

Inflammation, COX-2 Inhibitors, and Cancer

Years ago, I had a patient who insisted that a melanoma on her large right toe was due to chronic injury and inflammation in the exact location that she later developed her cancer. This connection intrigued me, and in the years following, I noted similar situations and observed the development of a literature that corroborated her claim. In time, I came to believe that inflammation was associated with malignancy, although it was not until the early 1990s that strong data began to indicate that inflammation was not only a trigger but also a fuel for promoting existing growth.

Today, there is no longer any question that inflammation often rages out of control in patients with advanced cancers. It is a key factor that accelerates the progression of disease and the clinical decline of the patient. Research shows that nonsteroidal anti-inflammatory drugs (NSAIDs), the most common of which are aspirin or ibuprofen, naproxen, and indomethacin, vastly lower the rate of breast cancer in women who take these drugs.¹ In addition, other research has found that when these are regularly taken among women already diagnosed with breast cancer, they were significantly less likely to have large tumors and positive lymph nodes—2 critical indicators of prognosis.²

While attending the recent poster sessions during the New Orleans 2004 American Society of Clinical Oncology meeting, I was struck by the swell of research investigating pharmaceutical COX-2 inhibitors as a therapeutic treatment option. These agents are being used in a large number of clinical trials for both prevention and cancer treatment. Anti-inflammatories are already approved for the prevention of precancerous colon polyps³; many studies now demonstrate improved outcome when combining COX-2 inhibitors with chemotherapy and radiation therapy for colorectal, breast, lung, prostate, esophageal, and other cancers.

I continue to be a proponent of anti-inflammatory and COX-2 inhibiting therapies, as I already have for many years now. In contradistinction to an all-out drug approach, however, I tend to favor using the more “gentle,” natural methods of inhibiting COX-2 pathways since they harbor little risk. I had begun using some of these broad-spectrum, nutraceutical formulations long before the advent of these new “super-aspirins” and even before the discovery that aspirin products and related NSAIDs had anticancer potential.

It was the NSAIDs’ well-known inherent risks that kept me encouraging these more natural approaches. The drugs can cause a spate of side effects. Women taking these regularly to prevent breast cancer are at increased risk for bleeding ulcers, gastritis, bone loss, and ringing in the ears. For a sizable percentage of women, the drop in their breast cancer risk came at too high a price. And, as it now turns out, this new generation of super-aspirins came at a price as well—an even higher price.

In fact, during the time our editorial office has been preparing this issue, the media have been full of reports on the cardiac risks of Vioxx, Bextra, Celebrex, and naproxen and the withdrawal from marketing of the first of these widely used, highly profitable drugs. While they carry short-term benefits of improved response to cancer therapy, they also propel longer-term concerns for increased cardiac risks. In a commentary following this editorial, I encourage exploration of the natural anti-inflammatory methods of integrative medicine as a potential replacement for these agents.

In this issue, we are also pleased to publish some very intriguing and innovative studies that address several important issues in integrative cancer care. Joseph Roscoe and colleagues at the University of Rochester report results of a pilot randomized study of polarity therapy, one of the energetically based therapies that have recently attracted some research interest. Margaret White and Marja Verhoef, who have contributed to this journal in the past, present a proposal for the use of participatory action principles in research on cancer clinical studies. Participatory action research focuses on real involvement of study participants in the conduct and design of the investigation and has received much attention in fields such as anthropology and ethnobotany. It has the ethical advantage of treating research subjects as intelligent human beings who communicate a meaningful perspective on what is occurring in their own bodies, rather than as the proverbial “guinea pigs” or passive subjects to be used by a researcher, who is customarily deemed the only reliable observer/reporter of information. Danette Hann and colleagues at the American Cancer Society Behavioral Research Center have contributed a survey of long-term breast cancer survivors and present interesting conclusions on the reasons and motivations for using complementary and alternative medicine techniques among this population of patients.

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Two of the studies in this issue address the use of vitamin C in cancer treatment. A comprehensive review by Michael Gonzalez of the University of Puerto Rico and his colleagues explains in detail the justification of the use of high-dose vitamin C in cancer treatment as an intravenous medication, rather than an oral one. The early trials of vitamin C by the conventional medical community were all done with oral use of lower doses of vitamin C, rather than the intravenous protocols used by most practitioners in the alternative community. This review casts doubt on the relevance of the outcomes of these trials. An article by Cheryl Krone of the Applied Research Institute in Palmerston, New Zealand, and John Ely at the University of Washington discusses mainly the use of blood-glucose-lowering strategies in cancer management but also highlights the relationship of hypoglycemic agents to vitamin C supplementation.

Two studies in the Patient Perspectives section of this issue highlight aspects of alternative medicine. This section is intended to allow for discussion of alternative therapies that are of substantial interest to patients, often from the viewpoint of the practitioner, with a view toward educating the wider integrative community about their characteristics and use. David Shannahoff-Khalsa has contributed an article on Kundalini yoga, in which he is a practitioner and teacher as well as a researcher. Ralph Moss gives us a detailed overview of the cancer clinics in Tijuana, Mexico, based on his recent trip to that area. While these clinics are usually written up in medical journals using a paradigm of what Moss terms *attack journalism*, this article instead approaches the clinics from the stance of an objective observer. Moss's global reputation as an advocate, and occasional critic, of alternative cancer treatment facilitated his access to these practitioners. Moss presents fascinating and important data on these clinics, the practitioners who work in them, and the patients who use them. He also presents a list of recommendations for the clinics themselves intended to assist them in establishing improved credibility.

Our Integrative Tumor Board for this issue concerns transitional cell carcinoma. Responders include

Drs Donald Lamm and Thomas Hogan of the Mayo Clinic in Scottsdale, Arizona; naturopath Eric Yarnell; and Monica Krise and June Lundy of the East Valley Regional Cancer Center in Chandler, Arizona, who discuss psychosocial oncology. This Tumor Board was organized by Assistant Editor Dan Rubin. Finally, an interview with Julian Safir on the new imaging technology 3TP helps us to round out our approach to integrative medicine, which includes new experimental diagnostic and treatment technologies as well as the oldest of medical traditions.

As this issue was going to press, we learned of the passing of Dr Hugh D. Riordan in early January 2005. Dr Riordan is a co-author of an article in this issue of *Integrative Cancer Therapies*. He was the Founding Director-President of the Center for the Improvement of Human Functioning International in Wichita, Kansas, was a former president of the American Holistic Medical Association, and was active in the field of alternative medicine for many years, including the use of orthomolecular vitamin C in cancer treatment. The staff of *Integrative Cancer Therapies* extends our condolences to the Riordan family and to Dr Riordan's associates.

References

1. Harris RE, Chlebowski RT, Jackson RD, et al. Breast cancer and nonsteroidal anti-inflammatory drugs: prospective results from the Women's Health Initiative. *Cancer Res.* 2003;63:6096-6101.
2. Schapira DV, Theodossiou C, Lyman GH. The effects of NSAIDs on breast cancer prognostic factors. *Oncol Rep.* 1999;25:433-435.
3. North GL. Celecoxib as adjunctive therapy for treatment of colon cancer. *Ann Pharmacother.* 2001;35:1638-1643.

Keith I. Block, MD

Editor-in-chief

Block Center for Integrative Cancer Care

Evanston, Illinois

College of Medicine

University of Illinois at Chicago

Chicago, Illinois