

Cancer-Related Fatigue Facts

No. 3 in a series providing the latest information for patients, caregivers and healthcare professionals.

Highlights

- Estimates are that more than 50 percent of people who have cancer experience cancer-related fatigue (CRF). It is often said to be the most common and distressing symptom reported by people living with cancer.
- CRF interferes with a person's ability to fulfill daily responsibilities and to enjoy life. It is a health problem that requires appropriate medical management.
- Compared with fatigue that healthy people experience, CRF is more severe, particularly relative to the person's activity or level of exertion. CRF is also less likely to be relieved by sleep or rest.
- CRF often begins before cancer is diagnosed, worsens during the course of treatment and may persist for months, or even years, after treatment is completed.
- CRF is generally either attributable to effects of the cancer or to the cancer treatment (for example, chemotherapy, radiation, immunotherapy), although the specific cause of a person's CRF may not be identifiable.
- Signs of CRF may include physical weakness, changes in mood or motivation, withdrawal from social activities, irritability and impaired ability to perform daily activities, concentrate or make decisions.
- It is important for patients to talk with their doctors if they experience signs of fatigue before, during or after treatment. Assessing fatigue can be a challenge for a number of reasons, and good patient-doctor communication is key to successful evaluation.
- While there is no standard treatment for CRF, the first step is often to identify and treat any underlying causes of CRF (for example, anemia or poor nutrition) and any other contributing health problems. Problems such as heart, liver or kidney disease, pain, depression and anxiety may intensify CRF.
- A number of therapies are available that may help restore energy in a person who has a blood cancer. These therapies include exercise, psychological support, nutritional and dietary assessment, improved sleep habits and medications.

Introduction

More than half of the people diagnosed with cancer experience cancer-related fatigue (CRF), which is characterized by excessive and persistent exhaustion that interferes with daily activity and function. CRF often begins before cancer is diagnosed, worsens during the course of treatment, and may persist for months—even years—after treatment ends. Fatigue can be difficult to assess because there are no objective measurements.

Unlike the fatigue that healthy people experience from time to time, CRF is more severe, often described as overwhelming exhaustion that cannot be overcome with rest or a good night's sleep. Many patients with leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma, myeloma or myeloproliferative diseases find CRF to be more distressing and disabling than other cancer-related symptoms such as pain, depression and nausea.

Although some doctors, caregivers, and people living with cancer consider CRF to be an inevitable part of cancer and its treatment, there are steps that people can take to ease fatigue. Medical treatment, regular exercise, good nutrition, psychological support, stress management and other lifestyle changes can help a person feel more energized and better able to cope with fatigue.

If untreated, CRF can negatively affect a person's physical and emotional well-being and quality of life. Fortunately, CRF awareness is growing, and research is uncovering treatments to help minimize or relieve fatigue. In addition, leading health organizations such as the National Institutes of Health and the National Comprehensive Cancer Network (NCCN) have called for better assessment and management of CRF as an integral part of quality, comprehensive cancer care.

This fact sheet addresses some common questions that people may have about CRF—likely causes, how it is measured, treatment options and self-care tips. As with any cancer-related symptom or side effect of treatment, it's important for individuals to tell members of their oncology team if and when they feel exhausted.

Causes of Cancer-Related Fatigue

CRF may arise due to

- The disease itself
- Treatment (for example, chemotherapy, radiation, surgery, immunotherapy, medications).

Fatigue Related to the Disease Itself. Blood cancer may cause or contribute to CRF. The exact biochemical or physiologic reasons for this are unclear and are the focus of ongoing investigation. Studies show that natural chemicals called “cytokines” may play a role. These substances are released by cancer cells when they die and are biomarkers of inflammation. Prolonged inflammatory responses can lead to fatigue.

Researchers are also investigating whether disruptions to the circadian rhythm (an approximately 24-hour sleep-wake cycle), impaired immune system functioning, disruptions in the production of serotonin (a hormone that influences a person's sense of well-being and helps regulate mood, anxiety and sleep) or problems involving the neuroendocrine system (the interaction between the nervous system and the hormones of the endocrine glands) might play a role.

Fatigue Related to Cancer Treatment. Fatigue is a side effect associated with a number of blood cancer therapies. A person who receives chemotherapy or other anticancer drugs, radiation therapy, and/or stem cell transplantation generally experiences some degree of fatigue.

CRF typically recedes in the months following treatment, but may be an ongoing problem. Changes in a person's routine resulting from treatment, and any financial stress that may be associated with cancer treatment, may also contribute to fatigue. See the free LLS booklet *Understanding Drug Therapy and Managing Side Effects* for more information about medications used to treat blood cancers and their possible side effects. The free LLS booklet *Financial Health Matters* may also prove to be useful.

Predisposing Factors in Cancer-Related Fatigue

The NCCN has identified several factors that contribute to, or are intensified by, CRF. Many of these factors respond to medical management.

- Anemia (decreased number of red cells)—Anemia leads to decreases in the body's supply of oxygen, nutrients and energy, causing a person with anemia to feel tired.
- Poor nutrition—Many cancer patients are at risk for nutrition-related problems due to loss of appetite or side effects of treatment that may cause nausea, vomiting, diarrhea or diminished nutrient absorption. Poor nutrition can cause a person to feel listless and down.
- Loss of physical fitness—A person who is overly tired is less likely to engage in physical activity; reduced physical activity leads to loss of muscle mass, which increases the exertion needed to perform basic activities.
- Sleep disturbances—More than half of patients with cancer have trouble sleeping, with one in four patients with cancer reporting moderate or severe symptoms of disordered sleep.
- Emotional distress—Coping with a cancer diagnosis can also contribute to fatigue and can disrupt sleep. Concentrating on and absorbing a great deal of new information, making decisions and coping with anxiety and depression can also create extra demands for energy.
- Pain—People who have blood cancer may experience pain that can disrupt sleep, limit activity, and intensify fatigue. In addition, many opioid analgesics (strong prescription pain medications) may cause changes in the body that contribute to fatigue. For information about pain management see the free LLS fact sheet *Pain Management*.
- Other health issues—Coexisting health problems (for example, an underactive thyroid; infection; problems with heart, lung, kidney, or liver function; or neurologic problems) may also cause or worsen fatigue.

Signs and Symptoms of Cancer-Related Fatigue

People with cancer who suffer with fatigue typically feel mentally and physically defeated; many are very hard on themselves because they are less active than they were before diagnosis and/or treatment. Other signs of fatigue include depressed mood or other mood changes; physical weakness; lack of motivation; avoidance of social activities; irritability; and impaired ability to concentrate, carry out normal daily activities or make decisions.

Signs of fatigue that may be evident from a medical history and physical examination or from laboratory tests include

- Difficulty climbing stairs or walking short distances
- Shortness of breath
- Anemia
- Weight gain or loss
- Intolerance to cold
- Changes to hair or skin
- Sleep disturbance
- Pain
- Muscle weakness
- Loss of sexual desire.

Fatigue can also be reflected in mood, cognition and social changes:

- Depressed and/or anxious mood
- Lack of motivation
- Negative thinking
- Inability to concentrate
- Clumsiness
- Loss of memory or mental alertness
- Withdrawal from leisure/social activities
- Unusual strain in relationships.

Coping with CRF and other symptoms can be frustrating, but there are steps that people with cancer can take to boost their energy and spirits. See *Take Care of Yourself* on page 8 for some ideas to ease fatigue and support overall wellness. See the free LLS booklet *Each New Day: Ideas for Coping with Blood Cancers* for more useful information and tips.

Assessing Cancer-Related Fatigue

CRF can affect a person's body, mind and spirit. It is important for patients to talk with their doctor if they experience signs of fatigue before, during or after treatment.

Assessing CRF can be challenging because

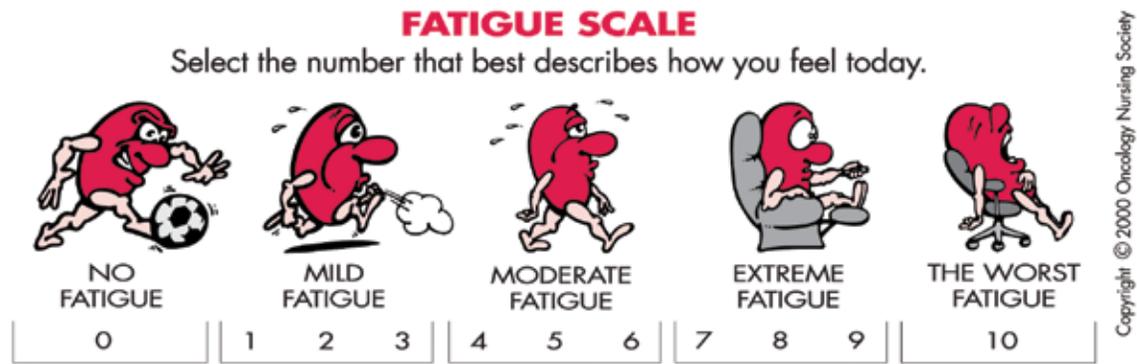
- Fatigue can fluctuate throughout the day and between treatments
- Distinguishing fatigue from other problems (for example, anemia, depression, anxiety) may be difficult
- Many patients believe that fatigue is an inevitable part of cancer treatment and do not mention it to their doctor
- Some patients may worry that addressing their fatigue could distract the doctor from treating the cancer, or they may worry that their fatigue is a sign of disease progression or a recurrence.

As with other cancer-related symptoms, such as pain, CRF is not necessarily an unavoidable part of a person's cancer journey. Treatment and lifestyle changes can make a difference and help improve energy levels.

The first step in assessing CRF is to identify and address any underlying physical problem, such as anemia, infection or treatment side effects that might be causing fatigue. While there are no lab tests to screen for CRF, doctors may decide to order one or more of the following tests to help identify potential causes:

- Complete blood count
- Transferrin level
- Total iron-binding capacity
- Ferritin level
- Iron level
- Folic acid level
- Vitamin B₁₂ level
- Thyroid function
- Corticosteroid or adrenocorticotrophic hormone level.

Doctors use a variety of other methods to assess CRF, including tools that take into account the patient's description of the presence and severity of fatigue, such as the Fatigue Symptom Inventory and the Oncology Nursing Society Fatigue Scale on page 6.



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These and other tools are designed to assess the severity, frequency and daily pattern of fatigue, as well as how it interferes with quality of life. A doctor may ask, “Since your last visit, how would you rate your worst fatigue on a scale of 0 to 10?” (0 = not at all fatigued; 10 = as fatigued as I could be).

Good patient-doctor communication is key to successful evaluation. It can be helpful for people living with cancer to note and report symptoms of fatigue at each doctor visit. Tell the doctor if the fatigue is

- Worse at certain times of day
- Associated with certain cancer therapies
- Worse or improved with certain activities.

Sleep patterns and any past treatments for fatigue are also useful information to share with the doctor.

Treatments for Cancer-Related Fatigue

Medications that relieve certain treatment side effects, such as nausea or loss of appetite, may improve sleep and nutritional status and, as a result, minimize feelings of fatigue. A combination of drug and nondrug treatments described below is often recommended.

Nondrug Options. A growing body of evidence suggests that physical exercise (walking, swimming, yoga, resistance training) and interventions that reduce stress and increase psychosocial support (counseling, stress management, coping strategies) can help reduce fatigue and increase energy levels. Exercise works by maintaining or building a person’s stamina and strength. Another theory is that by increasing circulation, exercise may reduce cytokines and other harmful substances in the body that can exacerbate fatigue. Randomized trials have shown that cognitive-behavioral strategies such as progressive muscle relaxation or relaxation breathing may improve CRF in those receiving radiation therapy or hematopoietic stem cell transplantation.

Other nondrug therapies currently in clinical studies include meditation, nutrition, various energy therapies that use gentle human touch to balance the flow of energy in the body, mindfulness-based stress reduction and restorative yoga. Research is ongoing to determine the usefulness of these approaches—alone and in combination—in relieving CRF.

Medications. While medications play a role in managing CRF, there is no consensus about which drugs are useful. Studies show that those who take drugs used to stimulate the central nervous system or to boost hemoglobin levels (for cancer patients with anemia) have greater improvements in CRF compared with those who received a placebo.

- Erythropoiesis Stimulating Agents (ESAs)—ESAs stimulate the body to make red cells. The ESAs epoetin alfa (Epogen[®], Procrit[®]) and darbepoetin alfa (Aranesp[®]) are drugs given by injection that are approved to treat chemotherapy-induced anemia. Recent safety concerns about the use of these drugs in certain cancer patients have resulted in revised guidance about their use from the US Food and Drug Administration (FDA). A cancer patient who is undergoing chemotherapy and is prescribed an ESA will be given information about the drug that will serve as a starting point for discussion with the doctor about the benefits and risks of taking an ESA.
- Psychostimulants—Because many people with cancer have sleep complaints, drugs that stimulate the central nervous system are of interest. Psychostimulants have been found to enhance alertness and reduce fatigue in people with multiple sclerosis and HIV infection. Although there is some data that supports the use of methylphenidate (Ritalin[®], Methylin[®]) or dexamethylphenidate (Focalin[®]) in the treatment of CRF, research is under way to address the question of whether methylphenidate is better than placebo in treating CRF. Common side effects of methylphenidate include irritability, anorexia, insomnia, nausea and rapid heart rate.
- Antidepressants—Studies have investigated two antidepressants in CRF: paroxetine (Paxil[®]) and bupropion (Wellbutrin[®] SR). Paroxetine is a selective serotonin reuptake inhibitor (SSRI) that appears to improve mood but does not reduce CRF in those receiving chemotherapy. This suggests that the underlying causes of fatigue and depression are distinct. Bupropion, which has been used to treat chronic fatigue syndrome and fatigue associated with multiple sclerosis, was associated with improvements in fatigue scores within 2 to 4 weeks of the start of treatment during an open-label study. Further research through randomized controlled trials is needed to better understand the relationship between depression and fatigue in people with cancer, as well as the usefulness of antidepressants in CRF.
- Corticosteroids—A recent review of four studies using progestational steroids found no benefit to patients with CRF after 8 weeks of treatment with these agents.

Under Study. Clinical trials with other medications and supplements including American ginseng, coenzyme Q10, L-carnitine (an amino acid supplement) and modafinil (Provigil[®]) are currently under way. There is little research on sleep drugs in people with cancer, which many experts say should be an area of inquiry.

Take Care of Yourself

Here are some suggestions that may help a person with CRF feel better.

Be Flexible. Don't measure yourself by prediagnosis energy levels. Set realistic goals. Allow yourself to shift your focus from fatigue (and what you may not be accomplishing) by listening to music, reading a book, meeting friends, watching a movie or going for a walk or a car ride.

Stay Active. Staying physically fit may help some people to ease fatigue. If you don't already have an exercise regimen, begin one gradually and aim to exercise at least three times a week, and adjust your routine if you feel overly tired. Focus on activities that will help you gradually build strength but don't deplete your energy level. Light exercise, such as walking, can also help you relax and sleep better.

Practice Good Nutrition. Patients with cancer are at risk for malnutrition and other problems resulting from either the cancer or the body's response to treatment (for example, loss of appetite, nausea, vomiting and malabsorption of nutrients in the foods you eat).

Eat a balanced diet that provides sufficient calories, protein, vitamins and minerals. Iron intake is important, so try to consume iron-rich foods such as green leafy vegetables and red meat. Maintain energy levels by eating frequent small meals or snacks throughout the day. You may find it useful to work with a dietitian to map out an eating plan to suit your caloric needs and to learn about easy to prepare, healthful meals. You should also drink plenty of noncaffeinated liquids to help eliminate toxins associated with treatments that may cause fatigue.

Consult your doctor for guidance about diet, exercise and daily activities. For more information about eating well, see the free LLS publication *Food and Nutrition Facts*.

Manage Stress. The effects of stress can be offset in part through exercise, relaxation techniques, meditation, spiritual and/or religious practices, socializing and counseling.

Address Sleep Habits. These suggestions may help improve sleep quality:

- Relax before bedtime by taking a warm bath or shower, meditating, or listening to calming music
- Go to bed at the same time every night
- Use the bedroom for sleep only and keep the room cool, quiet and dark
- Use comfortable bedding and sleepwear
- Avoid caffeine, alcohol and stimulation before bedtime
- Forgo long daytime naps that can interfere with nighttime sleep.

Ask for Help. Ask for help with routine tasks such as shopping, cooking, housekeeping, laundry or driving. Rest when you feel tired.

Plan Ahead. Schedule treatments for those times that will have the least effect on your job or other activities. For example, many patients who work find that scheduling treatment in the afternoon or at the end of the week enables them to be the most productive at their jobs.

Keep a Journal. Keep track of your fatigue, including severity (on a 0 to 10 scale), timing, duration, activities or treatments that make it worse or better, and how it interferes with daily activities. A detailed record—which includes your fatigue symptoms such as tired legs or eyes; poor concentration; weakness or sleepiness; shortness of breath after light activity; difficulty performing tasks such as cooking, cleaning, taking a shower or making the bed; irritability or impatience—will help you discuss possible causes, treatments and coping strategies with your doctor.

Also note daily activities, medications and treatments, eating and sleeping habits, weight changes and financial stressors. Write down strategies that have worked to reduce fatigue, such as undertaking difficult tasks when your energy is highest, or pacing yourself and scheduling rest.

Seek Support. Support groups are comforting and informative for many patients and their families. The Leukemia & Lymphoma Society (LLS) can help with referrals to support groups and the First Connection program, which links newly diagnosed patients with similarly diagnosed cancer survivors.

We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the country and in Canada. To find the chapter nearest you, visit our Web site, www.LLS.org, or contact

The Leukemia & Lymphoma Society

1311 Mamaroneck Ave.

White Plains, NY 10605

Information Resource Center (IRC): (800) 955-4572

Email: infocenter@LLS.org

Callers to the Information Resource Center may speak directly with an Information Specialist, Monday to Friday, 9 a.m. to 6 p.m., ET. You may also contact an Information Specialist by clicking on Live Help (10 a.m. to 5 p.m., ET) at www.LLS.org or by sending an email. Information Specialists can answer general questions about diagnosis and treatment options, offer guidance and support, and assist with clinical trial searches for leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative diseases. The LLS Web site has information about how to find a clinical trial, including a link to TrialCheck®, a clinical trials search service provided by LLS.

LLS also provides fact sheets and booklets that can be ordered by phone or through Free Materials on the Web site.

Other Resources

Oncology Nursing Society (ONS) Web Site

An information service, including information about fatigue, for oncology nurses, other healthcare professionals, people with cancer and their families and friends.

866-257-4ONS (866-257-4667)

www.cancersymptoms.org/fatigue/index.shtml

National Comprehensive Cancer Network

888-909-6226

www.nccn.org

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