

Side Effect Management in Lymphoma

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably.

The body has two main types of lymphocytes: B lymphocytes (B cells) and T lymphocytes (T cells). Cancerous lymphocytes can travel to many parts of the body (including the lymph nodes, spleen, bone marrow, blood, or other organs) and may form a mass called a tumor.



SIDE EFFECTS OF TREATMENTS

Lymphoma is often painless and asymptomatic early on, but it can cause symptoms including swollen lymph nodes (for example, in the neck, armpits, or groin), fever, drenching night sweats, drastic and unexplained weight loss, fatigue, and discomfort, among other symptoms. Treatments for lymphoma, including chemotherapy, monoclonal antibodies, immunotherapy, radiation, and steroids often have side effects. Each patient is different, so the side effects that occur and how severe they are may be different as well. Some patients experience many side effects and others have very few, but nearly all patients will experience some. Side effects may vary based on treatment, lymphoma type and stage, and the patient's age, other medical conditions, and overall health status. Although most side effects are temporary and resolve after therapy, they can cause a great deal of distress.

Chemotherapy drugs kill cancer cells, but these drugs may also kill healthy cells. When healthy cells in the bone marrow are killed, it can cause side effects such as anemia (low red blood cell counts), thrombocytopenia (low platelet counts), and leukopenia (low white blood cell counts). Thrombocytopenia may increase the risk of bleeding. Leukopenia decreases the ability of the immune system to fight infection, making patients more prone to infection. Anemia may lead to symptoms of fatigue, shortness of breath, or dizziness.

Chemotherapy can be physically demanding and may cause:

- Changes in smell and taste
- Mouth sores
- Diarrhea
- Nausea and vomiting
- Fatigue
- Weight loss
- Hair loss
- Constipation
- Nerve pain

Monoclonal antibodies (a type of immunotherapy, which helps promote the body's immune response against the lymphoma) commonly have fewer side effects than most cancer treatments, but they can affect normal cells as well as cancer cells. This can lead to an increased risk of infection, allergic reactions, fever, chills, weakness, headache, nausea/vomiting, diarrhea, low blood pressure, chest tightness, and rashes.

Other types of immunotherapy, including antibody-drug conjugates, radioimmunotherapy (RIT), cytokines, immunomodulatory drugs (IMiDs), chimeric antigen receptor T-cell (CAR-T) therapy, and checkpoint inhibitors are also associated with various side effects. These may include anemia, arrhythmias, constipation, cough, diarrhea, fatigue, fever/chills, flu-like symptoms, itching, low blood cell counts, lung inflammation, neuropathy, nausea, pneumonia, rashes, shortness of breath, swelling, thinning hair, and upper respiratory tract infection.

Patients undergoing CAR-T therapy receive their treatment in the hospital where they can be closely monitored. Side effects include temporarily low blood cell counts, feeling tired (fatigue), and an increased risk of infection. In some patients, B cells are destroyed by the treatment in addition to the cancer cells, causing a condition called B-cell aplasia. B cells make antibodies that protect people from infections so when this happens, patients may need to periodically receive antibodies. The antibodies are given through a vein by intravenous infusion.

Two side effects that are potentially serious can occur after CAR-T therapy. These are cytokine release syndrome (CRS) and neurologic complications. CRS causes fever, rash, headache, body fluid shifts, and changes in blood pressure. Neurologic toxic effects can range from headaches to confusion, delirium, and seizures. The symptoms of CRS and neurological complications can occur within minutes or hours of beginning treatment, or may occur days to weeks later.

Radiation uses high-energy x-rays to kill cancer cells. Most side effects of radiation appear in the part of the body receiving the treatment, but radiation can also result in overall fatigue. Skin changes, such as pain, itching, or redness, almost always go away after radiation therapy is completed.

Steroids can cause a specific set of side effects including insomnia (not being able to fall asleep or stay asleep), increased appetite, mood/personality changes (feeling more irritable, angry, sad, or anxious than usual), weight gain, increased blood pressure, and increased blood sugar.

DIET

Diet is a key part of managing both lymphoma and the side effects of lymphoma treatment, as it provides the body with the nutrients and energy necessary for health. Many side effects can affect how patients feel about food and eating. Eating smaller meals more often rather than a few large meals each day may help patients feel less nauseous and make it easier to eat when appetite is diminished. Foods rich in carbohydrates such as starches can also help decrease nausea, whereas fatty foods may make nausea worse. Liquid nutritional drinks are a good way of getting enough vitamins and calories when patients have loss of appetite, nausea, or mouth sores. Drinking a lot of liquid is important for preventing dehydration, which often results from nausea, vomiting, and diarrhea. If drinking fluid is difficult, you can try sucking on ice chips.

During times when patients feel well enough to eat, a diet of fresh fruits and vegetables, protein, carbohydrates, and dairy products can help increase and maintain their strength and energy and improve their body's healing ability.

Avoiding particular foods can ease some treatment side effects. Certain foods may cause discomfort if patients have mouth sores from chemotherapy and radiation. Foods that are crunchy, salty, acidic (like citrus fruits), or spicy should be avoided. Dietary considerations are also important when a patient's sense of taste and smell changes. Some foods that were pleasurable before beginning cancer treatment may not be pleasurable during treatment and vice versa. In contrast, liquids or soft foods can make eating less painful if the patient has a dry mouth or difficulty swallowing solid foods. Use a blender to process solid foods and include puddings, ice cream, soup or soft fruits in your diet. It is important to experiment with different foods and find out what tastes good during treatment for lymphoma.

Dietary considerations are also important when white blood cell counts are low, which can result in the body having a harder time fighting infection. Avoid soft cheeses and cheeses with mold (such as brie, feta, or blue), and avoid raw or undercooked meat, fish, poultry, eggs, or tofu to reduce the risk of getting an infection. Wash fresh fruits and vegetables with soap to kill germs, and avoid fruits and vegetables that cannot be properly scrubbed and washed.

Some treatments can cause thinning of the bones and increase the risk of osteoporosis and fracture. It is important to reduce alcohol intake and eat foods rich in calcium and vitamin D. In addition, lifestyle changes like quitting smoking and engaging in weight-bearing exercises (like jogging or walking, if possible) are also important to reduce these risks.

Vitamins and dietary supplements may affect lymphoma treatment. Patients should let their doctor know if they are taking any vitamins, minerals, or herbal supplements. In addition, alcohol may be very irritating if the mouth is sore during cancer treatment. It may also affect the body differently during treatment or even interact with the chemotherapy drugs.

It is important for patients to discuss with their doctor whether drinking alcohol is safe in their particular circumstance. For more information, please view the Nutrition and the Integrative Oncology fact sheets on the Lymphoma Research Foundation's (LRF's) website at www.lymphoma.org/publications.

LIFESTYLE

Lymphoma and its treatments can cause fatigue. Changing routines may help accomplish daily tasks more easily. Prioritize the most important activities and let people who want to help do so. Planning chores or breaking down big tasks into smaller ones can help decrease tiredness. Remember that staying active and maintaining an exercise routine (as much as is comfortable) is vitally important for keeping the body as strong and energetic as possible. Try and keep regular sleeping habits, taking the time to fit in short naps (20 to 30 minutes) to help recharge the body and mind during the day. Enjoy what you do, but do it in small increments with breaks for rest.

Intimate relationships may be affected during and following diagnosis and treatment for lymphoma. Intimacy can be impacted by psychological factors (such as changes in body image and increased emotional strain) as well as physical changes (such as fatigue, pain, and vaginal dryness). Patients may experience changes in all, some, or none of the phases of sexual response (desire, arousal, orgasm, resolution). Open communication, time, and patience are important while finding the most helpful remedy. Patients should discuss with their healthcare team what sexual changes patients tend to experience during and after treatment and what can be done to prepare for and manage these changes if they occur.

If white blood cell counts are low as a result of chemotherapy, avoiding people who are coughing, sneezing, or known to be ill can help reduce the risk of infection. Avoid crowds during outbreaks of flu and other communicable diseases. Washing hands or using a hand sanitizer after visiting public places or touching items used by others is important. Patients should let their doctor know if they develop a fever during chemotherapy, as this may be a sign of an infection. Vaccination during chemotherapy or radiation therapy should generally be avoided because response to the vaccine may be decreased. Talk with your doctor and healthcare team to receive their specific recommendations for vaccination and timing, particularly for the flu and COVID-19 vaccines.

Cancer and cancer therapy may also affect thinking, memory, concentration, and attention. This is sometimes referred to as "chemo brain" or "brain fog". Modest lifestyle modifications may be helpful, like keeping simple notes in a notebook, setting up reminder lists, following structured routines, and, if necessary, delaying important decisions or tasks that require intense concentration. Exercising the mind with puzzles and brain teasers helps as well. Physical exercise and sufficient sleep may also be helpful.

Some treatments may also cause problems with nerve function (neuropathy), which commonly start as numbness/tingling in the hands or feet. If this is the case, be careful while handling cutting objects and hot liquids to reduce the risk of injury. Walking slowly and hanging on to handrails, putting no-slip mats in the bathtub and wearing footwear with rubber soles can also help to reduce the risk of falls.



MEDICATIONS AND PRODUCTS TO MANAGE SIDE EFFECTS

GASTROINTESTINAL SIDE EFFECTS

Nausea and vomiting are well-known side effects of chemotherapy and can sometimes be severe. Nausea and vomiting can prevent patients from doing the things they want to do, and they can even interfere with or halt treatment. For chemotherapy regimens that commonly cause nausea, anti-nausea medications (antiemetics) are often used preventively with each chemotherapy cycle. Examples of antiemetic drugs used prior to chemotherapy include 5-hydroxytryptamine type 3 receptor antagonists (like granisetron [Kytril], ondansetron [Zofran] and palonosetron [Aloxi]), dexamethasone (or equivalent), and neurokinin 1 (NK1)-receptor antagonists (like aprepitant and fosaprepitant [Emend]). The goal is to prevent nausea from occurring in the first place. If nausea or vomiting does occur, it is important to take the anti-nausea medications soon after symptoms start to prevent them from becoming severe. Patients should let their doctor know about their nausea or vomiting, as additional medications can be used to relieve and prevent both nausea and vomiting.

Both diarrhea and constipation can also be side effects of chemotherapy and radiation. These symptoms may be prevented or treated with medications, so it is important that patients discuss these symptoms with their doctor or nurse as well.

MOUTH SORES

Certain cancer treatments can result in mouth sores or ulcers in the lining of the mouth, gums, tongue, or lips. Dehydration, poor mouth care, oxygen therapy, alcohol or tobacco use, and insufficient nutrients may also cause sores. They can be painful and distressing and range from inconvenient to severe. Mouth sores can interfere with eating and drinking, and they can potentially become infected. Healing can take two to four weeks, which may interfere with the continuation of treatment.

Although there is no guaranteed way to prevent mouth sores, there are ways to reduce the risk of getting them and mitigating their effects. Resolve any dental issues with a dentist before beginning chemotherapy, as these can worsen once treatment begins. After starting treatment, please notify your physician prior to having any dental procedures. Frequent mouth sores may be caused by a herpes simplex virus, which can be treated with antiviral medications. Staying hydrated by drinking two to three quarts of water each day can help prevent sores. Sucking on ice chips during treatment and for the first half hour following treatment can help reduce the risk of mouth sores following some types of chemotherapy. If you develop mouth sores, drinking with a straw can help shield sensitive areas of the mouth. If it becomes difficult to use a soft bristle toothbrush due to sores and sensitivity, foam swabs are available to limit the irritation.

Avoid alcohol-containing mouthwashes, as this may dry out your mouth. Saltwater rinses or a combination of baking soda and warm water can be used instead. Whitening toothpastes should be avoided, as they contain abrasives that can irritate sores.

Rinsing with magnesium-based liquid medications (such as Maalox or milk of magnesia) can help promote healing of sores.

Some medications such as palifermin (Kepivance) stimulate the growth of cells on the surface of the mouth and may help the sores recover more quickly. There are also medications that coat the entire lining of the mouth to form a film, protecting against sores and minimizing pain during eating and drinking. Topical painkillers containing benzocaine (such as Anbesol or Orajel) can also help to numb sore areas. Other medications are available to decrease the pain or discomfort caused by mouth sores. There are also products that can help ease dry mouth to prevent mouth sores that may result from activities like tooth brushing and flossing. Patients should discuss their oral health with their doctor, dentist, and healthcare team prior to and during treatment to help prevent and manage any mouth sores that develop.

INSOMNIA

Insufficient sleep can impact energy levels, attention, cognitive function, and mood. Persistent insomnia has been associated with anxiety and depression. Insufficient sleep may also affect the immune system. Adequate sleep may even increase a person's pain tolerance. Many people with cancer experience sleep disturbances that can impact their quality of life. This can be due to pain, hospitalization, treatments, and/or the psychological impact of their disease. Difficulties with sleeping should be discussed with a doctor, as there are multiple approaches to improving sleep depending on the cause and the patient's preferences.

Not every medicine will work for everyone, but it is important to remember that there are many options, and it may take some time to find the right drug or treatment.

Meditation, guided imagery, deep breathing, reading, yoga, and listening to music can provide distraction from symptoms and help patients overcome insomnia.



PROTECTIVE CLOTHES AND ACCESSORIES

Chemotherapy can make the skin more sensitive to sunlight and increase the risk of sunburns or rashes. Hats, scarves, and wigs reduce sun exposure in patients with hair loss and can lessen the distress associated with hair loss, which can negatively impact self-image. It is important to wear sunscreen on sun-exposed areas when planning to spend a prolonged period of time in direct sunlight. During and after radiation treatment, carefully protect the radiation site from exposure to sunlight. It is most important to not become sunburnt.



RELAXATION TECHNIQUES

Mindful relaxation techniques, such as meditation and yoga, are often helpful for accessing inner energy and directing thoughts toward healing and health. Guided imagery works to lessen tension in the body caused by worry and replace it with positive images that might reduce pain and other side effects. These methods have also been shown to aid the recovery process by reducing pain, improving mood, attitude, self-image, and outlook. For more information, please view the Integrative Oncology fact sheet on the LRF's website at www.lymphoma.org/publications.

FOLLOW-UP

Patients with lymphoma should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required at various times during remission (disappearance of signs and symptoms of lymphoma) to evaluate the need for additional treatment.

Some treatments can cause long-term or late side effects, which can vary based on the duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these side effects during follow-up care. Visits may become less frequent the longer the disease remains in remission.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any side effects resulting from treatment or potential disease recurrences. LRF's award-winning Focus on Lymphoma app (www.FocusOnLymphoma.org) can help patients manage this documentation.

LRF'S HELPLINE AND LYMPHOMA SUPPORT NETWORK

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. The LRF Helpline staff members are available to answer your general questions about a lymphoma diagnosis and treatment information, as well as provide individual support and referrals to you and your loved ones. Callers may request the services of a language interpreter. A part of the Helpline is

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LRF's one-to-one peer support programs, Lymphoma Support Network. This program connects patients and caregivers with volunteers who have experience with lymphomas, similar treatments, or challenges, for mutual emotional support and encouragement. You may find this useful whether you or a loved one is newly diagnosed, in treatment, or in remission.

LRF FOCUS ON LYMPHOMA MOBILE APP

Focus on Lymphoma is the first app to provide patients and their caregivers with tailored content based on lymphoma subtype, and actionable tools to better manage diagnosis and treatment. Comprehensive lymphoma management, conveniently in one secure and easy-to-navigate app, no matter where you are on the care continuum. Get the right information, first, with resources from the entire Lymphoma Research Foundation content library, use unique tracking and reminder tools, and connect with a community of specialists and patients. To learn more this resource, visit our website at lymphoma.org/mobileapp, or contact the LRF Helpline at 800-500-9976 or helpline@lymphoma.org.

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and CLL/SLL including our award-winning mobile app. LRF also provides many educational activities, including our in-person meetings, webinars for people with lymphoma, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. To learn more about any of these resources, visit our website at www.lymphoma.org or contact the Helpline at (800) 500-9976 or helpline@lymphoma.org.

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