the infants were at high risk of the HBV carrier state but the effects of breastfeeding on mother-to-infant HBV transmission were not studied. In our study from serum of all 10 HBeAg-positive, HBsAg-carrier mothers contained HBV DNA. No HBV DNA was found in the infant’s serum after the administration of HBlg, for as long as moderate levels of anti-HBs persisted. As anti-HBs disappeared, both HBV DNA and HBsAg were detected in the serum (9 months of age) despite four doses of hepatitis B vaccine. These findings suggested at least three possible causes of vaccination failure. The first possibility is that HBV infection of the fetus in utero made the child immunologically tolerant to HBV antigens, so that HB vaccine was not effective. Secondly, early administration of HBlg could have protected the child from viraemia, but HBV had already infected leucocytes, liver cells, or other cells and was reactivated later. The third possibility is that the baby was genetically a low responder to the epitopes of the vaccine antigens and was horizontally infected. The induction of immunological tolerance by intratransfer infection could explain the vaccine failure in this baby. To explore the second possibility leucocytes from the infant would have to be examined during the perinatal period. Shen and colleagues described two cases of HBV DNA detected in cord blood leucocytes. Nonresponsiveness to HBsAg is associated with genes in the HLA DR regions. The third possibility may explain the fact that the baby’s sister was also a low responder to hepatitis B vaccine.

These findings suggest the need for a follow-up study of whether breastfeeding by HBV-carrier mothers is advisable.

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References continued at foot of next column

EFFECT OF PSYCHOSOCIAL TREATMENT ON SURVIVAL OF PATIENTS WITH METASTATIC BREAST CANCER

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Summary

The effect of psychosocial intervention on time of survival of 86 patients with metastatic breast cancer was studied prospectively. The 1 year intervention consisted of weekly supportive group therapy with self-hypnosis for pain. Both the treatment (n = 50) and control groups (n = 36) had routine oncological care. At 10 year follow-up, only 3 of the patients were alive, and death records were obtained for the other 83. Survival from time of randomisation and onset of intervention was a mean 36-6 (SD 37-6) months in the intervention group compared with 18-9 (10-8) months in the control group, a significant difference. Survival plots indicated that divergence in survival began at 20 months after entry, or 8 months after intervention ended.

Introduction

Many studies have demonstrated positive psychosocial effects of group therapy in cancer patients, including improvements in mood, adjustment, and pain. However, few studies have prospectively examined medical effects. In general, patients who receive psychotherapy survived longer. Our objective was to assess whether group therapy in patients with metastatic breast cancer had any effect on survival. This group intervention has been reported to improve the psychological well-being of such patients. We started with the belief that positive psychological and symptomatic effects could occur without affecting the course of the disease; we expected to improve the quality of life without affecting its quantity. Here we describe a 10 year follow-up of the effect of psychosocial intervention on disease progression and mortality.

Patients and Methods

Patients

Only subjects with documented metastatic carcinoma of the breast were included. 109 women were referred by their oncologists. Those patients who agreed were called upon by our research interviewer, who told them about the study and invited them to participate.

T. MITSUDA AND OTHERS: REFERENCES—continued

16. Ip HMH, Lele PN, Wong VCW, Kuhn MG. Prevention of hepatitis B virus carrier state in infants according to maternal serum levels of HBV DNA. Lancet 1989; i: 405-09.
The intervention lasted for a year while both control and treatment groups received their routine oncological care. The three intervention groups met weekly for 90 min, led by a psychiatrist or social worker with a therapist who had breast cancer in remission. The groups were structured to encourage discussion of how to cope with cancer, but at no time were patients led to believe that participation would affect the course of disease. Group therapy patients were encouraged to come regularly and express their feelings about the illness and its effect on their lives. Physical problems, including side-effects of chemotherapy or radiotherapy, were discussed and a self-hypnosis strategy was taught for pain control. Social isolation was countered by developing strong relations among members. Members encouraged one another to be more assertive with doctors. Patients focused on how to extract meaning from tragedy by using their experience to help other patients and their families. One major function of the leaders was to keep the groups directed toward facing and grieving losses.

### Analysis

The analysis used Cox’s proportional hazards model to examine whether intervention affected survival. This model was chosen so that we could assess the influence of treatment assignment over and above the effect of pre-randomisation prognostic variables by O’Brien’s logit-rank procedure. The log-rank test was also used to ensure that main effect differences were significant although the hazards of survival differed. We also drew Kaplan-Meier plots, and $\chi^2$ tests where appropriate.

### Results

Most striking was the difference in survival from time of randomisation, when intervention began, until date of death. Survival time for the treatment group was significantly longer compared with controls (table III and figure). In addition the interval from first metastasis to death was significantly longer for the group randomised to treatment. Thus the intervention group lived on average twice as long as did controls.

Since initial staging differed, we examined whether the group randomised to treatment was not as ill and therefore survived longer. The following points make this unlikely: (1) all patients had metastatic disease at recruitment and

### Table I—Details of Control and Intervention Patients

<table>
<thead>
<tr>
<th>Age At initial diagnosis</th>
<th>Control (n=36)</th>
<th>Intervention (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range)</td>
<td>49 (10-5)</td>
<td>49.9 (10-0)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>54.6 (10.2)</td>
<td>54.7 (9-9)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>25 (69%)</td>
<td>26 (52%)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>6 (17%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Simple mastectomy</td>
<td>2 (6%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Modified radical mastectomy</td>
<td>11 (31%)</td>
<td>18 (36%)</td>
</tr>
<tr>
<td>Radical mastectomy</td>
<td>17 (47%)</td>
<td>25 (52%)</td>
</tr>
</tbody>
</table>

*Spread of metastasis scaled as: 0 = no spread, 1 = one site, 2 = more than one site of a particular type, and 3 (bone only) = four or more sites.

### Table II—Disease course pre-entry (months)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Median (range)</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Control</td>
<td>Intervention</td>
</tr>
<tr>
<td>I</td>
<td>1 (0-1)</td>
<td>1 (0)</td>
</tr>
<tr>
<td>II</td>
<td>18 (50%)</td>
<td>16 (32%)</td>
</tr>
<tr>
<td>III</td>
<td>5 (14%)</td>
<td>11 (22%)</td>
</tr>
<tr>
<td>IV</td>
<td>17 (19%)</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>

*Mean (SD) or no of cases.

**Table III—Survival (months)**

<table>
<thead>
<tr>
<th>Survival from</th>
<th>Control</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study entry to death</td>
<td>18.9 (10.8)</td>
<td>36.6 (37.6)</td>
</tr>
<tr>
<td>Initial medical visit to death</td>
<td>81.2 (53.9)</td>
<td>94.6 (61.0)</td>
</tr>
<tr>
<td>First metastasis to death</td>
<td>43.2 (20.5)</td>
<td>50.4 (45.4)</td>
</tr>
</tbody>
</table>

Mean (SD).

*p < 0.0001, Cox; p < 0.005, log-rank. **p < 0.01, Cox; p < 0.04, log-rank.

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The groups were similar at study entry except for a nearly significant difference in staging at initial diagnosis (tables I and II). Staging information, based on medical records at study entry, was available for 70 of the 86 patients. Initial staging favoured the intervention group. Initial staging took place, on average, 59-8 (SD
randomisation, and therefore had a fairly uniform prognosis; (2) there were no differences in other important prognostic variables; and (3) although initial staging was, as expected, significantly correlated with time from initial medical visit to date of first metastasis (Spearman's \( r = -0.42 \), \( n = 70 \), \( p < 0.0003 \)), this variable was not correlated with any survival variables, including the outcome variable that differentiated between treatment and control groups—i.e., time from entry to date of death (\( r = 0.03 \), \( n = 70 \)).

To address this potential problem directly, the between-group differences were examined controlling for initial staging. The difference in survival from randomisation to death between the treatment and control groups remained highly significant (\( n = 70 \), \( p < 0.0001 \)). Staging had little influence on this survival variable (\( p < 0.86 \)). Likewise the difference between the dates of metastasis and death remained significant (\( p < 0.02 \)). In addition, examination of Kaplan-Meier curves for treatment versus control patients matched for initial staging revealed a pattern similar to that seen for the overall sample in the figure. Survival between intervention and control groups was different within each homogeneous staging group. This analysis indicated that initial staging differences do not account for the observed differences in survival between the groups.

Although there were no significant differences between treatment and control groups in chemotherapy and irradiation before randomisation, we tested the significance of the main effect for survival while controlling for each of these variables with the O'Brien procedure, entering the medical treatment variable first and then group status. In each case the treatment/control difference held. Of most interest was the significance of the treatment/control difference in survival after entering those variables that were close to being significantly different: days of irradiation (\( n = 69 \), \( p < 0.0005 \)) and androgen (\( n = 86 \), \( p < 0.0004 \)) and steroid treatment (\( n = 86 \), \( p < 0.0004 \)). Differences in time from first metastasis to death also remained significant with this analysis. Thus these variables do not account for the enhanced survival.

There was variation in attendance among those randomised to group therapy. Illness accounted for some of this variation. Indeed, 15 patients in the treatment group and 8 controls died during the year. Some other patients moved away or were reluctant to attend their group. To examine between-group differences among those patients who where more actively involved, we did the same Cox regression analysis on the 54 patients who completed both a baseline and at least one of the three follow-up questionnaires during the year. The difference in survival time from randomisation to death between treatment and control groups again remained significant (\( p < 0.0001 \)), even when staging was controlled (\( n = 42 \), \( p < 0.0001 \)), and when log-ranks were used (\( p < 0.03 \)).

**Discussion**

Patients with metastatic breast cancer randomised to weekly group therapy for a year lived significantly longer than did controls, by an average of nearly 18 months. This difference was statistically and clinically significant. Our results are consistent with but greater in magnitude than those of Grossarth-Maticek et al., and overcome the problem of differences in time from initial diagnosis to study entry which limited the findings of Morgenstern et al. In agreement with Cassileth et al. and Jamison et al., we found that a battery of extensive psychological assessments before intervention did not significantly predict survival. Indeed the only variable to affect survival time significantly was our complex psychosocial intervention. The effect of group interaction on longevity was not apparent in the year of intervention. Treatment and control groups did not diverge until about 8 months after the year was over (figure), which may be explained, as would the result of a somatic treatment, as a cumulative mild effect on time until death.

Our follow-up study was done to investigate whether psychosocial intervention, which significantly reduced anxiety, depression, and pain, would do so without having any effect on the course of the disease. We intended, in particular, to examine the often overstated claims made by those who teach cancer patients that the right mental attitude will help to conquer the disease. In these interventions patients often devote much time and energy to creating images of their immune cells defeating the cancer cells. At no time did we take such an approach. The emphasis in our programme was on living as fully as possible, improving communication with family members and doctors, facing and mastering fears about death and dying, and controlling pain and other symptoms. To the extent that this intervention influenced the course of the disease, it did not do so because of any intention on the part of the therapists or the patients that their participation would affect survival time.

What could account for the differences observed? Social support may be an important factor in survival. Even when matched for health habits, social relations affect survival. The provision of social support for isolated individuals under stress can improve health outcome. Social support is important in mediating how individuals cope with stress. For example, married cancer patients survive longer than unmarried patients. In our study there was a higher proportion of married patients in the control group (70% vs 57%). The fact that treatment patients had longer survival may indicate the efficacy of psychosocial intervention. One role of the group might have been to provide a place to belong and to express feelings. Clearly the patients in these groups felt an intense bonding with one another and a sense of acceptance through sharing a common dilemma. 1 patient with oesophageal strictures secondary to irradiation described her sense of estrangement...
from the world; while struggling to swallow soup at a restaurant, she thought: "These people don't realise how fortunate they are just to be able to eat". The therapy group patients visited each other in hospital, wrote poems, and even had a meeting at the home of a dying member. Thus the groups countered the social alienation that often divides cancer patients from their well-meaning but anxious family and friends.

Involvement in the group may have allowed patients to mobilise their resources better, perhaps by complying more vigorously with medical treatment or by improving appetite and diet through reduced depression. Treated patients learnt about hypnosis for pain control, and therefore may have been more able to maintain exercise and other routine activities. Neuroendocrine and immune systems may be a major link between emotional processes and cancer course.\textsuperscript{18,24} Future studies of the impact of psychosocial interventions on medical illness might profitably examine variables such as compliance, health habits, diet, and immune and neuroendocrine function.

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