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Does exercise affect health in women with breast cancer?

by **Barbara Gladson**

Most women between the ages of 45 and 60 know someone who has breast cancer, and some have developed the disease themselves. Women know that many of today's treatments (surgery, radiation, and chemotherapy) result in improved prognosis and decreased mortality rates. However, what they may not know is that exercise has been shown to improve the quality of life for both patients with cancer and cancer survivors. Exercise may even reduce the risk of developing the disease after menopause.

Breast cancer and its treatments produce negative effects both mentally and physically. Chemotherapy has been shown to produce extreme fatigue, nausea, vomiting, anemia, neutropenia, thrombocytopenia, peripheral neuropathies, de-conditioning, and, in general, a reduced quality of life (QOL). Chemotherapy is usually administered either intravenously or orally in repeated cycles approximately 3 weeks apart over a 3 to 6 month span. Bone marrow depression leaves the patient vulnerable to life-threatening infections, bleeding, and fatigue, often delaying the next cycle of treatment. Therefore, it is useful to study treatments that can lessen the effects of bone marrow depression.

There is a strong rationale for examining exercise during chemotherapy treatments since exercise affects immunity in a manner important for cancer defense. For example, neoplastic cells may be eliminated by cancer cell-specific $CD8^+$ cytotoxic cells or the natural killer (NK) cells of the immune system. Moderate exercise in healthy individuals has been found to produce an increase in white cell count, and regular exercise in cancer survivors has been shown to increase the immune system's ability to kill cancer cells. Specifically, exercise in this population can increase natural killer (NK) cell cytotoxic activity and produce a decrease in the duration

of neutropenia. This is important since diminished activity in the NK cells has been associated with the development, advancement, and recurrence of cancer. In addition, exercise during chemotherapy has been shown to produce beneficial effects on function, fatigue, nausea, mood and QOL, as well as reducing the length of time of neutropenia. Specifically, moderate exercise results in an increased white count and an increased production of a variety of cytokines which lessen the effects of other pro-inflammatory cytokines. Current theory regarding exercise and cancer suggests that enhanced immune function and diminished incidence of cancer occurs with regular exercise in the moderate range over a minimum period of 12 weeks. But excessive and intensive exercise may increase the risk of cancer.

It is clear that as white cell counts fall, the frequency, duration and severity of infections increase. It has also been observed that patients differ in their susceptibility to infection within the confines of their specific cancer and neutropenia. This implies that there are other factors at work here besides neutrophils that are involved in preventing infection in these neutropenic patients.

One factor contributing to the severity of infections might be mannose-binding lectin (MBL) gene polymorphisms producing low levels of MBL, a member of the subfamily of C-type lectin proteins. MBL has been shown to initiate the lectin pathway of complement activation by binding to mannose and glucose residues that exist on various microorganisms. MBL controls the activation of complement and also binds to receptors on phagocytes and enhances their activity.

The plasma level of MBL depends on a variety of factors including polymorphisms, ethnicity and age. A single amino acid substitution can result in a marked decrease in MBL level, particularly in persons carrying the polymorphisms homozygously. MBL deficiency is associated with infection in infants, autoimmune disorders, cystic fibrosis and even cardiovascular disease. Several studies have shown that low levels of MBL are associated with an increased susceptibility to infection, particularly in immunocompromised states following chemotherapy and are associated with a poorer prognosis. A study examining 100 children undergoing chemotherapy demonstrated that low MBL levels correlated to frequency and duration of neutropenia. A prospective study of 54 adults with hematologic cancers also demonstrated that low levels of MBL obtained prior to chemotherapy were associated with a significant infection.

The level of MBL deficiency likely varies with different diseases. It is estimated that about 25% of Caucasians have an MBL level < 500 ng/ml, which is suboptimal for protection against infection. Patients with malignancies may need at least 1000 ng/ml to decrease the incidence of infection. Infusion of purified MBL to MBL-deficient subjects in doses designed to restore levels to normal have been safely given resulting in opsonic activity. To the author's best knowledge, there have been no attempts to study MBL in breast cancer patients undergoing chemotherapy and no attempts to demonstrate changing MBL levels in response to exercise.

We are beginning a study to evaluate the effects of mild-moderate exercise on neutrophil count, MBL levels, exercise capacity and quality of life on women undergoing chemotherapy for breast cancer. Regarding MBL, we are interested in determining if there is a correlation between baseline level and the development of neutropenia during treatment.

Thirty women with recently diagnosed breast cancer, scheduled to begin a standard post-surgical chemotherapy protocol known to induce neutropenia, will be randomly assigned to an exercise plus chemotherapy group or to a chemotherapy alone (standard care) group. The women are expected to receive at least 4 cycles of chemotherapy over a 12-week period. The supervised exercise intervention will take place during cycle 1 (3 times/week for 3 weeks) and consist of aerobic and resistance training. The treatment group will then continue with a home program for the remainder of their chemotherapy cycles, approximately 9 additional weeks. The control group will receive a home stretching program and weekly supportive phone calls to monitor progress.

Complete blood counts (CBC), MBL levels, psychosocial measures, quality of life, and exercise testing will be obtained at the beginning of the study. CBCs will be obtained weekly as part of standard of care. The exercise testing along with the quality of life assessments will be repeated at the end of both cycle 2 and cycle 4.

If our study finds that low levels of MBL correlate with increased frequency and severity of infection, then future study will examine the effectiveness of MBL reconstitution therapy. Perhaps this therapy will become an important adjunct to pharmacotherapeutics, since presumably greater doses of chemo may be given without the fear of infection. The same can be true for exercise. It is reasonable to expect that if physical activity reduces neutropenia, then in the future oncologists will be writing exercise prescriptions along with the prescription for chemotherapy. How wonderful it would be if treatment for cancer includes a gym membership.

Barbara Gladson is an associate professor in both the UMDNJ-School of Health Related Professions and the UMDNJ-Graduate School of Biomedical Sciences. She received a BS degree in Occupational Therapy from the University of Pennsylvania, an MS in Physical Therapy from Columbia University, and a PhD in Pharmacology from UMDNJ. Dr. Gladson's past research includes electrophysiological studies on ion channels responsible for glucagon release and clinical research on hand injuries. She is currently involved in the development of the UMDNJ Biopharma Educational Initiative, developing academic programs for the pharmaceutical industry.

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Developing healthy outlooks for families at risk for child physical abuse

by **Melissa K. Runyon**

Child physical abuse (CPA) and violence within families is a highly prevalent public health problem. CPA has been associated with a wide range of debilitating psychosocial sequelae, such as post-traumatic stress disorder (PTSD), depression, behavioral problems, and violence towards others. The documented long-term effects of CPA, in conjunction with its widespread prevalence, support the urgent need to develop and refine evidence-based, culturally competent treatment strategies that target this population. The goal is to meet the needs of both the children and parents and to reduce the recurrence of CPA.

In 1990, while completing a Master of Science degree in clinical psychology at Eastern Kentucky University, I submitted paperwork to obtain a practicum at the University Counseling Center, where I would provide

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