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To treat, perchance to cure

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Manipulating the endogenous immune system to treat and even cure cancer has intrigued clinical scientists since the dawn of modern medicine. In the late 19th and early 20th centuries, William Coley experimented with mixtures of bacterial endotoxins. “Coley’s toxins,” as they were called, clearly prodded the tumors to respond by nonspecific immune amplification. But tumor shrinkage came at the cost of unpredictable toxicity and occasional death from treatment.

Fast forward to 2008. Just this past week, the media were buzzing about a case report of a melanoma patient receiving a particular clonal subset of his own CD4 cells, directed against a disease-specific antigen, expanded *ex vivo* and reinfused. The treatment led to a long-term complete remission of extensive metastatic disease. Melanoma is a particularly good target for immunotherapy, with modest success already demonstrated for such therapies as high-dose interleukin-2 and interferon alpha, which apparently work through pleiotropic immune stimulation. This method overcomes the innate flawed response against established disease.

Other, more calibrated approaches to stimulating immunity are now in late-phase clinical trials. In this issue, Dr. Kim Margolin reviews in depth the development of anti-CTLA-4 therapy through the use of monoclonal antibodies (see page 367). The rationale for such treatment is based on extensive work elucidating the nature of the T-cell response. In fact, understanding this response with its feedback loops was essential in conceiving a treatment that interrupts physiologic T-cell blockade, allowing a robust antitumor response in melanoma. Dr. Margolin’s article gives a summary of the provocative clinical trial results to date and the ongoing studies with this class of agents.

The spectrum of topics this month is diverse, moving from immunology to psychosocial issues as addressed in the stem cell transplant setting by Dr. Scott Siegel (see page 407). He raises the issue, supported by recent studies, that the quality of psychosocial support might be as important in influencing overall survival as such long-recognized factors as disease status for patients requiring intensive chemotherapy and stem cell transplant. Does enhanced psychosocial support lead

to better outcomes due to better adherence with medical care in a complex delivery system? Or could the immune system be influenced positively when emotional needs are met? We don’t know the answer yet, but the intriguing possible mechanisms are discussed in Dr. Siegel’s paper.

Other articles of interest in this issue include the excellent review of endoscopic ultrasonography in pancreatic cancer by Drs. Andrew Fedoravicius and Douglas Adler (see page 382). Based on the clinically useful information it provides, this technology is gaining wide acceptance. You’ll be lobbying your gastroenterologists to add this capability after reviewing the data. On page 416, Drs. Prudence Lam and Rebecca Sands present the results of an interesting study using teenage volunteers to survey underserved women in Boston about their perspectives on breast cancer screening and early detection. Such innovative and creative approaches to this population will surely be important in reducing the disparity in cancer outcomes that arise from socioeconomic differences alone.

Please also read the case report and review of the diagnosis and management of cancer in pregnancy—in this instance Hodgkin’s lymphoma—by Dr. Amy Patel and her colleagues, beginning on page 389. We also feature a brief but important review of cutaneous toxicity associated with epidermal growth factor receptor inhibitors, written by Dr. Mario Lacouture and his colleagues, a group that has been leading investigation into treating this prevalent side effect (see page 413).

Last, but certainly not least, don’t miss the Washington Update by Ted Okon on page 396. As I write this, Congress has still not passed legislation reversing the 10.1% cut in Medicare payments to all physicians. Even if legislators do manage to postpone the cut, oncologists face an administrative nightmare, as claims are held until the situation is resolved. While we all keep dreaming of the day we can precisely stimulate the immune system to cure cancer, I wonder if our practices will survive to deliver that breakthrough.



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