, metabolic) localized geographically, suggesting a common etiology.(*22*) Comparing all 65 counties, serum cholesterol was highly correlated ($p<0.001$) with these Western diseases. This was striking because serum cholesterol was very low compared to Western experience (range of 94-

162 mg/dL and mean of 127 mg/dL for rural China, vs. range of 155-274 mg/dL and mean of 212 mg/dL for the U.S). This correlation within this very low range of serum cholesterol extends to the same correlation observed at a much higher range of serum cholesterol in the U.S., thus supporting the interpretation that disease risk begins to increase as soon as even small amounts of animal protein appear in the diet.

Fourth, additional affirmation of this animal protein effect was observed for hepatitis B virus and primary liver cancer in a second study in rural China in 1989.(*23*) Even though average animal protein intake in rural China was only about 10% of the U.S., it was within that low range of intake that serum cholesterol was directly correlated with chronic degenerative disease (including heart disease) mortality and active hepatitis B antigen (active virus), but inversely correlated with viral antibody (inactive virus)—all correlations were highly significant ($p<0.001$). These responses collectively indicated an unusual disease sensitivity to even small intakes of animal protein.(*24*) In a mouse model transgenic for hepatitis B virus, increasing animal protein increased cancer while depressing natural killer cell activity (now referred to as t cells).(*25*)

Fifth, the widely accepted impression that animal protein is "high quality" or has "high biological value", compared to plant protein, is emphatically false. A century ago,(*26*) the belief that animal protein provided superior health compared to plant protein was supposedly legitimized in laboratory rat studies by showing that a higher proportion of the consumed animal protein is retained in the animal rat body. This is to be expected because of the similarity of amino acid compositions of the fed protein and the rat body protein. The same applies to human body protein. But now it is clear that so-called high quality protein from animal sources also increases serum cholesterol and heart disease,(*27, 28*) insulin-like growth factor and cancer growth,(*29*) and other previously mentioned mechanisms that favor Western diseases. The mystique of 'high quality' animal protein, widely used in marketing, should be abolished.

Sixth, although not directly pertinent to heart disease etiology, it should be noted that animal protein, as casein, would be shown to be the most potent chemical carcinogen ever discovered, were it to be tested in the official bioassay test program for chemical carcinogens.(*30*) I mention this here to demonstrate, once again, how serious adverse effects of animal protein will be ignored, at any cost, so as not to question its alleged 'high quality' property which causes heart disease. In effect, many have believed in the claim that animal protein was unique in its high quality, thus had to be consumed. This is false because plant-based protein is able to supply all the protein needed for good health without causing the adverse effects existing for animal protein.

Seventh, over a century ago, research evidence impressively showed that intake of animal protein, not cholesterol, was the main cause of elevated serum cholesterol(*27*) and, furthermore, that switching from an animal protein diet to a plant protein diet improved physical conditioning.(*31, 32*)

Concluding Remarks

Two highly questionable belief systems have resisted constructive discussions on the etiology and clinical management of heart disease, in respect to food. One belief, a reductionist perspective, holds that individual nutrients like cholesterol and saturated fat—entirely or mainly in animal foods—are the chief causes of heart disease. But little could be done, food-wise, because animal-based protein was "high quality" and it needed to be consumed. Moreover, increases in serum cholesterol (especially low-density lipoprotein, LDL), thought to be the chief risk factor for heart disease, could be managed by pharmacologic means (statins). The second belief—a mirror image of the first—was the wholist perspective showing that consuming whole plant foods involving countless nutrients work together could decrease heart disease.(*11, 12*) Also, when animal food consumption decreases, plant food consumption increases, which further depresses disease occurrence.

The second belief system on wholism requires further comment because it opposes the common belief by almost everyone—public and professional—that nutrition, as provided by food, is the summation of the activities of individual nutrients in the food. That is, assigning causality to single nutrients operating independently contrasts with the very promising evidence showing countless nutrients in food work together in unison in a living system, as in cells, to create the health-giving nutritional effect. I don't suggest that it will ever be possible to determine the details of such a system because it will always be in a constant state of flux. I am inclined to describe it as an image of nature, always reacting, by default, to create human health and harmony, especially in the face of adversity. I am very much persuaded by the concept described by

Aristotle and others in ancient times, "The whole is greater than the sum of its parts".

This concept of wholism is even more inspiring when considering its reach beyond individual cells. Evidence clearly shows, for example, that cells communicate with each other, not only within their immediate environments, but beyond to distant parts of the body, where there are different cells and different organs performing different functions. Neural and hormonal systems exist throughout the body, and they are capable of instant messaging.

Some may consider these comments to be beyond the scope of the usual discussion of a link between nutrition and heart disease, which focuses on specific causes, specific mechanisms accounting for their activities, and specific disease outcomes. This is often said to be the best of science. In some ways, it is. But there is more. It is the forest that includes the trees, so to speak. Whatever shortcomings are perceived, however, consider this commentary as an attempt to broaden the discussion of the effect of nutrition on heart disease. This effect cannot be underestimated. Indeed, I suggest that heart disease is primarily a nutritional disorder.

One way to appreciate this dimension is to understand the comprehensive nature of nutrition function as well as the comprehensive nature of disease outcome. Nutrition involves countless nutrients, which, when they are part of the same food group, work in unison to produce the same effect. On outcome, the etiologies and treatment of degenerative diseases have much more in common than their separate anatomical and pathological identities may indicate. Thus, there is a need to investigate, understand, and compare these similarities, especially given the way nutrition works wholistically on different body systems. Such investigations can be very useful. For this author, there is no convincing evidence, for example, that optimum nutrition for one degenerative disease, in its directional effect, will be opposite that for another degenerative disease. Nature cannot work in this way, lest it self-destruct. The size and character of an effect will differ of course, but still there is little or no evidence showing that nutritional efficacy for one degenerative disease will be opposite that for another degenerative disease.

It is well-nigh time to consider moving past our myopic focus on independent causes, independent mechanisms of action, and independent disease outcomes as if this is the best of science or, more importantly, is the best for overall human health. Focusing only on the trees loses sight of the forest. It is abundantly clear that reductionist persuasion is good for commerce, but human lives are at stake and a huge existential environmental problem threatens the very existence of our planet as we know it. Colleagues in biomedical science and practice need to join their socioeconomic colleagues to collectively find ways to create a win-win solution for all, especially for all the public.

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