

Fatigue, Weight Gain, and Altered Sexuality in Patients With Breast Cancer: Exploration of a Symptom Cluster

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Purpose/Objectives: To identify the symptom cluster of fatigue, weight gain, and altered sexuality caused by treatment for breast cancer.

Data Sources: Published research and literature review articles.

Data Synthesis: Fatigue, weight gain, and altered sexuality commonly occur after breast cancer chemotherapy. Each symptom has a significant impact on quality of life; however, viewing them as a symptom cluster magnifies their impact.

Conclusions: These symptoms have yet to be studied as a cluster. Exercise appears to be an intervention common to each that may be effective in reducing the severity of these treatment side effects.

Implications for Nursing: Nurses should view symptoms caused by breast cancer treatment holistically, keeping in mind that a reciprocal relationship often exists among symptoms. Identification of symptom clusters with empirically derived interventions may enhance quality of care and quality of life for patients.

Key Points . . .

- Treatment-induced fatigue is the most pervasive symptom of breast cancer chemotherapy experienced by women.
- Weight gain caused by breast cancer chemotherapy may have implications for morbidity and mortality from breast cancer and other chronic health problems.
- The menopausal side effects of chemotherapy coupled with changes in body appearance have a negative effect on sexuality.
- Exercise may be an intervention that can have a positive effect on this cluster of symptoms.

Breast cancer treatments seldom produce a single symptom as their response. Rather, women respond to cancer therapy with symptoms that occur together in groups or clusters (American Cancer Society, 2003). Fatigue, weight gain, and altered sexuality are frequent side effects of breast cancer treatment (Berger & Walker, 2001; Goodwin, 2001; Nail, 2002; Stead, 2003; Wilmoth & Tingle, 2001). Barton-Burke (1997) postulated a link among fatigue, weight gain, and sexuality caused by cancer treatments (see Figure 1); however, the relationship has not been explored thoroughly.

The concept of symptom clusters has advanced the understanding of synergistic effects of cancer treatment side effects and has the potential to increase efficacy of nursing interventions (Dodd, Janson, et al., 2001). A symptom cluster has been defined as three or more symptoms that are related and experienced concurrently. The treatment side effects all affect a patient at the same time and may even have an interactive effect on each other. The symptoms may not have the same etiology but do have a synergistic effect and may be broad predictors of morbidity (Dodd, Miaskowski, & Paul, 2001). This article will explore the literature on fatigue, weight gain, and altered sexuality as a potential cluster of symptoms that affects women with breast cancer. An understanding of this symptom cluster will aid in directing limited resources toward designing innovative interventions for the more than 2 million breast cancer survivors in the United States (Schnipper, 2003).

Fatigue

Cancer-related fatigue (CRF) is “a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning” (National Comprehensive Cancer Network [NCCN], 2003, p. FT-1). The most common side effect of all cancer treatments, fatigue affects 70%–100% of patients with cancer receiving radiation therapy or chemotherapy (Bower et al., 2000; NCCN). Many patients report that fatigue is more limiting than nausea and vomiting or pain and is not as well controlled (Stone, 2002). Fatigue has been reported to be greater in those recently diagnosed with non-small cell lung cancer than those with newly diagnosed breast cancer (Stone, Richards, A'Hern, & Hardy, 2000).

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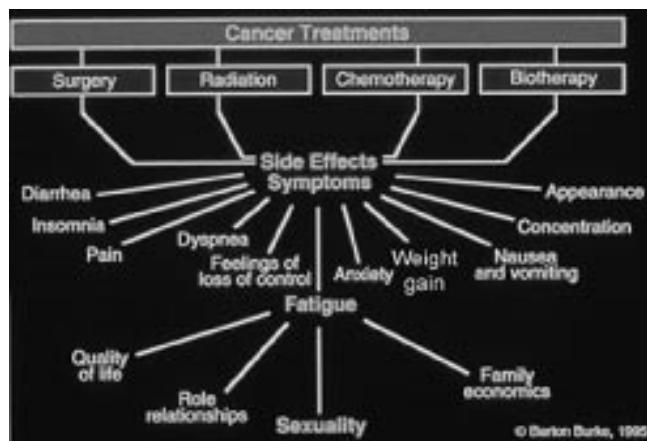


Figure 1. The Impact of Cancer and Its Treatments

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Studies examining the prevalence of fatigue in patients with breast cancer have found that as many as 99% experience some level of fatigue during the course of treatment and that more than 60% rate their level of fatigue as moderate to severe (Bower et al.). Fatigue has mental and physical components (Barsevick, Whitmer, & Walker, 2001; Cimprich, 1993) and a frequency of occurrence that is similar among patients who had breast-conserving surgery and those who received modified radical mastectomies (Shimozuma, Ganz, Petersen, & Hirji, 1999). A pattern of fatigue emerged from a study that consisted primarily of patients with breast, lung, and colon cancer who were treated with either radiation therapy or chemotherapy (Barsevick, Whitmer, Sweeney, & Nail, 2002). The pattern differed by type of treatment. Radiation-induced fatigue increased during treatment and decreased by the third month after treatment, whereas chemotherapy led to fatigue that peaked two to five days after each cycle and for the week after treatment. Fatigue also appears to continue after conclusion of treatment in patients with breast and ovarian cancer (Payne, 2002). Fatigue now is recognized as a major clinical problem in all cancer diagnoses and is the focus of intense research (Nail).

Suggested causes of CRF, regardless of the type of cancer diagnosis, include depression and sleep disturbance, side effects of chemotherapy, anemia, decreased ability to process nutrients, and increased energy requirements (Stone, 2002; Tavio, Milan, & Tirelli, 2002). Biochemical explanations for CRF in patients with breast and ovarian cancer include low hemoglobin and high bilirubin levels that alter oxygenation and altered melatonin production that leads to sleep disturbances (Payne, 2002). This begins a downward spiral as fatigued patients respond by being less active, which leads to muscle atrophy and decreased cardiovascular and respiratory functioning, causing increased fatigue (Mock et al., 1998; Stone). The result of this downward spiral can be loss of physical function and chronic fatigue that may persist for months or even years after successful treatment (Barsevick et al., 2002; Evans, 2002; Grant, 2000; Okuyama et al., 2000; Portenoy, 2000; Portenoy & Itri, 1999).

Models currently used to explain the concept of fatigue evolved in the absence of substantiated pathophysiologic theo-

ries of CRF and focus on energy utilization and conservation (Ream & Richardson, 1996). The Psychobiological-Entropy Model (Winningham, MacVicar, Bondoc, Anderson, & Minton, 1989) postulated that primary fatigue leads to decreased activity and that secondary fatigue results in a downward spiral of decreased activity, fatigue, and reduced functional status. Therefore, interventions must be directed at primary and secondary fatigue. Levine's Energy Conservation Model has four principles—conservation of energy, structural integrity, personal integrity, and social integrity (Fawcett, 2000)—that aid an individual in maintaining wholeness. Mock has conceptualized that enhancing structural integrity through exercise will moderate fatigue experienced by patients with breast cancer (V. Mock, personal communication, May 3, 2003).

Interventions

Interventions for CRF can be grouped as pharmacologic, nonpharmacologic, or psychosocial (Nail, 2002; NCCN, 2003). Pharmacologic interventions include administration of erythropoietin, psychostimulants, and antidepressants to moderate fatigue. Use of psychostimulants and antidepressants still is in the evaluation phase, whereas erythropoietin appears to increase energy levels by improving hemoglobin levels in patients with nonmyeloid malignancies (Nail; NCCN). Practice guidelines for management of CRF include correction of sleep disorders, counseling in sleep hygiene, and the careful use of hypnotics (Mock et al., 2000; Portenoy & Itri, 1999).

Nonpharmacologic interventions for fatigue include energy conservation, sleep and rest, and exercise. Exercise in the form of activity-enhancement programs such as structured walking (Dimeo et al., 1996; Mock et al., 1994, 1997, 2001; NCCN, 2003; Schwartz, 1998) and an individualized home-based exercise program combining aerobic exercise and strength resistance training (Coleman, Coon, et al., 2003; Coleman, Hall-Barrow, Coon, & Stewart, 2003) has resulted in reduced fatigue levels. Exercise can decrease patients' fatigue and improve physical performance and psychological outlook (Dimeo, 2001; Dimeo et al., 1997; MacVicar, Winningham, & Nickel, 1989; Mock et al., 1997). Psychosocial interventions for fatigue include stress management, nutritional support, and patient and family education about fatigue (NCCN). Standards of care indicate that all patients with cancer should be screened for fatigue at all visits, that patients and families require education about fatigue, and that CRF must be included in clinical outcome studies (NCCN).

Weight Gain

A second symptom experienced by many women receiving chemotherapy for the treatment of breast cancer is weight gain. This is a unique symptom of cancer chemotherapy that appears primarily in women with breast cancer; thus, little literature has explored this symptom in populations with other cancer diagnoses. Weight gain typically varies from 2.5–6.2 kg (5.5–13.64 lbs.) (Rock et al., 1999), although gains of more than 22 lbs. are not unusual (McInnes & Knobf, 2001). The largest gains are seen most often in premenopausal women (Demark-Wahnefried, Rimer, & Winer, 1997; McInnes & Knobf; Schwartz, 2000a). In one study of breast cancer survivors (N = 44) who gained 5 lbs. or more, weight gain was maintained by 68% of the study sample two years after treatment and by 40% three years after treatment (McInnes &

Knobf). Weight gain not only affects a woman's self-concept and sexuality but also has health risks, including the normal risks of being overweight such as heart disease and diabetes, and may increase the risk of breast cancer recurrence and death from breast cancer (Goodwin et al., 1993; McInnes & Knobf; Schwartz, 2000a). Obesity is associated with hormonal profiles that are likely to stimulate breast cancer growth (Kawachi, 1999).

The cause of weight gain in patients with breast cancer is unknown but may be related to decreased activity, decreased metabolism, and hormonal changes (McInnes & Knobf, 2001; Schwartz, 2000a). Some data indicate that chemotherapy provokes changes in body composition and metabolic requirements that may have a role in weight gain as well as a role in the fatigue that occurs during treatment (Demark-Wahnefried, Hars, et al., 1997; Demark-Wahnefried, Winer, & Rimer, 1993; Kutynec, McCargar, Barr, & Hislop, 1999). The assumption of the role of overeating and subsequent energy imbalance leading to weight gain in this population has not been validated (Demark-Wahnefried et al., 2001).

Interventions

Interventions for weight gain associated with chemotherapy in patients with breast cancer have not been studied as extensively as those for fatigue resulting from treatment. The few studies on weight gain focused either on nutritional counseling and weight management programs that included exercise (Goodwin et al., 1998) or on exercise alone (Schwartz, 2000a, 2000b; Winningham et al., 1989). This limited research suggests that weight gain associated with treatment can be controlled with exercise.

A group of breast cancer survivors ($n = 219$) who exercised maintained their weight compared to a control group of non-exercisers, whose weight continually increased (Schwartz, 2000a). In the study, regular exercisers were women who participated in aerobic activity for at least 15 minutes per day and at least four days per week; their most common activity was walking. The exercise and nonexercise groups did not report a difference in rates of anorexia or nausea, suggesting that exercise, not appetite, was responsible for the differences in weight gain. Furthermore, patients with breast cancer reported greater benefits from exercise than patients with non-Hodgkin lymphoma (Schwartz, 2000a).

Exercise has been found to control weight gain as well as reduce levels of fatigue (Schwartz, 2000b). In the study, 78 breast cancer survivors who adhered to a home-based program of exercise had significantly lower weight gain at the third and fourth chemotherapy cycle than those in the nonexercise group. Additionally, exercisers had significantly lower fatigue scores and higher functional ability than nonexercisers. The report provides a strong link between the symptoms of weight gain and fatigue and suggests that exercise is an intervention that may ameliorate both symptoms.

A study of the relationship between weight gain and psychological well-being in a nonobese, noncancer population ($N = 3,747$ women) found that women who gained more than 5 kg (11 lbs.) in a 10-year period reported lower overall well-being, higher negative affect, and lower positive affect (Rumpel, Ingram, Harris, & Madans, 1994). Similarly, weight gain during and after treatment has been found to have a negative impact on affect (Bremer, Moore, Bourbon, Hess, & Bremer, 1997), correlate positively with labile emotions

(Levine, Raczyński, & Carpenter, 1991), and be distressing and demoralizing (Knobf, Mullen, Xistris, & Moritz, 1983).

Although the studies have merit and suggest that exercise with or without nutritional modification can reduce the degree of weight gain associated with chemotherapy, randomized clinical trials are required to provide clear guidelines for practice. McInnes and Knobf (2001) recommended that future work in this area should examine body fat, weight change, hormonal status, and basal metabolic rate with and without exercise. Furthermore, additional work is needed on the suggested relationships between weight gain and fatigue and between weight gain and body image in patients with breast cancer. This will provide evidence on which to base recommended nursing interventions.

Altered Sexuality

A third symptom experienced by many patients with cancer is altered sexual function. The incidence is reported by 20%–90% of all patients with cancer (Andersen, 1985) with 25%–80% of female patients experiencing alterations in sexuality as a result of cancer or cancer treatment (Bruner & Boyd, 1999). Some reports suggest that about 50% of patients with breast cancer experience long-term sexual problems, including decreased desire, decreased arousal, changes in responsiveness to physical sensations, difficulty reaching orgasm, painful intercourse, and loss of pleasure from sex (Fleming & Kleinbart, 2001).

Breast cancer surgery has little impact on physiologic sexual functioning but does have major implications for body appearance and the psychological aspect of sexuality for women and their partners that, in turn, may affect their pattern of sexual activity (Yurek, Farrar, & Andersen, 2000). Women receiving breast reconstruction after modified radical mastectomy report lower rates of sexual activity and reduced sexual responsiveness than women receiving either modified mastectomy alone or lumpectomy (Yurek et al.). These procedures can lead to some loss of sensation in the breast. The loss of sensation also is experienced after breast reconstruction (Schover, 1991; Schover et al., 1995; Wilmoth & Ross, 1997; Wilmoth & Townsend, 1995). Keloid formation that occurs postoperatively along the site of the surgical incision can have a devastating effect on body appearance for African American women. Anecdotal evidence suggests that family history of keloid formation can influence women's decisions about type of surgery and whether to have breast reconstruction procedures.

Physical sexual changes that can result from chemotherapy include menopausal symptoms such as hot flashes, vaginal dryness, and dyspareunia, either on a temporary or permanent basis. These changes frequently result in altered sexual response such as desire, arousal, and orgasm (Shell, 2002). Lack of desire has been reported to affect as many as 11% of cancer survivors, arousal difficulties have been reported by 15%, and orgasm infrequency or inability has affected 4%–12% (Andersen, 1993; Andersen, Anderson, & deProse, 1989; Andersen, Van der Does, & Anderson, 1992). Side effects of adjuvant treatment that affect sexual response include nausea, fatigue, hair loss, and weight gain (Fleming & Kleinbart, 2001). In addition to these side effects, chemotherapy can cause destruction of ovarian follicles of premenopausal women, which mimics the response that ovaries have to hormonal changes during

menopause (Knobf, 1998). Symptoms of chemotherapy-induced menopause include atrophy of vulvar tissues, loss of tissue elasticity, decreased vaginal blood flow, decreased lubrication, hot flashes, mood swings, fatigue, and irritability (Fleming & Kleinbart; Ganz, Rowland, Desmond, Meyerowitz, & Wyatt, 1998; Knobf, 1998, 2001). These symptoms may be experienced for as long as 30 months post-treatment (Nystedt, Berglund, Bolund, Fornander, & Rutqvist, 2003).

Endocrine treatments for breast cancer have sexual consequences, including decreased desire, decreased orgasmic response, and soreness and shrinkage of the vagina (Kaplan, 1992; Swain, 1996). Vaginal discharge and hot flashes also are common problems during endocrine therapy, particularly in premenopausal women, but appear to decrease by the third year of treatment (Nystedt et al., 2003). These side effects are magnified and last longer in women also treated with chemotherapy.

Body image related to treatment for breast cancer is another factor that affects sexuality. Fatigue, weight gain, and changes in body image can occur with chemotherapy or endocrine therapy (Nystedt et al., 2003) and can contribute to women feeling sexually undesirable (Fleming & Kleinbart, 2001). Not only does weight gain affect women's self-esteem and sexual desire, it also may have an impact on their partners' attraction to them (Holmberg, Scott, Alexy, & Fife, 2001). In one case study, the husband of a patient with breast cancer admitted that he was less stimulated because of her weight gain and smaller reconstructed breasts (Fleming & Kleinbart). Surgical scars, missing or changed breasts, keloid formation in African American women, and alterations in skin tone and color also affect body appearance and may have a negative effect on psychological sexual functioning (Wilmoth, 2001; Wilmoth & Sanders, 2001). In the postoperative weeks, women who had modified radical mastectomies with or without reconstruction reported higher levels of traumatic stress and situational distress from their body changes. Forty percent of the women receiving reconstruction had not resumed intercourse at the time of assessment one month postoperatively (Yurek et al., 2000) and reported a more negative impact on their sex lives than women without reconstruction (Rowland et al., 2000). Thus, body change appears to be linked with sexual activity, at least in women receiving reconstruction.

Barton-Burke (1997) postulated a cyclical relationship between fatigue and sexuality (see Figure 2). Although little literature links the symptoms, one qualitative study (N = 10) indicated that women link fatigue and weight gain as contributing to changes in their sexuality (Holmberg et al., 2001). Intuitively, fatigue leaves little energy or desire to engage in sexual activity. According to a survey by the Fatigue Coalition, more than 70% of patients with cancer believe that fatigue can lead to feelings of hopelessness and laziness and can make relationships with other people difficult, leading to loneliness and isolation (CancerSymptoms.org, 2002). Although not of an empirical nature, the report suggests a link between fatigue and sexual interaction that bears further investigation. Even though patient education materials also imply links among cancer treatments, fatigue, and altered sexuality (Bullard, Bullard, Rosenbaum, & Rosenbaum, 2003), much empirical work remains to be done to validate this as a symptom cluster.

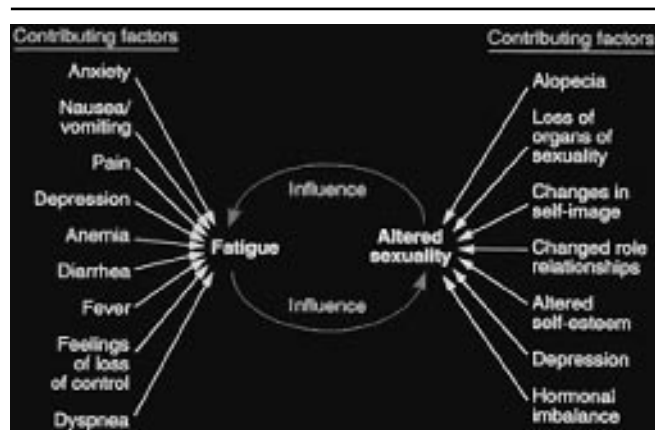


Figure 2. Fatigue's Influence on Altered Sexuality

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Interventions

The literature has few empirically derived interventions to reduce the altered sexual functioning that occurs secondary to cancer therapies. One study used a nurse practitioner trained to provide a specific comprehensive menopausal assessment (CMA). The CMA consisted of a comprehensive assessment of menopausal symptoms and an individualized plan of education, counseling, and pharmacologic support. Women in the study group (n = 33) reported significant improvement in menopausal symptoms ($p = 0.004$) and significantly improved sexual functioning ($p = 0.02$) but no measurable improvement in quality of life over women in the usual care group (n = 39) (Ganz et al., 2000).

Research in healthy perimenopausal women suggests positive sexual benefits from regular exercise. In one study of physical activity as it affects symptoms of perimenopause, women participating in regular physical activity reported fewer sexual symptoms (Li, Holm, Gulanick, Lanuza, & Penckofer, 1999). One group of studies found that exercising just before viewing an erotic stimulus increased both vaginal blood volume and vaginal pulse amplitude, indicating that activation of the sympathetic nervous system increased the body's susceptibility to arousal (Meston, 2000). This was true for women with normal sexual functioning as well as those with decreased sexual desire. However, in women with difficulty achieving orgasm, exercise decreased arousal (Meston). Conversely, findings from another study indicate that increased muscle tone as a result of exercise may increase orgasmic pleasure (Li et al.). This work has not been replicated in women with breast cancer. More work remains to be done in the development of an intervention that is clinically useful and effective in targeting the sexual sequelae of breast cancer treatments.

Discussion

Barton-Burke (1997) suggested a causal relationship among treatments for breast cancer, fatigue, weight gain, and sexuality that is only beginning to be explored. Analysis of the literature suggests a link among the symptoms of fatigue, weight gain, and altered sexuality. The literature also appears to suggest that exercise may be a common intervention for each of the symptoms.

Exercise has been shown to elevate mood and energy and decrease depression, anxiety, and moderate weight gain in patients with breast cancer (Pickett et al., 2002; Schwartz, 1998, 2000a). Therefore, exercise has a moderating effect on the physical and psychological causes of fatigue and weight gain. Numerous studies have demonstrated that regular aerobic activity is effective in decreasing fatigue in patients with cancer (Evans, 2002; Stone, 2002; Tavio et al., 2002). Exercise is effective even if a patient was active prior to diagnosis. Other studies also have reported that aerobic exercise interventions allowed patients with breast cancer to maintain their weight, lose weight, or decrease body fat while increasing muscle mass, compared to control groups who did not exercise and gained weight and body fat (McInnes & Knobf, 2001).

Exercise may be an intervention for altered sexual function caused by breast cancer treatment. Regular exercise can reduce depression and anxiety in healthy people as well as those with chronic illness (Ahmadi, Samavatt, Sayyad, & Ghanizadeh, 2002; Neidig, Smith, & Brashers, 2003; Pinto, Trunzo, Reiss, & Shiu, 2002; Suh, Jung, Kim, Park, & Yang, 2002) and enhance the sense of well-being, which has a positive effect on body image and sexual functioning (Pinto & Maruyama, 1999). One explanation for enhanced sexual functioning after exercise is an increased level of endorphins produced by physical activity with a subsequent positive influence on mood (Li et al., 1999). This increased level of endorphins also can help to decrease the psychosomatic symptoms associated with chemotherapy-induced menopause, such as mood swings, irritability, and insomnia (Li et al.). Other theories that contribute to the explanation of the positive effects that exercise has on psychosomatic symptoms include distraction from negative thoughts, improved body image leading to improved self-esteem, and increased social interaction (Li et al.). With decreased anxiety and depression, better and more stabilized mood, and increased self-esteem, women may have increased sexual desire.

Conclusion

Women with breast cancer do not experience just fatigue, weight gain, or altered sexuality. Instead, these symptoms can

be experienced concurrently, and each symptom may influence the other. Cancer and cancer treatments cause patients to be fatigued, which has a high level of impact on their lives (Evans, 2002; Mock et al., 1998; Nail, 2002; Stone, 2002; Tavio et al., 2002). As a result of fatigue, patients decrease their levels of physical activity, contributing to weight gain (Knobf, 2001; Schwartz, 2000a, 2000b). Logically, if women are experiencing fatigue that significantly affects their quality of life, their sexual desire probably will be decreased. Another factor contributing to altered sexuality is chemotherapy-induced menopause. Chemotherapy-induced menopause also contributes to weight gain experienced by these women (Knobf, 2001). Because all of these symptoms are experienced concurrently and are related, they could be defined as a symptom cluster (Dodd, Miaskowski, et al., 2001).

Fatigue, weight gain, and altered sexuality are nursing-sensitive outcomes that result from breast cancer treatment. Nurses have developed effective interventions for fatigue in women with breast cancer and are developing programs to minimize weight gain caused by treatment. Nurses can be on the cutting edge in developing interventions for the symptom of altered sexuality. Altered sexuality appears to be the synergistic symptom climax of the previously discussed symptoms of fatigue and weight gain. If a woman feels overweight, mutilated, prematurely aged, and chronically fatigued from her cancer treatment, she probably will have alterations in her sexuality. The range and scope of these alterations have a negative impact on quality of life as well as quality of relationships with significant others. The literature strongly suggests that exercise is a common intervention for each of the symptoms in this cluster. A descriptive study to find the prevalence of the three symptoms and the relationship to exercise among women receiving treatment for breast cancer is the logical next step. Then, a clinical trial of a supervised program of exercise for the treatment of the symptom cluster may be indicated.

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For more information . . .

- CancerSymptoms.org: Fatigue
www.cancersymptoms.org/symptoms/fatigue
- Cancer Care: Cancer fatigue
www.cancercare.org/Fatigue/Fatiguemain.cfm
- Archives of CANCER-FATIGUE@LISTSERV.ACOR.ORG
listserv.acor.org/archives/cancer-fatigue.html

Links can be found at www.ons.org.