Untold Nutrition

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Nutrition is generally investigated, and findings interpreted, in reference to the activities of individual nutrients. Nutrient composition of foods, food labeling, food fortification, and nutrient recommendations are mostly founded on this assumption, a practice commonly known as reductionism. While such information on specifics is important and occasionally useful in practice, it ignores the coordinated, integrated and virtually symphonic nutrient activity (wholism) that occurs in vivo.

With reductionism providing the framework, public confusion abounds and huge monetary and social costs are incurred. Two examples are briefly presented to illustrate, the long time misunderstandings (1) about saturated and total fat as causes of cancer and heart disease and (2) the emergence of the nutrient supplement industry. A new definition of the science of nutrition is urgently needed.

Nutrition has long been viewed through the lens of reductionism, which focuses on parts instead of the whole. The vast majority of experimental studies have focused on individual nutrients, their structural identities, their mechanisms of action and their effects on specific outcomes. This strategy has served the purpose of sharpening the message about functions of individual nutrients but, far too often, these findings are not synthesized into a whole food context.

The activities of individual nutrients—often determined in laboratory (in vitro) experiments—are substantially modified upon consumption. Nutrients interact with each other and with other chemicals in food, both during intestinal digestion and absorption and after, during their metabolism and tissue distribution. Nutrient functions also vary with nutrient dose and their effects on specific outcomes. This strategy has served the purpose of sharpening the message about functions of individual nutrients but, far too often, these findings are not synthesized into a whole food context.

The first is the vitamin supplement industry, now running at $32 billion annually, according to a 2011 industry report (1). Its modern day history started in the mid-1980s after it got a marketing boost in 1976 with the Proxmire Amendment of the food and drug regulations. This legislation permitted food companies to sell vitamins and minerals without a doctor’s prescription (2). The industry also got a scientific boost from the publication of the 1982 National Academy of Science (NAS) report on Diet, Nutrition and Cancer (3) that set goals for using a lower fat diet (<30%) and the consumption of more fruits, vegetables, and grains based on their nutrient contents. Although this NAS expert committee based their goals in reference to the nutrient contents of foods, they explicitly cautioned that these goals applied to whole foods, not to the individual nutrients contained therein, as in nutrient supplements.

Still, the emerging vitamin supplement industry at that time ignored the warning and claimed otherwise, landing them in a 3-year administrative court hearing before the U.S. Federal Trade Commission. Being a witness on behalf of the NAS to those hearings, I saw firsthand the intense, well-funded effort by the industry to argue that the NAS goals referred to individual nutrients, thus supporting their efforts to develop nutrient supplements for the marketplace (4). Now, 20–30 years later, a large number of randomized clinical trials
have been undertaken to test the efficacy of these supplements and the results have been found wanting (5–9).

Summaries, which mostly represent meta-analyses of more than 100 trials and hundreds of thousands of experimental subjects, overwhelmingly show no long-term benefit for vitamin supplements, along with worrisome findings that certain vitamins may even increase disease occurrence for diabetes (5, 9), heart disease (6, 7), and cancer (7). Supplementation with omega-3 fats also was said to have no long-term benefits, even posing increased risk for diabetes (8, 9). More worrisome is the fact that these findings, first appearing more than 10 years ago, have had no discernible effect on their market. The public desire for quick fixes through pills (i.e., reductionism) is overwhelming, especially when money can be made. The activities of individual nutrients observed in carefully controlled research conditions will not necessarily be the same, at least quantitatively, when these nutrients are consumed in the form of whole food.

A second example of nutritional reductionism has a lifetime of many decades. Total dietary fat (as well as dietary cholesterol and saturated fat) has long been considered a major cause of cardiovascular disease (10, 11) and some cancers (12–14), culminating in major policy recommendations to reduce its intake (3, 15, 16). This conviction has had major implications far beyond what may be known to the casual observer. This story began about a century ago with experimental animal studies that mistakenly and mysteriously concluded that fat was a primary cause of these diseases. Some, but not all, of this early research, conducted by German and Russian scientists, certainly indicated that dietary fat elevated serum cholesterol and arteriosclerotic lesions [as reviewed by Kritchevsky (17)], but these findings were somewhat equivocal and inconsistent until the 1920s when it was shown that protein was a much more important cause of atherosclerosis than dietary fat (18–20). These 1920s studies also showed that serum cholesterol was not the cause of heart disease and, further, that dietary cholesterol had little or no effect on serum cholesterol (19).

Somewhat later, additional insight emerged when it was animal-protein [especially casein (21, 22) but also lactalbumin (23)] not plant-based protein that increased serum cholesterol and enhanced development of early heart disease. This casein effect was substantial, being about 5 times greater than the soy protein effect (21, 22). A substantial cholesterol-lowering effect of soy protein also was shown in human studies (24), and subsequently in still more human studies, as reviewed by a soy industry consultant (25). Eventually, this cholesterol-lowering effect of soy was judged to be an acceptable claim by the FDA in 1999 (26).

When it was shown that soy protein decreased serum cholesterol in rabbits by 70–80% (21, 22) [as reported by Kritchevsky (23)] and in humans by as much as 30–40% (27), it was called a cholesterol-lowering (hypercholesterolemic) effect by soy, a marketable idea. But this observation also could just as easily have been said to be a cholesterol-increasing (hypercholesterolemic) effect of animal protein (especially casein). In doing so, the soy protein effect would have been considered an indication of a natural, healthy condition promoted by plant proteins in general, whereas the casein effect would have indicated an unnatural, unhealthy condition. Therefore, during that history, it is animal protein that should have been labeled as the main cause of increased serum cholesterol and heart disease, not total fat, animal fat, and/or cholesterol.

A very similar story can be told for the association of dietary fat with cancer, especially cancers of the breast (28) and colon (29). Dietary fat as a cause of cancer became a leading hypothesis at a conference in Miami, Florida, and published in the November 1975 issue of Cancer Research. Also, the previously mentioned NAS 1982 report on diet, nutrition and cancer (3) suggested as their first-listed goal a reduction of dietary fat to 30% of total calories. Thereafter, several other public policy reports also made similar recommendations to decrease fat consumption (15, 30–32).

The association of fat with breast cancer in population-based studies was especially impressive (Fig. 1) (33). However, this oft-cited paper (33) also showed that this association of total dietary fat with breast cancer (Fig. 1A) was explained by the consumption of saturated fat (Fig. 1B) (typically found in animal-based foods), not polyunsaturated fat (Fig. 1C) (typically found in plant-based foods). Essentially the same dietary fat associations exist for colon and prostate cancers as well (34).

I find these opposing associations of animal and plant fat diets with breast cancer (Fig. 1A–1C) to be especially revealing. Animal fat—thus also total fat—is highly correlated with animal protein (r = 0.94), according to a large database on food and health for different countries (35). This impressive association therefore suggests that dietary animal protein could be an equally important cause of cancer, similar to the conclusion drawn for the association of animal protein with heart disease discussed above. And because chronic degenerative diseases typically common to Western industrially developed countries are substantially correlated with each other (29, 36, 37), this interpretation is likely to apply to these other diseases as well. An association of protein with cancer is consistent with experimental animal reports from the 1940s and 1950s showing animal protein to promote development of cancers of various sites (38–40).

Similarly, in a long series of laboratory animal experiments in my laboratory, the animal-based protein, casein, proved to be a powerful promoter of primary liver cancer initiated either by a powerful chemical carcinogen (41–48) or by a viral carcinogen (49, 50). Increasing dietary casein above recommended protein levels (~10% of diet calories) dramatically promotes tumor formation (~100% of experimental animals) (41), whereas switching to diets containing low dietary protein (~10% of diet calories) reverses cancer development (~0% of experimental animals) (42, 48). A series of many experiments
FIG. 1. Correlations of age-adjusted breast cancer mortality with total dietary fat (A), saturated fat (B) and polyunsaturated fat (C). Regressions are eyeball, based on authors findings that total fat (A) and saturated fat (B) were significantly correlated with breast cancer mortality while polyunsaturated fat (C) was not correlated. This figure is reprinted from Carroll et al. (33). From Carroll KK, Braden LM, Bell JA, and Kalamegham R: Fat and cancer. Cancer 58, 1818–1825, 1986. Copyright © 2006 by John Wiley Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc. (Continued)
on this protein effect illustrated a multimechanistic and highly integrated network of metabolic reactions converging to produce the outcome (42, 44, 51–59). This evidence is more than sufficient to qualify casein, when fed in excess of the recommended level of protein (i.e., the RDA equivalent) as the most significant chemical carcinogen ever identified (60) as important causes of human cancer should be abandoned.

In short, an important role for animal-based protein in cancer causation has long been overshadowed in favor of the false hypothesis that it was total fat and especially animal-based fat (mostly saturated fat) that causes these diseases (28, 33).

Searching for specific nutrients as independent causes of heart disease, cancer, and related diseases has been a routine assumption and practice of long standing, which causes more confusion than clarity. First, it is the combined, integrated effects of all nutrients that is far more relevant than the independent effects of individual nutrients. Second, in the examples cited here, although it is acceptable to choose a few nutrients as indicators of a total diet (as with antioxidants or dietary fiber indicating plant-based foods or saturated fat favoring animal-based foods), choosing saturated fat either as a primary causal factor or as an indicator of a high risk dietary pattern has proven to be very misleading.

It is not that fat or protein or other individual nutrients do not have independent and direct-acting properties that could contribute to increased or decreased disease risk. This is important information provided by reductionist research. But this information should not be used out of its context. It should be used to help explain the larger environment of which it is a part and to which it contributes.

Early during the history of heart disease, a choice was made in favor of fat instead of protein as a (or “the”) principle cause of this disease. This choice has survived for almost an entire century, becoming embedded in our collective consciousness. The correct choice should have been animal-based protein, not as a single nutrient causing heart disease or cancer but, more importantly, as a marker of a diet that causes these diseases.

This is a highly significant and relevant observation because diets ever richer in animal protein-based foods also are ever more deficient in plant-based foods. This exchange assumes, of course, that total food or calorie consumption is mostly a zero-sum game. Plant-based foods in the whole food form are far, far richer in antioxidants, complex (natural) carbohydrates, and vitamins while also having lower and more appropriate concentrations of protein and fat. This dietary pattern sets up a broad and worthy hypothesis involving very complex causes (e.g., plant-based foods) and outcomes that offer a frame of reference for interpreting detailed and
mechanistic findings of reductionist research. These detailed findings inform us of the biochemical properties of the participating nutrient parts, which either support or deny such a broad hypothesis, thus helping us to understand the healthful properties arising from the wholeness of food and dietary lifestyles.

I believe that focusing on the properties of isolated nutrients beyond their whole food context is more akin to pharmacology; considering whole foods containing countless nutrient-like substances that act within a natural context describes nutrition; and limiting our thinking to out-of-context parts considers only the threads of a tapestry, not the tapestry itself.

Trying to understand nutrition from a perspective of its parts as if they were acting independently explains why nutrition is so confusing for so many people, professionals included. Within this scenario, choosing which specific nutrients or nutrient combinations are responsible for hypothetical cause-effect relationships offers a long list of choices whose interpretative analyses are likely to be much more subjective. Without a biologically plausible context, we risk becoming entrapped in trying to understand the meaning of nutrient parts instead of the whole diet, or even the whole dietary lifestyle. Nutrition, if and when it is understood as a wholistic (spelling intended) phenomenon, only then can its real meaning be understood and applied.

REFERENCES