

HYPNOTHERAPEUTIC INSIGHTS AND INTERVENTIONS: A CANCER ODYSSEY

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Abstract

Despite advances in molecular biology and therapeutics, cancer continues to be a major source of morbidity and mortality. The diagnosis and treatment are often stressful, and high levels of psychological and psychiatric disorders have been reported consistently over the last 20 years.

However, there is evidence that much of this distress is preventable by providing a support service that is open-access and fully integrated functionally and geographically with other parts of cancer services. This paper reviews the findings of some of the interventional research carried out by the author and his colleagues over the past 20 years. These studies have provided evidence that relaxation therapy, guided imagery and hypnotherapy can be very beneficial in helping patients cope with the diagnosis and treatment. Intriguingly, there is some evidence that they may prolong life, although further studies are required to clarify this. In the meantime, however, it is clear that much can be done to prevent, as well as to treat, cancer-related problems.

Key words: breast cancer, guided imagery, psychoneuroimmunology, relaxation

Introduction

Depending on the classification system used, there are over 250 types of cancer. Causes, stage at presentation, treatments and outcomes differ considerably. Unfortunately, at least one in every three people will develop cancer and, despite significant advances in molecular biology and in therapeutics over the last few decades, one in every four people still dies from the disease (<http://www.cancerresearchuk.org/aboutcancer/whatisacancer>).

The causes of cancer are usually complex and multifactorial. However, since the dawn of medical history, there has been a suggestion that psychosocial factors may play a part in the onset and/or the progression of malignant disease. For example, the revered Greek physician Galen, one-time physician to the Emperors Marcus Aurelius, Commodus and Septimius Severus, wrote that, in his clinical experience, women with a melancholic temperament (i.e. prone to depression) were more likely to develop breast cancer.

More recently, in his classic textbook *Surgical Pathology* (published in 1870), Sir James Paget, the famous surgeon and pathologist, suggested that mental state and life events predisposed to cancer: ‘The cases are so frequent in which deep anxiety, deferred hope and disappointment are quickly followed by the growth and increase of cancer that

we can hardly doubt that mental depression is a weighty addition to the other influences favouring the development of the cancerous condition.'

Even more recently, the concept of a Type C, or 'cancer-prone personality', has been proposed. Obviously, if it is a valid concept, the defining characteristics must be very common because cancer is so common. Key characteristics are said to be a lack of assertiveness, a high level of social conformity, a strong tendency towards emotional suppression (the British 'stiff upper lip') and a predisposition to depression (Bahnsen, 1980; Ratcliffe, Dawson and Walker, 1995; Temoshok, 1985; Watson and Greer, 1983).

It is important to emphasize that studies that have investigated the relevance of the Type C personality to the development or progression of cancer have certainly not produced conclusive results. We should also be careful to distinguish studies investigating the possible relevance of the Type C personality to the onset of cancer from those that have investigated its putative role in cancer progression. There is no logical reason why factors predisposing to the onset of cancer should necessarily be important in the progression of established disease. Conversely, factors that cause disease progression are not necessarily relevant to disease onset.

One of the classical studies often cited in support of the view that psychological factors affect disease progression was carried out by Greer and colleagues (Pettingale, Morris, Greer and Haybittle, 1985). Fifteen years after diagnosis, they followed up a cohort of patients with breast cancer and found that those who had coped initially by adopting the fighting spirit or by minimizing, denying or avoiding the implications, lived longer than those who responded with fatalism, hopelessness or anxious preoccupation (Greer, Morris, Pettingale and Haybittle, 1990; Greer, 1991).

However, follow-up studies such as this are a methodological mine field, for the simple reason that correlation and causation are by no means the same. For example, it may be that patients who have a particularly large tumour, or who have a particularly aggressive tumour, are more likely to respond by hopelessness and helplessness. Alternatively, it may be that some of the genes that predispose to various types of cancer manifest themselves not just in terms of an increased risk of malignant disease, but also in terms of features of the Type C personality. The only sure way to resolve this issue is by means of prospective, randomized, controlled, clinical trials in which the effects on survival of interventions designed to alter coping are evaluated systematically (Walker and Anderson, 1999; Walker, Heys and Eremin, 1999).

The impact of the diagnosis and treatment

It is not surprising that the diagnosis and treatment of cancer are often associated with distress of various types, for example, anxiety, depression, sexual problems, nausea, vomiting, fatigue, body image problems, pain and the 'Damocles syndrome'. Patients with the Damocles syndrome become locked in the future, unable to enjoy the present for fear of recurrent disease.

Given these considerations, it is hardly surprising that well conducted studies throughout the world have found high levels of psychiatric morbidity in patients following the diagnosis. In one of the early studies carried out in North America, 215 patients with different types and stages of cancer were assessed. Almost one in every two (47%) suffered from a diagnosable psychiatric disorder (Derogatis, Morrow, Fetting, Penman, Piasefsky, Schmale, Henrichs and Carnicke, 1983). In the UK, Maguire and colleagues followed up a cohort of women for a year following breast surgery. They found that 25% of the women suffered from clinically significant anxiety and/or

depression and 33% had moderate or severe sexual problems (Maguire, Lee, Bevington, Kuchemann, Crabtree and Cornell, 1978). Even more strikingly, the same group found that no fewer than 81% of women receiving adjuvant combination chemotherapy for breast cancer developed a psychiatric disorder (Maguire, Tait, Brooke, Thomas, Howat, Sellwood and Bush, 1980).

Recent studies have confirmed a high rate of morbidity. For example, in a study of 269 women with early breast cancer, 49.6% were clinically anxious and 37.2% were clinically depressed in the first 3 months after diagnosis (Hall, A'Hern and Fallowfield, 1999). The same group carried out an even larger study and found that 36% of 2297 patients attending outpatient clinics in 34 cancer centres in the UK scored above cut-off on the General Health Questionnaire (12 item version) (Fallowfield, Ratcliffe, Jenkins and Saul, 2001). In a study of 987 patients with newly diagnosed inoperable lung cancer, Hopwood and Stephens (2000) found that 33% of the patients were clinically depressed, and that, in many cases, depression was persistent.

These continuing widely reported high levels of morbidity in patients are clearly alarming. However, cancer not only affects individuals; it also affects families. How do they cope? In a study of the mental health of partners of women with breast cancer (Anderson, Walker and Walker, 2000), we found that, at diagnosis, the distress level was significantly higher in partners of women with breast cancer than it was in the patients themselves. As we followed up these women and their partners over a period of 24 weeks after the diagnosis, we found that distress levels very closely followed each other. In other words, a decrease in the distress level of one of the dyad was likely to be followed by a decrease in the distress level of the other. There may be an important therapeutic message here: by helping partners, we may be able to help patients.

In a useful paper, Harrison and Maguire (1994) reviewed predictors of psychological and psychiatric disorders in patients with cancer. They concluded that the following are risk factors: a previous history of mood disturbance, high emotionality, low ego strength, poor performance status ('fitness'), certain types of treatments (e.g. colostomy), lack of social support, passive or avoidant coping, inadequate or inappropriate information, and communication problems. To this we might add the number of unresolved concerns (Worden and Weisman, 1984) and the partner's distress level (Anderson, Walker and Walker, 2000).

Several of these predictors, such as a history of mood disturbance and performance status, cannot be altered. However, at least potentially, a number of these risk factors can be altered, for example ego strength, coping style, extent of the partner's distress, amount of support, number of unresolved concerns, adequacy of information, and satisfaction with communication.

The importance of information and communication was evaluated in one of our early studies (Paraskevaidis, Kitchener and Walker, 1993). We followed up 118 women who had been treated previously for gynaecological cancer. Most patients were in remission. Those who had clinically significant anxiety and depression were much more likely to be dissatisfied with the relationships that they had with the hospital doctors and were more likely to have been less satisfied with the information they received following the diagnosis.

Perhaps distress and morbidity can be prevented by improving satisfaction with communication, and by making sure that the information we give is the information that is going to assist and enable the patient to cope (Walker, 1996). However, whilst accurate information can be vitally enabling, information given at the wrong time, in the wrong way or by the wrong person can be very damaging to patients and their relatives. In our

study of women with gynaecological cancer, although many said they would have coped better with more information, there was a small subgroup that believed they would have coped better with less information (Paraskevaidis et al., 1993). Hence, there is a need for communication skills training for all health professionals, during basic training and afterwards (Fallowfield, Jenkins, Farewell, Saul, Duffy and Eves, 2002; Klein, Kitchener, Tracy and Walker, 2000; Walker, 1996).

Prevention, better than cure?

With these considerations about risk factors in mind, 10 years ago in Aberdeen, UK, we designed a service that we hoped would minimize distress and improve quality of life. The result was a Behavioural Oncology Unit that included a drop-in centre that was fully integrated functionally, and physically, with the medical and surgical oncology services. We cultivated a professional but informal atmosphere and we gave our staff special training to make sure that they had the skills necessary to elicit cancer-related concerns and, equally importantly, to respond effectively to these. We customized the information given and provided the opportunity for peer group and staff support. The Unit was physically a part of the Professorial Surgical Unit and patients received their chemotherapy under the supervision of a consultant medical oncologist within the Behavioural Oncology Unit. It was possible for us to make sure that, from the patient's point of view, investigations and treatments were carried out with the minimum delay, the minimum fuss, and the maximum coordination.

In one of our studies, 96 women attending the Unit because of newly diagnosed locally advanced breast cancer were studied intensively over a period of 37 weeks (Walker, Walker, Ogston, Heys, Ah-See, Miller, Hutcheon, Sarkar and Eremin, 1999). They were assessed using a number of tests, including the Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983). Immediately after the diagnosis had been made, when they were in-patients in the Professorial Surgical Unit waiting to start their chemotherapy, 21% scored 11 or above on the anxiety sub-scale of the HADS. This is usually taken to indicate clinically significant anxiety. However, the figure of 21% is not very interesting. We had carried out surveys of other groups of women in the North East of Scotland, for example, surveys of female police officers, female psychiatric nurses and wives of police officers. We had consistently found a point prevalence of 15–25% in community samples. These women with newly diagnosed breast cancer were undoubtedly stressed; but they were not clinically *dis*-stressed.

Eighteen weeks later, having had six cycles of chemotherapy and whilst awaiting surgery, the point prevalence had fallen to 5%. This is obviously much lower than it had been at diagnosis, and much lower than it was in the so-called healthy population of North East Scotland. Thirty-seven weeks after the diagnosis, following chemotherapy, surgery, hormone therapy and radiotherapy, the point prevalence had fallen further to a very striking 2%. Moreover, it was not just some psychometric quirk of the Hospital Anxiety and Depression Scale. Other psychometric tests and structured clinical interviews using standardized psychiatric criteria (DSM-III-R; American Psychiatric Association, 1990), confirmed the low rate of morbidity.

By applying simple, obvious, but key principles following the diagnosis and during and after treatment, these women were mentally healthier than they had been at the time of diagnosis, and they were healthier than were previously studied community cohorts of women. These exciting data suggest that a great deal can be done to prevent the widely

reported high rates of psychological and psychiatric morbidity, and a new service based on these principles has now been established in Kingston upon Hull, UK (Walker, Walker and Sharp, 2003a and 2003b).

The psychoneuroimmunological effects of relaxation and imagery

A large and burgeoning literature shows that certain types of stress, especially certain types of chronic stress, have predictable effects on host defences, particularly by suppressing natural killer (NK) cell activity (Gruzelier, Clow, Evans, Lazar and Walker, 1998; Walker, 1999; Walker and Eremin, 1995).

It had been previously shown in healthy volunteers (Johnson, Walker, Whiting, Heys and Eremin, 1996), and in patients with melanoma (Fawzy, Cousins, Fawzy, Kemeny, Elashoff and Morton, 1990; Fawzy, Kemeny, Fawzy, Elashoff, Morton, Cousins and Fahey, 1990) that a psychological intervention could offset stress-induced immunosuppression. The brain is 'hard-wired' to the autonomic nervous system and the endocrine system, and these systems are known to play a part in the modulation of host defences. It is clear that the brain can communicate with host defences via these and other less well-defined pathways. It is not surprising, therefore, that what happens in the brain, particularly in the frontal lobes, in the limbic system and in the hypothalamus, can alter host defences (Walker, 2000).

With funding from the Cancer Research Campaign, we were able to evaluate the effects of a simple intervention designed to reduce stress and to teach patients a method of feeling more in control. The main outcomes were quality of life, mood, coping, host defences and response to chemotherapy (Walker, Walker, Ogston et al., 1999).

Of a consecutive series of 97 women presenting with large, or locally advanced, breast carcinoma, 96 (99%) agreed to participate. Following the diagnosis, with their written informed consent, the women were randomized to a high level of support in the Aberdeen Behavioural Oncology Unit or to a similar high level of support plus our experimental intervention, relaxation plus guided imagery.

We issued our patients with a portfolio of 10 coloured cartoons as a resource. We also encouraged the women to develop their own images, and many of them did. One of our patients visualized three female warriors with spears attacking a large cluster of cancer cells. At a different stage in her treatment, she visualized a three-headed dragon breathing fire.

Patients received 'live' training sessions to help them learn progressive muscular relaxation, cue-controlled relaxation and guided imagery. In addition, they were given audiocassette recordings for daily practice at home. They were asked to keep a detailed diary of home practice and to rate the extent to which they had been able to relax and visualize.

All patients were given six cycles of chemotherapy every three weeks (cyclophosphamide, vincristine, adriamycin and prednisolone). Thereafter, they underwent surgery (breast conservation or mastectomy, depending on the woman's preference and what was surgically feasible). Four weeks after surgery, they received 20 fractions of radiotherapy over a period of 4 weeks, and they were followed up 4 weeks and 12 weeks after radiotherapy, a 37-week protocol in all. Blood samples were taken on 10 occasions, and psychological tests were administered 12 times during the 37 weeks.

At baseline, we carried out a comprehensive assessment of personality, coping, mood, mental state, quality of life and host defences. Our main measures of outcome were quality of life, mood, coping, host defences and response to chemotherapy.

Clinical assessment of the response of the tumour(s) to chemotherapy was carried out after six cycles of chemotherapy using standard internationally recognized criteria (UICC). Pathological response was assessed post-surgically from the excised specimen using a previously published 1–5 scale.

As expected, during chemotherapy women in the control group showed a significant decline in self-rated global quality of life. In contrast, those women randomized to relaxation and guided imagery showed a slight improvement in quality of life. In the control group, mood deteriorated during chemotherapy, whereas in the experimental group it improved quite dramatically.

Emotional suppression, as assessed by the Courtauld Emotional Control Scale (Watson and Greer, 1983), was stable in the control group. In the experimental group, however, women clearly became much more emotionally expressive. Similarly, the intervention modified social conformity as measured by the L scale of the Eysenck Personality Questionnaire (Eysenck and Eysenck, 1991). Social conformity was relatively stable in the control group, whereas there was a progressive decline in the experimental group. These data showed that the experimental intervention had a significant effect on important coping strategies.

The two groups did not differ significantly in terms of either clinical or pathological response. However, using logistic regression and multiple regression, two independent predictors of chemotherapy response were discovered. These were tumour size at diagnosis, and mood disturbance at diagnosis. The larger the tumour, the poorer was the response. The greater the mood disturbance at diagnosis, the poorer was the response (Walker, Heys, Walker, Ogston, Miller, Hutcheon, Sarkar, Ah-See and Eremin, 1999).

Between-group analyses revealed that the intervention increased lymphokine activated killer (LAK) cell activity, and increased the total number of T cells (CD2+), mature T cells (CD3+) and activated T cells (CD25+). Also, the intervention reduced the circulating levels of tumour factor alpha (TNF- α). Within the experimental group, we were able to correlate the women's self reports of imagery vividness as recorded in their daily diaries with changes in LAK and NK cell activity during chemotherapy and at the final follow-up time point. There was a high, positive and statistically significant correlation. The more vivid the imagery, the higher the NK and LAK cells activity was after chemotherapy, and 12 weeks after completion of radiotherapy (Ogston, Walker, Simpson, Fielden, Segar, Heys, Ah-See, Hutcheon, Sarkar, Walker and Eremin, 1997).

To summarize, the psychological effects of relaxation and guided imagery included improved mood and quality of life and enhanced coping. The intervention did not affect response to chemotherapy, although mood disturbance was a significant independent predictor of a poor clinical response and a poor pathological response to chemotherapy. We concluded that relaxation and guided imagery improved key aspects of quality of life and that there were statistically significant effects of host defences. However, we are not yet in a position to determine the clinical significance of these biological changes. Statistical and clinical significance are not the same, and only careful follow-up will show whether these alterations in host defences will translate into something that is clinically meaningful in terms of tumour biology.

Psychosocial interventions and survival

Although a number of negative studies have been reported, five well-designed positive studies have been reported (Anderson and Walker, 2002):

- 86 patients with metastatic breast cancer (Spiegel, Bloom, Kraemer and Gottheil, 1989);
- 94 patients with haematological malignancies (Richardson, Shelton, Krailo and Levine, 1990);
- 68 patients malignant melanoma (Fawzy, Fawzy, Hyun, Elashoff, Guthrie, Fahey and Morton, 1993);
- 271 patients with gastro-intestinal cancers (Kuchler, Henne-Bruns, Rappat, Graul, Holst, Williams and Wood-Dauphinee, 1999);
- 63 patients with lymphoma (Walker, 1998; Walker, Ratcliffe and Dawson, 2000).

In our study, 63 patients with Hodgkin's disease or non-Hodgkin's lymphoma were randomized to one of three interventions: individual training in progressive muscular relaxation and cue controlled relaxation; individual relaxation training plus hypnotherapy (direct hypnotic suggestion, a novel technique that we called nausea management training and ego strengthening); or standard treatment. The purpose of relaxation and hypnotherapy was to try to reduce the severity and prevalence of chemotherapy side effects – nausea, vomiting and anticipatory anxiety (Walker, 1992; Walker, Dawson, Pollet, Ratcliffe and Hamilton, 1988). In addition to reducing treatment-related side effects, the 5-year follow-up results suggested that the interventions had also prolonged survival (Ratcliffe, Dawson and Walker, 1995; Walker, 1998).

A long-term follow-up has now been carried out (the median time from diagnosis was 13 years and 5 months). Thirty-seven per cent of the patients randomized to standard treatment compared with exactly 50% of those randomized to relaxation with, or without, hypnotherapy were still alive 13 years later. The median survival of those in the standard treatment group was 74 months compared with a median survival of 115 months in those randomized to relaxation with, or without, hypnotherapy.

When those who had survived were compared one variable at a time with those who had died (univariate analysis), those who had died were older; they had more advanced disease at diagnosis, and they were more likely to have non-Hodgkin's lymphoma. This is unsurprising and, therefore, reassuring. In addition, however, social conformity scores (Eysenck Personality Inventory L scale), and depression scores (Hospital Anxiety and Depression Scale D scale), were also significant. On this univariate analysis, however, the effect of the interventions was not statistically significant.

The problem with univariate analyses is that the different variables are often themselves intercorrelated: what we really want to find out is which variables are genuinely *independent* predictors of survival. Using a conservative form of multivariate analysis – Cox proportional hazards: simultaneous entry – the interventions were shown to have a statistically significant effect on survival, along with stage of disease, depression and social conformity.

When the patients were divided into three groups according to their scores on social conformity (L scores), the Kaplan-Myer survival curves showed a most interesting pattern (Figure 1). Because of the small numbers, the two interventions have been combined. The interventions clearly had no effect on survival on the low scorers. The curves for the middle third of scorers are suggestive, and there is a highly statistically significant effect for the high scorers (7 or above). *All* of the high scorers in the control group were dead by 2 years, whereas over 30% of the high scorers in the experimental group were still alive after 13 years (Walker et al., 2000). These results were even more striking than they had been when we carried out a 5-year follow-up (Ratcliffe et al., 1995; Walker, 1998).

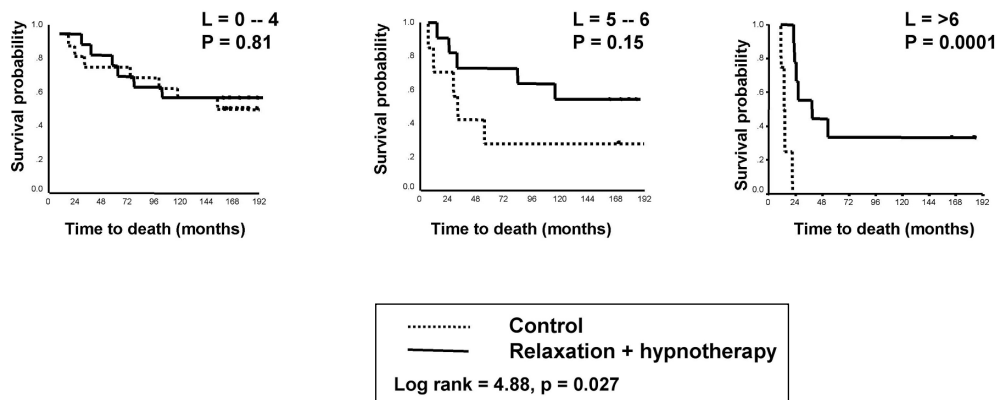


Figure 1. Social conformity scores (L) and survival

In summary, the interventions prolonged survival. In addition, social conformity, mood disturbance and stage at diagnosis were independent prognostic factors for survival. Sub-group analyses showed that the survival advantage was related to social conformity scores. High scorers benefited most from the interventions.

Obviously, this study needs to be replicated. It was not designed as a survival study. However, if psychosocial interventions can improve quantity as well as quality of life, what mechanisms might be involved? There are several possibilities:

- Because of treatment side effects, some patients decide not to persevere with life-prolonging, or even curative, treatments. There is strong evidence that psychological interventions can improve treatment compliance (Richardson et al., 1990; Walker, 1985; Walker et al., 1988).
- Interventions may encourage health-promoting lifestyle changes.
- As already described, in our breast cancer study we found that mood disturbance predicted poorer clinical and pathological responses to chemotherapy via an as yet undefined mechanism. Psychosocial interventions may affect survival by improving mood, thereby improving response to chemotherapy.
- Interventions have measurable effects on host defences, and there is reason to believe that they also affect hormones, etc. To the extent that host defences and hormones are relevant to tumour progression, interventions may influence survival through these pathways.
- Finally, a small, but significant number of patients develop serious infectious complications during chemotherapy. If interventions can prevent or ameliorate some of the chemotherapy-induced immunosuppression, they may reduce the number of associated deaths from neutropenic sepsis (Walker, 2000).

The study suggests that, if psychosocial interventions do prolong survival, they may not do so across the board. The findings suggest that two 'Type C' factors, depression proneness and social conformity, may mediate the survival effect. However, further work is required to determine which patients (in terms of personality, type of cancer, and stage at presentation) might benefit from particular interventions. Although the data are immensely exciting, we must be careful not to raise patients' expectations unrealistically.

Conclusions

The biopsychosocial approach to cancer holds out the promise of profound new insights into the malignant process and cancer therapeutics. If future studies confirm that psychosocial interventions, such as relaxation therapy, visualization and hypnotherapy, not only improve quality of life, but also prolong survival significantly, that will be a huge bonus. However, we must not wait for these studies. By applying what we have already learned, undoubtedly we can improve the lives of our patients and their families – now!

Note

- 1 By way of analogy, electroconvulsive therapy (ECT) is an effective treatment for some types of depression. However, no one would seriously suggest that depression is caused by a lack of externally delivered electricity such as is used in ECT.

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