Dear Readers,

I particularly enjoy this time of the year. I like being reminded that spring is here, and that nature will begin a new cycle. We are part of this cycle. We, too, will continue to grow and change. It is a time to set new goals. Spending time outdoors in nature should be one of those goals for each of us.

Best regards,
Dr. Silvana Martino

BIOLOGY BASICS

CHEMOBRAIN

The effects of cancer therapy on the brain were first noted with radiation therapy. It was observed that patients who received radiation to the brain experienced thinking and memory problems. On occasions when a patient received radiation to the brain twice, a “locked in” syndrome was noted, where the patients appeared aware, but unable to express themselves and communicate. The more brain tissue was radiated and the higher the dose of radiation given, the more likely one would observe these side effects. This led to the development of radiation techniques that spare as much brain tissue as possible such that one targets the brain lesions specifically rather than radiating the whole brain as the preferred way to treat brain tumors and brain metastases. The effects of radiation on brain function seemed logical, since this was a therapy directed at brain tissue.

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Even in patients who were not receiving brain radiation, changes in thinking and memory were subsequently observed. Such changes were reported by patients who received hormonal therapy as treatment for their breast cancer. A similarity was noted between symptoms reported by women treated with hormonal therapy and women going through the menopause.

More recently, it was observed that even patients who received neither radiation to the brain nor hormonal therapy also had certain complaints of impairment in mental function. This resulted in the appreciation that chemotherapy was also capable of inducing these symptoms and thus, the expression “chemobrain” was coined.

The symptoms of this syndrome are varied and include: (1) a decrease in recall and memory, (2) the inability to concentrate on a task, (3) a feeling of being in a mental fog, (4) the inability to remember basic facts such as dates and names, (5) difficulty remembering common words, (6) inability to complete a sentence, (7) the inability to perform several tasks simultaneously—multitasking, (8) the inability to learn new skills, (9) a feeling that the mind is slower and less organized, and (10) performing tasks at a slower pace.

The symptoms of chemobrain can develop during or after therapy. The reported incidence of chemobrain ranges widely from a few percent to 70% of patients treated. It is difficult to quantify in part because it depends on how one classifies and measures chemobrain. For most patients who develop chemobrain, it is temporary, resolving from six months to two years from onset. For a minority, it is a long term issue.

It is unclear at present whether certain chemotherapy drugs are more likely to cause this problem versus other drugs. Likewise, it is unclear whether the combination of chemotherapy and hormonal therapy are more likely to result in chemobrain versus either type of drug alone. Patients who receive high doses of chemotherapy, such as have been used as part of a bone marrow transplant, appear more likely to experience this problem.

The diagnosis of chemobrain is difficult to make since there is no specific test that can be performed to establish the diagnosis. There are many other medical events that mimic chemobrain and/or co-exist with chemobrain. These include: (1) cancer, (2) other drugs such as anti-nauseants, steroids, anesthesia, sedatives, antidepressants and others, (3) low blood counts, (4) fatigue, (5) poor sleep, (6) other medical conditions such as diabetes, high blood pressure, infections, (7) hormonal changes such as reduced estrogen levels, (8) the use of hormones, (9) nutritional deficiency, (10) aging, and (11) emotional states such as increased stress, anxiety, fear, and depression.

Attempts to measure the effects of chemobrain have had limited success. For many patients, the symptoms are sufficiently mild and non-specific as to make it difficult to measure anything different. Often, baseline levels of mental functions are lacking for affected individuals so, it is not clear how much of the noted symptoms might have been present before therapy. It is also not clear whether there are types of patients who are more prone to develop this side effect. Some believe that this syndrome is more apparent in people who are more “high functioning.” What is clear, is that these symptoms are disturbing and disruptive to a person’s life. These symptoms can interfere with activities of daily living, work performance and school performance. It has also become clear that these symptoms are real and not imagined by the patient.
At present, there are no reliable preventive strategies; nor, are there good therapies. It is important to correct other confounding issues such as depression or poor sleep, keeping in mind that drugs with a sedative quality can further interfere with mental functions. The drug modafinil (Provigil) has been used with modest results.

Certain behaviors can be helpful especially with memory function such as keeping lists of important dates and things to do. Maintaining a routine such as always placing the keys and purse in specific places can also be useful. In my own practice, I have found that simply informing family and coworkers of your situation can be helpful as they can be enlisted to help you with things you may not easily remember. It is important to keep in mind that the symptoms of chemobrain are temporary and improve with time.

Considerable research is now being devoted to this problem. Special scans are now available that allow visualization of brain function. Prospective trials are underway to distinguish between the effects of chemotherapy versus hormonal therapy. Whether different chemotherapy drugs have different effects on the brain is also being investigated. Various drugs are being studied that may reduce or prevent chemobrain. If such studies are available in your area, I encourage you to participate.

FDA-approved biological product. Zarxio’s parent product is filgrastim (Neupogen), a drug used to increase the body’s ability to produce white blood cells. Filgrastim, itself, is a man-made version of a naturally occurring protein known as granulocyte-colony stimulating factor (G-CSF). This approval pathway was established to expedite the drug approval process, and requires less product-specific data than the FDA’s traditional regulatory channels. It accepts efficacy and safety data from the previously approved reference drug.

The new drug is being developed by Sandoz Biopharmaceuticals, a division of Novartis. It is manufactured using recombinant technology in cells from the E. coli bacteria. Approval of Zarxio was based on results from multiple studies including 2 clinical trials. One of these studies and perhaps the most clinically relevant was the double-blind phase III PIONEER trial that compared the efficacy and safety of Zarxio with the U.S. licensed formulation of Neupogen in breast cancer patients treated with six cycles of Taxotere/Adriamycin/Cytoxan chemotherapy. The data presented demonstrated that the two agents, Neupogen and Zarxio, gave similar results in their ability to control white blood cell counts. Side effects were also similar.

The data were previously presented in January, 2015, and reviewed by the Oncology Drug Advisory Panel (ODAC) - a group of experts who serve in an advisory capacity to the FDA. The panel voted unanimously to recommend approval of Zarxio.

Sandoz already distributes a biosimilar version of filgrastim under the brand name Zarzio in over 40 countries including many in Europe. In some countries there is a suggestion that the use of biosimilar products has reduced health care costs. Whether this will be the result in the U.S. is the question. We can certainly anticipate other biological products to fall under the category of “biosimilars” and to also seek FDA approval.
QUESTIONS AND ANSWERS

(Q) Dr. Martino, my father has recently been diagnosed with cancer of the pancreas. The only other person with cancer in his family is a brother with melanoma. There is no one in my father’s family with breast cancer. His oncologist has told him that he should consider being tested for the breast cancer genes. Our family does not understand why the doctor has made this recommendation. Can you help us?

(A) I believe that your father’s oncologist is aware that the breast cancer genes, particularly BRCA2, predict not only for breast cancer, but also predict a higher risk of ovarian cancer, prostate cancer, melanoma, pancreatic cancer and others. The doctor was likely made suspicious by recognizing that two brothers, one with melanoma and one with pancreatic cancer may share a common gene as the cause of their cancers. This is especially so if the family is of Ashkenazi Jewish descent, either of the brothers were relatively young at their diagnosis and also if there are only a few women in the family who might have developed breast or ovarian cancers. I would consider the oncologist’s advice. Based on your father’s results, other members of his family, yourself included, may also need to be tested.

(Q) Dr. Martino, one of my closest friends was recently diagnosed with a recurrence of breast cancer. We have always been very close and done many things together. Now I find that she is shutting me out. She tells me that she is too tired to do things with me. She does not always answer my calls or emails but has her husband do it for her. I want to be helpful to her, but she is making it very difficult. What can I do?

(A) Perhaps the first thing you can do is understand that, at least for now, life has changed for your friend. A recurrence of cancer is always very frightening not only for the person but for their entire family. She probably is very tired and does not have the energy she had before either physically or emotionally. She and her family need time to adjust to this new reality. Give her space. Let her know that you care for her and want to be helpful and ask her in what manner you can be most helpful to her. She may not have the time or energy to do the things you enjoyed together such as shopping or socializing. Offer to do things that may relieve her of some burdens such as driving her children to events or doing her laundry or providing meals. Realize that her needs are different now. Above all, do not feel offended by her change in behavior. She still needs your friendship, but it may take a different form now.

INTERVIEW

As you may have already observed, I have become more passionate about health maintenance with physical exercise, proper diet, and weight control. Though these elements are most often viewed as ways to prevent disease, I think that they are equally as important once there is a diagnosis of an illness such as cancer. I also strongly believe because of my own personal experience, that having a guide or a personal trainer has clear advantages. There are exercise therapists that specialize in working with cancer patients. Ms. Lewis is such a therapist. What follows is an interview that I did of her so that we could better understand what this field entails.

Becoming a Cancer Exercise Specialist (CES), With Ms. Nadja Lewis

Dr. Martino: Ms. Lewis, in the past you have been my personal trainer and have contributed to the Breast Cancer Advisor. Since you and I were together, I am aware that you have trained as a Cancer Exercise Specialist. I did not know that there was such a specialty within your field. Please tell me what motivated you to obtain this additional training?

Ms. Lewis: Being a Certified Personal Trainer brings me great pleasure. As I studied and earned additional certificates -
(Senior Fitness Specialist), (Brains and Balance Specialist), I felt good but still kept wondering, how can I reach others? Who really needs help? The answer - cancer patients!

**Dr. Martino:** Can you explain what is involved in acquiring this certification?

**Ms. Lewis:** In order to become a Cancer Exercise Specialist, one must possess the following prerequisites/qualifications:

- An accredited health/fitness related certification
- Adult CPR/AED certification
- Bachelor’s Degree (in any field) with at least 500 hours of experience training older adults or individuals with chronic conditions
- Adequate knowledge of, and skill in, risk factor identification, fitness appraisal, exercise recommendations, and basic nutrition

Training to become a CES is not an easy task. One must gain in-depth knowledge of the cancer process including:

- Incidence and prevalence of the most common cancers
- Common forms of cancer treatment and side effects
- The benefits of exercise after a diagnosis of cancer
- Exercise testing, prescription, and programming
- Nutrition and weight management

Special emphasis is given to the topic of lymphedema; how to identify, prevent, and manage it. Also, there is added emphasis on exercise for breast cancer survivors.

To be an effective CES, one has to really learn about the entire cancer process - from diagnosis, to all stages of cancer treatment, possible side-effects, reconstructive procedures, and how they apply to and/or contradict exercise programming.

In order to ensure ongoing competency and to maintain a high standard for qualified professionals, CES qualifications must be renewed every two years.

**Dr. Martino:** Are there cancer patients most suited for physical fitness? Will you work with certain particular types of patients or is it simply anyone who is interested?

**Ms. Lewis:** A CES will design an exercise program for people dealing with cancer, no matter what the stage may be; just diagnosed, undergoing treatment, and/or after treatment/surgery. As a CES, I want to make sure that cancer survivors realize they no longer have to just sit back and accept that they have limitations. Exercise will help patients who have limited range of motion, poor posture, chronic fatigue, and lymphedema to name a few. Consistent exercise can help them improve a great deal.

I wanted to become a CES to offer cancer patients a chance for hope, a chance to feel better, and a chance to possibly keep some cancers away. I will work with any patient, once we have received the doctor’s approval.

**Dr. Martino:** As a CES, is it only exercise that you deal with, or are there other aspects of health that are part of your training?

**Ms. Lewis:** As you know Dr. Martino, a good diet is essential. Consistent exercise and a healthy diet go hand in hand. A CES will help their clients understand the value of certain foods, which foods they should avoid, and which ones are essential. There are three main nutritional goals for someone living with cancer:

1. To maintain a healthy body weight
2. To find a nutritional plan that will supply the body with enough fuel and nutrients for repair and healing, that will also aid in the body’s ability to eliminate toxins
3. To prevent recurrence of cancer and the development of a second malignancy

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Dr. Martino: Cancer and cancer treatments tend to take a lot of energy from a patient. When do you suggest patients start an exercise program? Is it best to wait until their therapy is over?

Ms. Lewis: The side effects of treatment often contribute to inactivity on the part of cancer patients, which can lead to secondary disabilities (disabilities not directly related to cancer or its treatment). These can include lack of strength and fatigue. It is important to note that the best time to start an exercise program is as quickly as possible, right after getting the doctor’s approval. Too many patients make the common mistake of waiting to ‘get/feel better’ which in turn prolongs the recovery process. Many cancer patients lose muscle strength due to lack of use. This is especially common in breast cancer patients. Moderate strength or resistance training will help to rebuild muscle mass and strength.

Dr. Martino: Not everyone can lift weights or handle intense exercise.

Ms. Lewis: That is correct; a CES will prescribe exercises specific to the individual and their medical condition.

Dr. Martino: Some patients, especially those with a diagnosis of breast cancer tend to gain weight after treatment.

Ms. Lewis: It is particularly easy to gain weight when you are inactive. Hormone use sometimes leads to weight gain as well. It is an absolute must to keep moving, stay active, and be careful of food choices. For many cancer patients, especially in later stages, weight loss and loss of muscle mass are the problem. Diet, like exercise, must be tailored to the patient.

Dr. Martino: Are there any exercise tips you care to share with our readers?

Ms. Lewis: There are several tips, here are a few:

- Rest is important, so listen to your body. When feeling tired, take a rest for a day, or do some gentle activities such as gardening or stretching.
- When your energy level is high, take advantage and exercise!
- To avoid injuries, proper form is critical when performing exercises. A CES, such as myself, can be a big help here.
- It is best to concentrate first on those body areas of greatest need. For example, women with breast cancer should focus on gaining flexibility and strength, in the arm and shoulder areas; while those with diminished bone density should really start with weight bearing exercises, such as brisk walking.
- Make water your best friend. Avoid dehydration; keep muscles pliable by drinking lots of water before, during, and after exercise.
- Exercise should be viewed as an ongoing journey to recovery. Make an appointment that cannot be broken with yourself to exercise as frequently as approved by your doctor.

Dr. Martino: Do you have any tips for doctors on this topic?

Ms. Lewis: Yes, each cancer patient has their unique set of needs and goals. Physicians and oncologists should do their part in encouraging patients to start being more active and more attentive to their diet. We know that doctors can be very influential and can motivate their patients.

Dr. Martino: Thank you, Ms. Lewis.

Ms. Lewis: Thank you.

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