

The concept of cure

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For many chronic diseases, none of the affected patients have the prospect of a complete cure, and patients have to learn to live with their disability. Cancer does not fall into this category; it is the most curable of the chronic diseases. Why, then, all the concern these days about using the word 'cure' when discussing treatment outcome with patients? The recent impressive results of the adjuvant trastuzumab (Herceptin®, Genentech Inc., San Francisco, CA) chemotherapy breast cancer study (*Nat Clin Pract Oncol* 3: 12–13) prompted one investigator to talk about the "cure of breast cancer", which triggered many news stories expressing concerns about "over promise". In fact, for decades, we have been curing an increasing number of patients with breast cancer, and, with the addition of this new adjuvant program, we will be curing many more. In part, this is why mortality rates from breast cancer are falling in the US and elsewhere in the world. The grand experiments of the 1960s, using childhood leukemia and Hodgkin's disease as experimental models, focused solely on addressing whether advanced cancers were curable by chemotherapy. The answer was yes, and this led to the use of adjuvant chemotherapy in the first place.

For almost all cancers, the risk of recurrence is clear from the shape of the relapse-free survival curves. For cancers curable by chemotherapy, and treated appropriately, relapse rates diminish over time, and disease rarely recurs after a specified period; this period is unique to each type and stage of cancer. After that specified time, patients in remission should be considered cured. In other cancers, the relapse rate is steady and linear and while long survival might be possible, cure is not achieved with current treatments.

Two phrases are key to this concept—"treated appropriately" and "rarely recurs". If doctors do not adhere to an established regimen, the true outcomes will most likely not be as expected. Unfortunately this scenario

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occurs frequently, usually by doctors who never had the confidence that they could cure patients in the first place. Doctors who deviate from using established regimens avoid any certainty in predicting outcome, to the patient's detriment. "Rarely recurs" seems clear enough; despite a diminishing risk of relapse over time, some patients' tumors inexplicably recur after long periods in remission. This does not negate the fact that most patients followed over the same period are cured. Patients understand this risk if the odds are carefully explained to them. Other issues such as employment, insurance, working in the uniformed services and providing for a family also revolve around the confidence in cure expressed by physicians.

By failing to call a cure a cure we also sometimes blind ourselves to unique opportunities. For example, despite the fact that complete remission can be attained using standard chemotherapy in a significant fraction of patients with advanced breast cancer, almost all such patients relapse and die of their disease. But, some patients who had advanced breast cancer are long survivors—invariably patients who were treated with myeloablative chemotherapy, supported by autologous marrow transplantation. I recently heard about a follow-up of such a study, originally published in 2000, (*Biol Blood Marrow Transplant* 6: 262–271) which used purified, autologous adult marrow stem cells, devoid of contaminating tumor cells, to support chemotherapy. At 7.5 years of follow-up, 32% of patients are alive and continuously free of disease (I Weissman, personal communication). The rate of relapse in this study diminished considerably and was uniquely different from the relapse rate after standard chemotherapy. Comparison with relapse-free survival curves indicates that these patients can be considered cured. Failure to recognize the ability to cure led to the premature abandonment of studies of this treatment approach. It's time we pay more, not less, attention to the concept of cure and give patients the benefit of the doubt.

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Competing interests

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