

A Tale of 2 Studies: Diet and Breast Cancer

Early in 2006, the cancer community saw the publication of the Women's Health Initiative (WHI) randomized trial on the effect of a low-fat diet on occurrence of breast cancer and heart disease.¹ The initial media response to this study was a flood of articles describing the study as "revolutionary" and a "Rolls-Royce" of clinical studies and featuring a generally uncritical acceptance of the results of the study.² Cooler heads soon prevailed.³ A more reflective reading of this study reveals problems with the implementation of the study in this large population, as well as problems with the design of the diet intervention that become obvious in hindsight with the knowledge about dietary fats that has emerged in the past 10 years. These problems have been discussed clearly by other writers⁴ and are worth serious attention by clinicians and researchers. What interests me the most at this time is the extraordinary contrast between this study and the preliminary results of the Women's Intervention Nutrition Study (WINS) on low-fat diets in breast cancer patients, presented at the 2005 American Society of Clinical Oncology (ASCO) meeting. This is currently available in abstract form as well as slide format on the ASCO Web site,⁵ along with a very enlightening discussion of the WINS results by Eric Winer, MD, of the Dana-Farber Cancer Institute.⁶

First, it is important to note that we still need to view the WINS results as a preliminary, although very intriguing, contribution to the question of the role of low-fat diets in cancer. The results have not been published at this writing, and many questions about the study remain unanswered. Comparing the 2 studies is, nevertheless, intriguing. The similarities and contrasts between the WHI and WINS should be noted. Both studies involved women of fairly similar ages (48 or 50 to 79 years). The WHI study was much larger ($n = 48\,835$ healthy women) than the WINS ($n = 2437$ early breast cancer patients). The WHI study found that a low-fat diet, over the course of 6 years, did not alter the incidence of breast cancer versus the control group. However, in women with the highest initial fat intake (women with an initial dietary fat percentage greater than 36.8%), there was a significant reduction in breast cancer risk (hazard ratio = 0.78). Women who initially had the highest white blood cell counts also had a significant reduction in risk (hazard ratio = 0.77). The WINS, in contrast, found that with 5 years of follow-up, the overall relapse-free survival was significantly better

in the low-fat diet group (hazard ratio = 0.76 for the entire population and, in addition, a significant 0.58 for estrogen-receptor-negative patients).

Why the difference? We have always assumed it would be easier to prevent cancer with diet than to control cancer once it was initiated, but that is not what these results imply. One of the possible explanations is that there may have been better adherence to the low-fat diet pattern in the WINS than in the WHI study. In the WHI study, subjects in the intervention group lowered their dietary fat percentage by 10.7 points relative to those in control group by the end of the first year. By the end of the sixth year, the 2 groups were only 8.1 percentage points apart.¹ Adherence to the dietary programs was measured in the 2 groups, using attendance at regular follow-up sessions. By year 6, only 31% of the intervention group showed a high level of adherence. In contrast, the most arresting slide from the WINS presentation showed the fat gram intake of the control and the low-fat groups. The control group appears to have slightly decreased their fat intake over 5 years of the study. The low-fat diet group, however, drastically decreased fat gram intake during the first year, and these new levels remained very nearly stable during the entire 5 years. So it is possible that more rigorous adherence on the part of the cancer patients—who had an obviously strong motivation to prevent recurrences—may explain the different results of the 2 studies. Perhaps technical differences in the execution of the dietary program and follow-up explain this difference, or perhaps it is simply the motivational aspect; in either case, we may better understand this difference once the WINS reaches publication.

Differences in the 2 populations may also explain the different results. The finding of the WHI study that the low-fat diet reduced cancer risks among women with the highest initial fat intake suggests that high fat intake may delineate a group at high risk for cancer who can be helped by the low-fat diet. The WHI study also found that the low-fat diet lowered the cancer risk of women with initially high white blood cell counts, which indicate persistent inflammation (the low levels of fat may lower the inflammatory potential of the diet, as previously discussed in this journal). So it appears that women with these 2 risk factors may be helped by a low-fat diet. Perhaps actual breast cancer patients are, in fact, people who did have a high-fat diet and/or persistent inflammation before their diagnosis. This could mean that the group in the

DOI: 10.1177/1534735406289102

WINS was, in fact, similar to the subgroups in the WHI study who appear to have benefited from the diet intervention.

There are other features of the dynamics of breast cancer and diet that might help explain the different findings, as pointed out by Winer in his discussion. Winer emphasizes the important role that body weight and insulin play in breast cancer recurrence.⁶ Recent studies have clearly indicated that higher body weight or body mass index (BMI) increases chances of breast cancer recurrence and death. Weight gain during or after chemotherapy is also strongly correlated with poor outcomes. Winer points out that excess body weight or adipose tissue can promote breast cancer growth in several ways: increasing estrogens, sex hormone binding globulin, insulin, and insulin-like growth factor-1 and its binding protein. High dietary fat could conceivably influence estrogen and sex hormone binding globulin but not the other factors that are associated with excessive weight. Winer speculates that effects on body weight and BMI may have been the reason for the results in the WINS.

From an integrative medicine perspective, the WHI study and WINS are interesting in several ways. Weight control, inflammation, fat content and fat type, motivation, and interventional techniques may all play a role in the story of these 2 studies. All of these factors point to what I feel is a need to approach patients not just with a diet change but with a multifaceted intervention that targets not only dietary fat percentage but also other elements of the diet such as fat composition and protein sources, along with exercise, without which most weight control efforts are doomed to failure. Sensitive support in making transitions of this kind is necessary from both health professionals and patients' families and friends. Certainly, these 2 studies themselves say little about the potential of full integrative regimens to contribute to cancer prevention or control. But the use of multifaceted and mutually reinforcing strategies of life change, with adequate psychological support, may make the difference that is needed to have a real impact on the progression of cancer, a multifaceted disease.

Whether or not the differences in the WHI study and WINS hinged on motivations, this issue of *Integrative Cancer Therapies (ICT)* does feature substantial articles on topics of motivation, mind, and spirit in oncology. Tiffany Hunt-Shanks and colleagues, associated with the American Cancer Society, present a detailed analysis of exercise practices of breast and prostate cancer patients from the viewpoint of the theory of planned behavior. Assessing the exercise intention of these patients to determine its dependence on attitudes, social norms, and perceptions of

behavioral control resulted in the discovery of different determinants for exercise behavior in the breast versus the prostate cancer patients. This is surely a useful approach for integrative practitioners who are concerned with helping patients make physical activity an important part of their plan of care.

Our lead article, a review of studies of mindfulness meditation in oncology, assesses the research to date on a technique that has received attention in many oncology centers. Mary Jane Ott and coauthors, of the Dana-Farber Cancer Center, have assembled an interesting group of studies, and their analysis points the way toward areas and methods of research that need more attention in the proper clinical application of this very relevant technique.

Margaret White and Marja Verhoef of the University of Calgary contribute a qualitative analysis of one of the continuing questions of integrative and alternative medicine: why some patients choose to forgo well-established conventional treatment in favor of alternatives. They examined the role of spirituality in these decisions, a new perspective that revealed a pervasive effect of spirituality on the cancer experience in a large subset of patients who avoid conventional therapies. Deeply moving images of treatment and health arose in the meditations of some of these patients, images that remind and challenge clinicians to remain open to the importance of spirituality in their patients' lives.

We bring back a feature of some of the earlier volumes of *ICT* in this issue: the Point-Counterpoint. This feature allows experts who work from different viewpoints to express their assessments of important questions in oncology. And the questions for this issue's Point-Counterpoint are definitely important: cancer patients' feelings of blame and guilt. These feelings can seem even more overwhelming to patients as our correlations of diet and lifestyle with cancer incidence become more powerful. Integrative practitioners need to be familiar with and handle their patients' feelings of blame and guilt with great care. Our interviews with Drs Roger Dafter of the University of California, Los Angeles, and Howard Greenwald of the University of Southern California pay special attention to the role of psychosocial factors in cancer prevention and progression. Glib assessments of patients' mental states and how they may relate to the state of their cancer have the potential to inflict real damage. Integrative and complementary practitioners need to pay attention to the research summaries and perspectives in this article and ensure that their discussions of both lifestyle and psycho-emotional antecedents of cancer are scientifically accurate as well as compassionate.

Another feature of *ICT* that many practitioners find very useful is the Integrative Tumor Board.

This issue's Tumor Board explores responses of integrative practitioners to a case of cholangiocarcinoma, a cancer for which dietary and lifestyle correlations are generally lacking. Can integrative medicine contribute to the well-being of patients in this situation? Are there special dietary concerns that need to be addressed with a patient with gallbladder disease? The practitioners who explore these issues are Drs N. Joseph Espat and Suhail Sharif of the University of Illinois at Chicago, who provide the surgical oncology background of the case; dietitians Jacki Glew of the Block Center for Integrative Cancer Care and Cheryl Sullivan of Ingalls Memorial Hospital in Chicago; and Dr Tina Kaczor, a naturopath practicing at the Clinic of Natural Medicine in Eugene, Oregon.

Finally, we also present a detailed review of supplements that may be useful as part of a core nutraceutical program in cancer. The specific aims of this program are inhibiting metastasis; boosting capacities of natural killer cells; preventing cachexia, embolisms, and tumor-induced osteolysis; and maintaining optimal micronutrient status. This review was spearheaded by Mark McCarty, who has applied his knowledge base in locating relevant scientific studies and understanding their importance in the overall biology of the cancer patient.

References

1. Prentice RL, Caan B, Chlebowski RT, et al. Low-fat dietary pattern and risk of invasive breast cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA*. 2006;295:629-642.
2. Kolata G. Low-fat diet does not cut health risk, study finds. *New York Times*. February 8, 2006. Available at: <http://query.nytimes.com/gst/fullpage.html?sec=health&res=9505E2DC143EF93BA35751C0A9609C8B63>. Accessed March 21, 2006.
3. Gillette F. A heaping serving of baked Kolata, hold the caveats. *Columbia Journalism Review*. February 9, 2006. Available at: http://www.cjrdaily.org/behind_the_news/a_heaping_serving_of_baked_kol.php. Accessed March 21, 2006.
4. Ornish D. The facts about fat. *Newsweek*. February 7, 2006. Available at: <http://www.msnbc.msn.com/id/11225530/site/newsweek/>. Accessed March 21, 2006.
5. Chlebowski RT, Blackburn GL, Elashoff RE, et al. Dietary fat reduction in postmenopausal women with primary breast cancer: Phase III Women's Intervention Nutrition Study (WINS). Available at: <http://www.asco.org>. Accessed March 16, 2006.
6. Winer E. Discussion of the WINS trial. Available at: <http://www.asco.org>. Accessed March 16, 2006.

Keith I. Block, MD

Editor-in-chief

Integrative Cancer Therapies

Block Center for Integrative Cancer Care

Evanston, Illinois

College of Medicine and College of Pharmacy

University of Illinois at Chicago

Chicago, Illinois