Eat your broccoli (and brussels sprouts)

Masses of circumstantial data link diet and disease, including a new report about a chemical in broccoli that detoxifies carcinogens *in vitro*, but it remains the case that very little is really known about food as medicine

THE idea that health is related directly to diet is an appealing one. If you just eat right dread disease can be kept at bay. Particularly in the United States where, during the past decade both the federal government and private scientific organizations such as the National Academy of Sciences have become powerful advocates of a 'healthy diet', eating right is associated with 'take charge' type of people who are in control of their lives, and therefore their bodies.

Take charge people eat oat bran, and lots of cruciform vegetables — like broccoli. They do not get cancer.

Studies too numerous to count, published in journals refereed and not, point to a link between diet and various forms of disease. The high-fat diets characteristic of Western nations are blamed for heart disease and cancer that, in incidence, is greater than that among peoples whose diets are rich in grains and vegetables. The official word from the Food and Nutrition Board of the Academy's Institute of Medicine is this: eat five or more servings of vegetables and fruits daily, especially green and yellow vegetables and citrus fruits. The advice is repeated on television by spokesmen for grocery store chains.

Fibre is important too. Last year, oat bran was 'in'. Now, thanks to a recent report in the March *Proceedings of the National Academy of Sciences* (**89**, 2394-2403), broccoli is in vogue. Broccoli contains a chemical called sulforaphane, first synthesized in 1948, that appears to be a potent inducer of an enzyme that detoxifies carcinogens in mouse hepatoma cells.

Paul Talalay and his colleagues at The Johns Hopkins University School of Medicine reported in *PNAS* the development of a test for the 'rapid detection of inducers of enzymes that protect against carcinogens.' Specifically, they measure an agent's capacity to stimulate quinone reductase in murine hepatoma cells grown in microlitre plate wells, and began with an analysis of various components of broccoli because of the many epidemiological studies that suggest that people who eat broccoli tend not to get cancer. Talalay says he chose it also because broccoli is widely consumed in the United States, despite George Bush's famous declaration that now that he is President he does not have to eat his broccoli anymore.

Talalay's rapid assay was developed with several premises in mind. First, that 'dietary composition is a major determinant of cancer risk in humans and experimental animals'. Second, that the 'consumption of vegetables, especially crucifers, reduces the risk of developing cancer'. And, third, that malignancy is regulated by so-called phase I enzymes that activate carcinogens and by phase II enzymes that detoxify them.

Focusing attention on chemicals in food that appear to detoxify carcinogens (rather than on carcinogens or mutagens that have been well-studied), Talalay and his colleagues report that their test turned up a number of anticancer substances, of which sulforaphane is the most potent. Peppers, potatoes and tomatoes appear to be low inducers of anticancer activity, whereas some vegetables (red leaf lettuce, beets, bok choi and cauliflower among them) actually showed some capacity for cytotoxicity. 'Cytotoxicity measurements are important,' Talalay writes, 'because phase II enzyme inducers may be toxic and/or carcinogenic.'

What are we to make of all this? Not much if you are thinking about dinner. The Talalay data, if they hold up in further experiments, represent a potentially useful step in the direction of sorting out the connection between food and disease at the level of cellular mechanism. A test for naturally occurring agents that may exert a protective effect could be useful in the long run in the development of medically useful drugs. In any case, efforts to distinguish fact from wishful thinking in the diet and cancer business are commendable.

But, contrary to enthusiastic press reports, it is premature (to put it mildly) to suggest that the broccoli-haters of the world have a duty to consume the stuff in the name of a long and healthy life. In fact, as others have noted before, taking all the data about health and disease and adding them together, still does not make the case that the average person (with no known genetic predisposition and no present disease) can prevent cancer by eating 'right'.

This is not an endorsement of a diet of greasy hamburgers and cotton candy. Rather, it is simply another occasion to consider the complex issues of doing science, estimating risk, and then communicating that risk to the public in an arena in which people are able to make individual choices (as opposed, for instance, to such global cases of potential risk as Chernobyl or global warming).

Even a brief review of past cases shows the risks of simplifying risk prevention. Beta carotene, a precursor of vitamin A, is thought to be an anticancer compound on the basis of data from dietary questionnaires and from some animal studies. In a clinical trial of 1,805 patients with nonmelanoma skin cancer, however, beta carotene failed to reduce the incidence of new cancers (*The New England Journal of Medicine* **323**, 789–795; 1990). An article in the same issue of *NEJM* (795–801) reported that clinical trials of 13-*cis*-retinonic acid failed to prevent recurrences of original tumours of the head and neck but did appear to prevent the development of new or 'second primary' tumours. Tests did not confirm expectations.

Then there is the unhelpful biological complication that Talalay himself referred to: some agents that induce anticancer enzymes may also be toxic. This phenomenon of the double-edged sword is a frequent impediment to clean data in cancer metabolism and pharmacology.

Animal biology presents another reason for caution. Despite diligent efforts of hundreds of scientists, it is not yet entirely clear why an agent that is carcinogenic in one animal is safe in another. Penicillin injected into the veins of a rat causes sarcoma. Alcohol is a carcinogen in humans but not in rodents. Crystalline silica causes lung tumours in rats but not in mice. Most people who get lung cancer smoke, but most people who smoke do not get lung cancer.

In short, when it comes to nutrition and disease, ignorance exceeds knowledge and a little knowledge, while scientifically valuable, cannot be readily translated into a menu for health. What is needed? The answer is all too predictable. Not only more, but better, research in nutrition. For fifty years, the science of nutrition was the elucidation of nutrients and deficiency states — vitamin D and scurvy, for instance. There followed important decades of epidemiological study during which associations about diet and disease accumulated. Now the era of molecular nutrition should be in full flower but it is not here quite yet. The field deserves the attention of the most sophisticated researchers.

Every month or so another 'broccoli' story makes news, reflecting an understandable desire for a silver bullet, a single answer. But given the present level of knowledge, there is only one right answer about diet and health. Do what your mother told you to do — eat a balanced diet and get some exercise. And hope you inherited good genes.

Barbara J. Culliton