Psychological Reports, 1989, 65, 315-321.

LENGTH OF SURVIVAL AND LYMPHOCYTE PERCENTAGE IN WOMEN WITH MAMMARY CANCER AS A FUNCTION OF PSYCHOTHERAPY[1]

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Summary.—50 patients suffering from terminal mammary cancer and visceral metastases received chemotherapy, and in addition half of them received psychotherapy, while half did not. A lymphocyte count was undertaken seven times in all, once before initiation of chemotherapy, the others after six applications of the therapy. As hypothesized, the 25 women who received psychotherapy lived longer and had significantly higher lymphocyte counts on Occasions 5, 6 and 7 than did the 25 women who did not receive psychotherapy. Of the types of psychotherapy employed, a specially designed form of behaviour therapy was significantly more helpful than dynamic psychotherapy in prolonging life.

There is now good evidence of an experimental kind that the CNS is involved in carcinogenesis (Metzler & Nitsch, 1986). In addition, there is evidence for the direct involvement of psychosocial factors. In a series of large-scale prospective studies, Grossarth-Maticek, Eysenck, and Vetter (1988) and Eysenck (1988) have shown that a new type of behaviour therapy (novational behaviour therapy) can be used successfully in prophylaxis, i.e., in the prevention of cancer in probands diagnosed as cancer-prone by virtue of personality, stress, and habits, such as smoking (Grossarth-Maticek, 1986; Eysenck, 1985, 1987a, 1987b, 1988; Grossarth-Maticek, Schmidt, Vetter, & Arndt, 1984; Grossarth-Maticek, Eysenck, Vetter, & Frentzel-Beyme, 1986). Novational behaviour therapy has also been used as a method of treatment in cases of terminal cancer to prolong life (Eysenck, 1987a, 1987b, 1988; Grossarth-Maticek, Eysenck, Vetter, & Frentzel-Beyme, 1986). The treatment is described in detail elsewhere (Grossarth-Maticek & Eysenck, in press).

Present Study

In the present study, 100 women with mammary carcinoma and visceral metastases constituted the sample. One hundred twenty-nine women with breast cancer and visceral metastases, to whom a Doxorubicin (adriblastine or adriamycin) combination chemotherapy had been proposed, were asked whether they would like to receive psychotherapy at the same time. Seventeen refused psychotherapy and another 56 declined chemotherapy. Fifty of the women who accepted chemotherapy were divided into pairs, matched on age, social background, extent of cancer, and medical treatment.

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A similar procedure was applied to 50 of those who refused chemotherapy, while the remainder were excluded from the design. One member of each pair was chosen at random to be treated with psychotherapy, while the other received no psychotherapy. A 2 x 2 design was therefore completed (psychotherapy/no psychotherapy; chemotherapy/no chemotherapy) with 25 women in each condition. Patients were allocated to the different psychotherapies at random. Twenty-four patients received creative novation therapy (Grossarth-Maticek & Eysenck, in press), 12 underwent depth psychotherapy, while the remaining 14 were treated with orthodox behaviour therapy (relaxation training and desensitization). Patients who accepted or refused chemotherapy were distributed proportionately to the different therapies.

The sequence of events is summarized in Table 1. Chemotherapy consisted of Doxorubicin (adriamycin) in combination with other agents. Doxorubicin was combined with cyclophosphamide (Endoxana) in 7 pairs, with fluoruracil in 13 pairs, and with vincristine, cyclophosphamide and prednisolone. Chemotherapy was administered in three to four week cycles and repeated between four and nine times. Thirty hours of psychotherapy were provided, as shown in Table 1. Various alterations were made in chemotherapy as appropriate.

TABLE 1
TEMPORAL DESCRIPTION OF THE EXPERIMENT

t_0	Diagnosis of breast cancer
	↓
t_1	Operation
	↓
t_2	Radiation or adjuvant chemotherapy
	↓
t_3	Diagnosis of viseral metastases
	↓
t_4	Combination chemotherapy proposed
	↓
t_4	Refusal or acceptance of chemotherapy and psychotherapy
	↓
t_6	10 hours of psychotherapy
	↓
t_7	First cycle of combination chemotherapy
	↓
t_8	10 hours of psychotherapy
	↓
t_9	Second cycle of combination chemotherapy
	↓
t_{10}	10 hours of psychotherapy
	↓
t_{11}	Third cycle of combination chemotherapy
t_{12}	. . . .

The outcome variables included the interval between surgery and the detection of metastases or new recidivism and the interval between metastases and death. These two intervals in combination comprise the total survival time. The results presented here concern the relation between intervention variables (chemotherapy and psychotherapy) and outcome variables (total survival time, changes in leucocyte concentration and lymphocyte percentage, and changes in psychosocial variables). Multiple linear regression and analyses of variance or covariance were employed in the statistical analyses.

Results

Length of Survival

We postulated the following: (H_1) Cancer patients who have undergone psychotherapy have a longer survival time than patients not treated by psychotherapy. (H_2) Psychotherapy and chemotherapy have a synergistic effect on survival time. (H_3) Different therapeutic interventions and concepts have different effects on survival time.

TABLE 2
Survival Time In Months According To Type Of Psychotherapy

Type of Psychotherapy	*n*	Survival Time In Months
A		
Neither chemotherapy nor psychotherapy	25	11.28
Psychotherapy	25	14.92
Chemotherapy	25	14.08
Both types of therapy	25	22.40
. . . . .		
B		
Behaviour therapy	14	15.29
Creative novation therapy	24	23.54
Depth psychotherapy	12	12.83
Total	50	18.66

Table 2 shows that all three hypotheses are in fact borne out. Cancer patients who have also undergone psychotherapy have a significantly ($p < .001$) longer survival time than patients not treated by psychotherapy. The statistical procedure used for testing our propositions was analysis of variance. The mean survival time of all patients was 15.7 mo. The maximum survival time was 38 mo., the minimum survival time was 6 mo. Persons who received neither chemotherapy nor psychotherapy lived 11.3 mo. after the diagnosis of visceral metastases, whereas patients with no chemotherapy but psychotherapy treatment lived 3.64 mo. longer on average (14.9 mo.). The effect of chemotherapy but no psychotherapy was 14.1 mo. survival

time, which was not significantly different from psychotherapy with no chemotherapy.

Psychotherapy and chemotherapy have a significant ($p < .05$) interaction effect on survival time. Those persons who had undergone both chemotherapy and psychotherapy had a mean survival time of 22.4 mo. Chemotherapy alone increased survival time by 2.8 (14.08—11.3) mo. If the effects of psychotherapy and chemotherapy were additive, one would expect a survival time of $11.3 + 2.8 + 3.6 = 17.7$ mo. for the group with combined therapies. However, the mean survival time of the chemotherapy plus psychotherapy group was 22.4 mo., exceeding the additive value by 4.7 mo. ($p = .05$). This indicates that a positive interaction between chemotherapy and psychotherapy takes place, and that this operates synergistically.

Since chemotherapy was not randomly assigned to subjects, it is possible that differences in the initial values of metastases detection time or psychosocial variables contribute to the pattern of results. These factors were therefore controlled by multiple regression. In the case of chemotherapy, the results of this procedure depended on the method of analysis. If chemotherapy was analysed as a dummy variable (yes = no), its effect after controlling for initial values of metastastes detection time and psychosocial variables was no longer significant. If, on the other hand, chemotherapy was analysed in terms of the number of treatment periods (which frequently extended beyond the three cycles illustrated in Table 1), it retained its statistical significance. In contrast, the effects of psychotherapy were scarcely reduced by controlling for these initial factors; this is to be expected, since psychotherapy was randomly allocated to subjects. After controlling for initial values of psychosocial values and detection of metastases time, the interventions taken together account for 37% of the variance in survival time.

The three forms of psychotherapy were not equivalent in their effects. The mean survival time in months of patients in the three conditions is shown in Table 2. Creative novation therapy led to significantly longer survival than either of the other procedures ($p < .001$). This difference remains significant even when initial conditions are controlled by analysis of covariance.

Percentage of Lymphocytes

Our findings that stress and personality combine to produce cancer have led to an hypothesis suggesting that certain peptides and hormones (e.g., cortisol) are related to personality traits (e.g., depression) and also influence the immune system (Eysenck, 1988). Thus, acute stress in humans and inescapable shock in animals increase cortisol levels, lead to depression and feelings of helplessness/hopelessness, and produce immunodepression, which facilitates the growth of cancer cells. Of course, the theory must be

much more complex than this, if only because endocrine secretions are involved in complex mutual interactions (e.g., ACTH, endogenous opiates), but we have here simply chosen cortisol to stand for a complex system of interacting peptides and hormones (Brambilla, *et al.*, 1978; Pena, 1983; Levy, 1985; Lloyd, 1987).

TABLE 3
LYMPHOCYTE TIME ACCORDING TO TYPE OF PSYCHOTHERAPY

Psychotherapy	t_1	t_2	t_3	t_4	t_5	t_6	t_7
None, %	23.24*	19.96	18.84	18.92	17.09	17.35	16.62
Some, %	21.08	16.09	18.68	19.68	21.80	22.38	24.38

*t_1, t_2, etc. = times of measurement.

If it is true that psychotherapy and in particular creative novation therapy can prevent cancer and prolong life in terminally ill patients, then the theory would suggest that *psychotherapy should have a positive effect on the lymphocyte percentage of the total amount of leucocytes*. To test this prediction, we measured the lymphocyte percentage of the total amount of

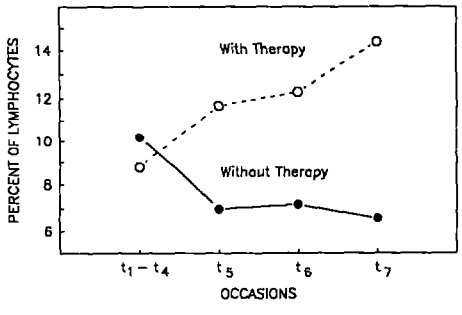

FIG. 1. Percent of lymphocytes as a function of psychotherapy

leucocytes seven times on the 50 women who had undergone chemotherapy. This first measurement took place before the beginning of the treatment, the second a fortnight after chemotherapy had started. After a month of chemotherapy treatment the lymphocyte percentage was measured again. This was repeated for the next chemotherapy application periods. Therefore, we had seven measurements in all.

Group Comparisons

The group of patients who were treated by chemotherapy but not by psychotherapy showed a steady *decrease* in lymphocyte percentage under chemotherapy as can be seen in Table 3. The group of patients who received both chemotherapy and psychotherapy showed a rapid decrease in lympho-

cyte percentage soon after chemotherapy had started but produced a steady *increase* in this percentage up to a higher level than at the beginning of chemotherapy.

Fig. 1 shows the main results. We have averaged t_1, t_2, t_3, and t_4, because we doubt if the ups and downs during these early periods are very relevant to our hypothesis and are more than statistical artifacts. The figure may give a more realistic impression of the effects of the therapeutic intervention. The quantitative effect of the therapy on the lymphocyte count over seven measures was certainly significant ($p < .01$) and high (the standardised regression coefficient was 0.53). The data leave little doubt about the verification of our hypothesis.

Discussion

If the basic concepts of our working hypothesis are correct, then sustained lymphocytopenia should be a characteristic feature of stress-invoked carcinoma. Lymphocytopenia can be correlated with increased plasma cortisol. Consequently, lymphocytopenia can be used as a useful and simple indicator in human prospective studies (Lloyd, 1987).

Glucocorticoids alter the immune competence of an organism and thereby the immunologic surveillance of latent 'initiated' tumour cells. In various animals both T and B lymphocyte and macrophage-mediated functions are inhibited by glucocorticoids (Baxter & Harris, 1975). Therefore, the elevation of circulating glucocorticoids induced by chronic psychosocial stress may inhibit immunosurveillance and consequently this may result in progression (promotion) of cancer; compare also Fox (1981).

Behaviour therapy, by altering an individual's reaction to stress and increasing his ability to cope with the stress, significantly alters the capacity of the immune system to kill cancer cells, as indicated by the increased percentage of lymphocytes. It would, of course, be necessary to investigate in similar experiments the effects of behaviour therapy on other indices of immune system efficacy, such as the number of NK cells. All that can be claimed at present is that the results of our study are in line with prediction.

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Accepted July 17, 1989.