Discussant's comments

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The first three speakers of this symposium showed that problems exist in extending too far the use of the Atwater values (ie, 4 kcal/g for protein and carbohydrate and 9 kcal/g for fat). It is important that we recognize these problems if we hope to understand the effect of a caloric change on the development of cancer.

Yet we need to keep two ideas in mind. First of all, we should continue to use these values to formulate and balance diets so that we equalize the intakes of other nutrients. If we are studying an effect of energy intake, be it fat or carbohydrate, we want to be sure that in changing these variables we don't change the intake of protein, vitamins, minerals, and fiber. We want to run as clean an experiment as possible changing one variable at a time.

Indeed, many of the early experimenters on diet and cancer failed to equalize protein-vitamin-mineral content, and many still fail to recognize that this is important. We should not get the idea that the Atwater numbers have no value.

On the other hand, as you heard this morning, these values are not adequate in trying to explain why a particular dietary change in energy may exert an effect. Clearly, this inadequacy is going to demand fine tuning in diet composition and level of intake in animal experimentation, which means many more experiments on many more animals.

Even when we invoke these principles of balancing diets, however, we will continue to encounter uncertainties and problems. It is the object of all experimenters to conduct a fair experiment. If we wish to carefully control intake, we can restrict food intake of one animal to that of another by pair-feeding or yoke-feeding, as Dr Leveille described. However, pair-feeding in itself can introduce bias into the experiment.

For example, if a dietary treatment alters the efficiency of energy expenditure, is it fair to restrict the intake of a control animal whose metabolic efficiency may be different? Physicists have long recognized the Heisenberg Uncertainty Principle, ie, that the very act of making a measurement affects the process being analyzed. So, too, do we have to contend with a similar principle—namely, that when you alter one component of a diet, you have to alter others, which affects metabolism of the other nutrients.

Now, if in addition, we include genetic aspects, such as those discussed by Dr Wolff, the complexity increases greatly. Indeed, experimenters in carcinogenesis have known for a long time that meaningful results will not be obtained unless experimental groups are relatively large, 25 or more animals per group, in contrast to the typical 5–10 animals per group adequate for the usual nutritional experiments. Moreover, species of animal and strain within species play a tremendous role in carcinogenesis with effects that are far greater than those seen in the usual experiments in nutrition.

Finally, I do not need to remind you that the central goal is the study of cancer in humans. Each approach that we use has its particular drawbacks. Epidemiological studies are often retrospective involving multiple variables. Even when they are not, the biology and environment of the subjects are uncertain.

Experiments with animals also have drawbacks and uncertainties. What is the best animal to use? Rodents are coprophagic. Hence, it is possible that consumption of feces could introduce factors that would influence the development of cancer in a way that would not be applicable to humans. You could find similar but different objections leveled against any experimental animal.

McCay et al (1, 2) have shown that caloric restriction can double the life span of rats and mice, yet no evidence suggests that caloric restriction will achieve anything similar in humans.

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Thus, the bottom line is that understanding any interaction between diet and cancer is going to require many more studies with various protocols and approaches. Even in the best of times, arguments, uncertainty, and controversy will exist. We will be subject to public pressure for definitive results, especially because dietary changes are easy solutions and because diet has been invoked to explain good and evil events since the dawn of history. Remember, for example, the tremendous impact that nutrition had on human health in the 1920s and 1930s. In the early 1920s thousands of people died of pellagra in the South; 70–80% of the children in the northern cities were estimated to have rickets. Yet these diseases have disappeared.

A faith seems evident on the part of the public and a hope on the part of many of us that we can repeat this success. We must remember, however, that cancer is a complex disease with a biology still not understood. And dietary effects on cancer are understood even less.

Because of these complexities and uncertainties, it is imperative that we move slowly and cautiously in proclaiming dietary changes and recommendations. We must also remember that cancer is but one of many diseases that may be influenced by diet. Finally, we must also recognize that a dietary recommendation that may appear to be appropriate for cancer may turn out to be inappropriate for another disease.

References
