Searching for Values for Up and Coming Nutrients

Helaine R.H. Rockett
Channing Lab

The relationship between nutrition and disease is rapidly expanding. Today researchers are looking beyond traditional nutrients for causes of human disease. The common macro and micro nutrients appear to be answering only some of the questions surrounding of cardiovascular disease, cancer, and other chronic diseases of public health importance. Although there are probably multiple causes of these diseases, nutrition is still viewed as a major cause and needs to be continually reevaluated in new lights. The question that I pose today is "Are we missing the big picture - examining the trees but ignoring the forest."

Three possible "new" ways I would like to present today are

1- Examining individual foods as opposed to individual nutrients to represent the diet.

2- Looking at "new" dietary components such as boron and chromium .

3- Researching non nutritive additives and naturally occurring compounds in our food supply.

I. Examining Foods vs. Nutrients

Diet is different than other risk factors in human health, in that, we all eat. This exposure is not all or nothing but occurs in varying degrees. Everyone eats protein, carbohydrate, fat, vitamins, and minerals but in different amounts. Diet is also different from other epidemiological focuses in that changes in a person's diet usually do not occur at an exact moment but over a period of time.

As research nutritionists we tend to think of foods in our diets as the "holding tank" for specific amounts of protein, carbohydrate, fats, vitamins and minerals. A carrot is not thought of as a carrot but more as a good source of vitamin A or more specifically beta carotene. Looking at foods as chemical compounds comes naturally not only because of our chemical/biological background but also because the measurement of a specific nutrient in a diet can support a hypothesis with mathematical precision.

But when a researcher looks at a diet via "foods" instead of nutrients another avenue is opened to explore how our diet is associated with disease risk. An example of this is in Peto's research, which shows a relationship between high intakes of green

and yellow vegetables and a decreased rate of lung cancer. He hypothesized that beta carotene might protect the oxidation of DNA (Peto et al,1981).[1] Another example is when Graham, et al, (1978) found that cruciferous vegetables were protective against colon cancer, supporting Wattenberg and Loub's hypothesis that indole compounds are protective against cancer (Wattenberg & Loub,1978). A third example is a study of the Eskimos diet of fatty fish and low incidence of coronary heart disease led to the hypothesis that omega 3 fatty acids are involved in preventing the formation of thromboxane, necessary for thrombus formation (Lands,1986)![1]

Diets are made up of whole foods not simply isolated nutrients. Mertz commented that foods are not completely represented when you look at only their nutritive composition.[5] Foods that have similar nutrient composition such as milk and yogurt can behave quite differently when consumed.

Foods are chemical mixtures with complex relationships that can enhance certain nutrients but antagonize the bioavailability of other nutrients. "It is certain that there are interactions between nutrients such that the presence of one nutrient at a given level can influence the action, availability or requirement of another nutrient."[2] We all know examples of this - vitamin C with vitamin E or iron. "The failure of studies to determine the level of both factors (foods as well as nutrients) limits the interpretability of individual studies, limits the ability to resolve apparent discrepancies in results between different studies, and may hamper sensible public health policy".[2]

Two examples of looking at foods as well as nutrients are Le Marchand, et al, study of Vegetable and Fruit Consumption in Relation to Prostate Cancer Risk in Hawaii; and Hankinson, et al, recent study of Nutrient Intake and Cataract Surgery in Women.

The initial study of Hawaiian Prostate Cancer was a case control study of 452 prostate cancer cases and 899 population controls during the time period of 1970 to 1983. The original analysis showed a positive association of risk of prostate cancer and the intake of beta carotene. This flew in the face of all current studies finding beta carotene as a nutrient preventing cancer. Several years later, the authors reexamined the data specifically looking at vegetables and fruits and found "With the exception of papaya, which was positively associated with risk among men aged 70 years and older, consumption of other yellow-orange fruits and vegetables, tomatoes, dark green vegetables and cruciferous vegetables was not associated with prostate cancer risk".[3]

The second study I refer to is a recent analysis from the Nurses Health Study. From 1980 to 1988, Hankinson and co-workers examined prospectively the relationship of diet(specifically vitamins C, E, carotene and riboflavin) to cataract extraction in 50,828 women. Carotene and vitamin A were inversely associated with

the disease. Women in the highest quintile of vitamin A intake had a 40% lower risk of having cataract surgery compared to the lowest quintile. Riboflavin as well as dietary vitamins C and E had no association with cataracts. There was an inverse relationship seen with long term supplemental intake of vitamin C but not with multivitamins. When they examined foods as well as nutrients they found no association with carrots (the highest source of beta carotene) but rather spinach was the food "most consistently associated with a lower relative risk."[4] " This may indicate that a carotenoid other than beta carotene is influencing risk. For example, spinach is high in lutein and zeaxanthin while carrots are low in these carotenoids. Whether these carotenoids or other nutrients in these foods are associated with cataracts is currently speculative."[4]

II. Looking at New Dietary Components

When studying diets via foods as well as nutrients we also target "future" dietary components that are not now popular, well assessed, or discovered. One element whose popularity has waxed and waned is chromium.

In 1969 Mertz and in 1970 Shroeder both were studying chromium. According to Mertz chromium deficiency in rats and monkeys produced impaired glucose tolerance, increased serum cholesterol, elevated blood sugar, sugar in the urine, increased growth of vascular fibrous plaque, decreased growth and decreased longevity. Chromium given as supplements reversed these conditions. The symptoms described above are very similar to adult onset diabetes mellitus in humans.

Anderson in 1981 found that countries with higher chromium intakes also had low rates of coronary heart disease (CHD). Another study compared chromium levels in hair and found they were inversely related to coronary heart disease(Cote et al., 1979). Levine(1968), Schroeder(1970), Riales and Abrink(1981) and Anderson(1983), all hypothesized that chromium reduces CHD risk by improving glucose tolerance, decreasing blood cholesterol levels, and raising HDL levels.

Guthrie in 1982 reviewed all the data on chromium and found a large range of discrepancies in values from around the world including from many reputable labs. He found that the reason for such discrepancies was due first to the ease of contamination with stainless steel. The second problem was that prior to 1978 the machines used to measure chromium were not sensitive enough to measure low levels of chromium. Chromium is measured as nanogram. A nanogram is one billionth of a gram or one millionth of a milligram.

Although measuring chromium has been a problem; an alternative method of studying the effects of chromium is to use it as a supplement. Studies that have given supplemental chromium to mild non insulin dependent diabetics have found an improvement in their glucose tolerance(Nath,1979, Offenbacher and Pi-Sunyer,1988).

Another food component that could deserve more research is boron. Boron is also an element that is difficult to measure accurately. As Hunt et al., reported there are three sources for variable intake :

1- concentration of boron in water and water based beverages
2- individual variety in choosing their diets- fruit and vegetables being especially high in boron
3- use of many personal care products - analgesics, antibiotics, antiseptics, decongestants,etc

Hunt and Nielsen have studied boron in animals since 1981 and found a relationship between boron and cholecalciferol. "Depressed growth and abnormal bone development were more marked in boron-deprived chicks fed a cholecalciferol-deficient diet than in those fed a cholecalciferol luxuriant diet."

Nielsen, et al, also found that when boron was given as a supplement (3 mg per day) to postmenopausal women, it decreased the amount of urinary calcium and magnesium. This seemed more marked in the women who were consuming a low magnesium diet. "These findings suggest that supplementation of a low boron diet with an amount of boron commonly found in diets high in fruits and vegetables induces changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization."[8]

III. Non Nutritive Additives and Naturally Occurring Compounds

Finally I wish to speak of non nutritive additives and naturally occurring compounds in our food supply. Many people feel that "no human diet can be entirely free from mutagens or agents that can be carcinogenic...".[11] Estimates of 10 to 70% of cancers in the United States may be caused by the food we eat.

Ames, et al, looked at naturally occurring carcinogenic compounds in our food supply. He assigned a HERP (Human Exposure Dose/ Rodent Potency) index to these foods and drinks to express animal tested carcinogens in human terms. It is not a direct relationship to human risk.

He examined contaminated well water (including Santa Clara (Silicon) Valley, California and Woburn, Massachusetts) to ordinary tap water. Only two of the 35 wells shut down in Silicon Valley had greater HERP values than tap water examined. The well water was not chlorinated thus did not have chloroform that is found in tap water. "Water from the most polluted well(HERP=.004% per liter of trichloroethylene) ...has HERP value orders of magnitude less than for the carcinogens in an equal volume of cola, beer, or wine".[11] And the HERP is much lower than "natural" foods such as a peanut butter sandwich.

Ames also looked at natural pesticides and chemicals, finding we consume at least "10,000 times more by weight of natural pesticides than of man made pesticide residues".[11] These natural chemicals protect plants from insects, fungi, and animals. They make up "5-10% of the plant's dry weight."[11] Many have been found to be carcinogenic. Examples of these are:

Psoralen- light activated carcinogens in celery- can cause occupational disease for celery pickers as well as produce checkers in supermarkets.

Molds - produce mycotoxins -"common pollutants of human foods particularly in the tropics" - one potent rodent carcinogen is aflatoxin. Aflatoxin is found in wheat, corn, nuts - specifically peanut butter.

Urethane- formed during a variety of fermentations has carcinogenic qualities. This is found in Japanese Sake wine as well as beer, yogurt, and bread.

Formaldehyde- found in many foods also considered carcinogenic. Shrimp, bread, cola and beer all contain levels of formaldehyde.

The purpose of looking at these natural carcinogens is not to discover that we can't eat anything but that there are natural substances in our foods that may not be benign and need to be considered when studying the human diet.

Now that I have presented nature's negative side, there is a growing faction of scientists that are looking at the positive side. On the surface research indicates that with all these carcinogens found naturally in our foods we should all be dead at 25! But nature must have chemopreventive compounds that are keeping us alive and it is here that more research is needed.

I have mentioned some prominent chemopreventive nutrients - Vitamin A and its many components but scientists are looking for other anticarcinogenic agents particularly in fruits and vegetables. It has been seen in many studies that the "consumption of higher levels of vegetables and fruit is associated consistently, although not universally, with a reduced risk of cancer at most sites, and particularly with the epithelial cancers of the alimentary and respiratory tracts".[14]

Preventive compounds in our foods can do one of four things to break the chain of a procarcinogen going to a proximate carcinogen and finally to the ultimate carcinogen:

1- initial prevention of the forming or absorbing of a carcinogen
2- modify the transformation into a carcinogen
3- accelerate the excretion or watering down of a carcinogen
4- finally, block any carcinogenic action once the carcinogen is formed.

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There are several non-nutritive compounds being studied for there anticarcinogenic properties. The following ones seem to be the ones in the forefront of research at this time: indoles, flavonoids, phenols, protease inhibitors and isoflavonoids.

"Indoles are formed through the hydrolysis of glucobrassin." [14] Glucobrassin is a glucosinolate and is found in the cruciferous vegetables. Indoles are formed when plant cells are damaged and an enzyme, myrosinase, mixes with the glucobrassicin. "The effects of indoles may be related to this increase enzyme activity."[14]

Flavonoids are benzopyrene derivatives widespread through plants because they are involved in the photosynthesis. "Flavonoids have antioxidant properties dependent on the degree of hydroxylation of the benzene ring".[14] Examples of flavonoids are quercetin, kaempferol, myricetin and chrysin.

Phenols are usually found in foods as glycosides. Some very common phenolic compounds are coumarin, caffeic, ferulic and ellagic acids. Scientists believe the anticarcinogenic properties of phenols are involved in the "induction of detoxication systems".[14]

Protease inhibitors are usually large proteins involved in inhibiting proteases. The Bowman-Birk type is currently being investigated for its anticarcinogen qualities. Some possible mechanisms are invading neoplasms, suppress the expression of neoplasia and tumor inhibition. Protease inhibitors are throughout the plant kingdom with seeds and legumes being especially rich sources.

Isoflavones have also been seen as potential anticarcinogenic compounds. Soybeans are particularly rich in isoflavones. The mechanism that may be cancer preventive is its involvement with estrogen. This may hold a key to the hormone dependent cancers.

Nutrition and its study as you can see is exploding into new areas of study as well as new ways of studying it. Our future is to look at the bigger picture - whole foods which are made up of a combination of nutritive and non nutritive components.

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