Toniolo and Akhmedkhanov Respond to “Serum Carotenoids and Breast Cancer” by Rohan

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We welcome Dr. Rohan’s thorough commentary (1) on our paper (2). His many pertinent comments were helpful in putting our results into a broader perspective. In his comments Dr. Rohan reviews the inconsistencies of published results concerning the role of carotenoids in breast cancer. Such inconsistencies remain when studies using different exposure assessment approaches and different designs are considered separately. What emerges, as is often the case in epidemiology, is a confusing picture, which our report has no presumption to redress. One of the problems that Dr. Rohan correctly identifies is that carotenoids are but one of the many chemical compounds that are part of the complex structure of fruits and vegetables. Some of these compounds are potentially anticarcinogenic and some are potentially harmful or carcinogenic, often depending on the method of food preparation. Such compounds are likely to interact with each other in complex ways, so that swallowing a handful of multivitamin pills is unlikely to ever come close to eating an apple. In this light, Dr. Rohan is correct in pointing to the potential pitfalls inherent in dealing with the complexity of diet by looking at a single class of chemicals or a particular dietary item, mostly because of the fundamental inability of observational studies to remove confounding.

A second interesting question addressed by Dr. Rohan has to do with the extent to which replacing the traditional exposure assessment approach based on questionnaire information with biologic measurements of body fluids may help to disentangle the complex issues involved in the relations between diet and cancer and between diet and breast cancer in particular. Dr. Rohan examines the issue with a skeptical eye and provides a number of good reasons for being skeptical. Indeed, biologic measurements introduce a whole new set of questions, the nature of which has been extensively debated (3), although solutions do not appear to be at hand. The most glaring problem is that, given the constraints of observational research, the vast majority of circumstances the measurements in question will have been performed from specimens obtained at a single point in time. Thus, unless the measurement has the ability to predict accurately the underlying average in the same body fluid for that person over an extended period of time, chances are that the results obtained with biologic measurements will not be appreciably less misclassified than any self-reported piece of information. In our case, we were fortunate to have at our disposal repeat sampling and data that indicated a strong intraclass correlation in measurements obtained from the same person within a 3-year span. In most circumstances, however, it is unlikely that extensive repeat sampling is available, so that this is a limitation that is going to stay with us. Perhaps, the complexity of the relation between diet and cancer should be addressed without shying away from using complex methods to assess exposure, including combining the use of biologic measurements with traditional questionnaire-based information. This appears to be the road followed by the large European Prospective Investigation into Cancer and Nutrition (EPIC) study coordinated by the International Agency for Research on Cancer (4).

With all the caveats above, it remains that our study suggests quite strongly that the use of a battery of carotenoid measurements of blood may provide useful information concerning the eating habits by study subjects of fruits and vegetables. When combined with solid background information on habitual diet, such measurements may provide a new set of tools to advance our still limited knowledge.

REFERENCES