Breast Cancer Consensus

On 11 September, a National Institutes of Health consensus panel on breast cancer therapy recommended that many older women with the disease be given hormonal therapy and that certain younger women, who have not yet reached menopause, be treated with chemotherapy. The hormonal therapy recommendation, in particular, should change medical practice in this country, according to panel chairman John Glick, who is chairman of the University of Pennsylvania Cancer Center. The panel stressed, however, that many uncertainties about the timing, types, and duration of breast cancer treatments still remain.

In 1985, approximately 120,000 women will be diagnosed as having breast cancer and will be treated with radiation or surgery. Although 90 percent of these women will have cancer only in their breast and possibly in their underarm lymph nodes, the cancer will spread in one-half of them and ultimately kill more than a third. The idea of adjuvant chemotherapy is to treat not only the visible breast cancer but also any microscopic metastases by giving women cytotoxic drugs that destroy cancer cells, or hormones that inhibit the cancer's growth. These treatments are given at almost the same time that the primary cancer is treated. The problem for the consensus panel was to determine whether adjuvant therapies are effective and, if so, which therapies are best for which groups of women.

In making its recommendations, the panel subdivided cancer patients into pre- and postmenopausal groups and then further subdivided those groups, considering separately women whose cancers had spread to their lymph nodes and those whose cancers were confined to their breasts. The panel also distinguished between women whose cancer cells had estrogen receptors on their surfaces and those whose cells did not have the receptors. The significance of the estrogen receptors is that the drug tamoxifen, which blocks the receptors, frequently stops the growth of these cells.

Half of all women with early breast cancer also have cancer cells in their lymph nodes. About two-thirds of women with breast cancer are postmenopausal and about two-thirds have tumors that contain estrogen receptors.

After subdividing the breast cancer patients, the panel concluded that the clinical trial data now available indicate that premenopausal women with positive lymph nodes should have chemotherapy and should be given a combination of cytotoxic drugs unless they are participating in a clinical trial evaluating single-drug therapy. It is not yet clear which drug combination is best, nor how long the chemotherapy should be continued, but there are indications that nothing is gained by continuing it for longer than 6 months. This treatment, the panel concluded, could reduce cancer deaths in premenopausal women by 25 percent. There is no good evidence that hormonal therapy improves survival in premenopausal women.

For postmenopausal women with positive lymph nodes whose tumors contain estrogen receptors, tamoxifen is recommended. The studies considered by the panel showed that this treatment results in a highly significant period of disease-free survival. Most of the studies have not continued long enough to show that the treated women actually live longer as well. Tamoxifen, notes Glick, has "virtually no side effects. It is the least toxic drug used in oncology." The routine use of tamoxifen in older women with positive lymph nodes and tumors with estrogen receptors could reduce breast cancer mortality rates from 30 percent to 25 percent in this age group.

Postmenopausal women with positive lymph nodes whose cancers lack estrogen receptors probably will not benefit from tamoxifen, according to the panel. But they may want to consider chemotherapy, particularly if they have four or more positive lymph nodes.

The group of women with negative lymph nodes poses a more difficult problem. The panel does not recommend treating them unless they are at particularly high risk for a recurrence of their cancer. The high-risk women, Glick says, include those who are under age 35, who have large tumors, whose tumors are growing rapidly, and whose tumors lack estrogen receptors. Those women may want to consider adjuvant chemotherapy, the panel notes.

As for the rest of the women with negative lymph nodes, Glick remarks, "I wish we could have reached a more definitive statement, but the data are not there." But women with negative lymph nodes could possibly benefit from adjuvant chemotherapy and should continue to be studied in clinical trials. In reaching its consensus, the panel considered data from 20 different clinical trials, involving tens of thousands of women. As statistician Richard Peto from Oxford University told the panel, "the sheer volume of information seen over the past few days is so vast that, paradoxically, it becomes almost uninformative."

But even more data were available than the panel—for sheer lack of time—could consider. Nearly all the available data were considered at a meeting of clinical investigators and statisticians, organized by Peto, that convened the weekend before the consensus conference. Peto and his colleagues evaluated data from about four to five dozen clinical trials of cytotoxic agents and three to four dozen trials of tamoxifen—and reached different conclusions than the consensus panel. The group concluded that all women who have not yet undergone menopause—regardless of whether they have positive lymph nodes—would benefit from chemotherapy. And all postmenopausal women—regardless of whether they have positive lymph nodes and regardless of whether they have cancers with estrogen receptors—would benefit from hormonal therapy.

Asked to comment on the stronger results reported by Peto, panel members stressed that the statisticians were looking at a much larger body of data. And, said Glick, the statisticians' results are not yet published in a peer-reviewed journal. But then again, neither are the consensus panel's.

Everyone agrees, however, that clinical trials of adjuvant chemotherapy for breast cancer are still very much needed. The consensus panel urges that every woman with breast cancer participate in a clinical trial, although it acknowledges that only about 10 percent do so now. As panel member John Russo, who is director of the Michigan Cancer Foundation in Detroit, notes, only 10 percent of younger women and only 5 percent of older women with breast cancer even respond to adjuvant therapy. And there are enough unanswered questions that women would have nothing to lose by entering clinical trials.—GINA KOLATA