

Understanding Lymphoma and Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma (CLL/SLL)



Part 5 — Survivorship and Living with The Side Effects of Treatment

Part 5 — Survivorship and Living with The Side Effects of Treatment

Chapter 19: Common Treatment Side Effects

Patients being treated for lymphoma may experience various side effects or toxicities caused by their treatment. All treatments have the potential to cause side effects. Fortunately, medications and other treatment strategies can effectively prevent or lessen the severity of most side effects. Before beginning treatment, patients should ask their healthcare team about the most common treatment side effects and how to prevent and manage them. Once treatment has begun, patients need to tell their doctor, nurse, nurse practitioner, or physician assistant about all side effects they experience. This chapter explains why side effects occur, the types of side effects caused by different treatments, and steps for minimizing them.

What Is the Difference Between Long-Term Effects and Late Effects?

Long-term effects are toxicities that occur during cancer treatment and continue for months or years. Fatigue, symptoms of menopause (the time that marks the end of a woman's menstrual cycles) and neuropathy (nerve problems) are examples of long-term effects. In contrast, *late* effects of treatment appear only after treatment has ended—sometimes months, years, or even decades after treatment is completed. Infertility, osteoporosis (disease that thins and weakens the bones), heart problems, and secondary cancers are examples of late effects.

Why Does Chemotherapy Cause Side Effects or Toxicities?

Chemotherapy causes side effects because of the nonspecific way these drugs work, which means that they affect cancer cells but also some types of healthy cells. Most chemotherapy drugs work by killing cells that grow and multiply faster than typical cells. Cancer cells are one type of cell that multiplies rapidly, which is why chemotherapy can be effective at killing them. However, a few types of normal cells in the body also multiply quickly, including the cells in hair roots, the mouth, the gastrointestinal tract (stomach and intestines), and bone marrow (the spongy tissue inside the

bones), so these may also be damaged or killed by chemotherapy. Some chemotherapy drugs can also damage cells in other organs and tissues.

The type and severity of side effects caused by chemotherapy vary widely depending on the specific drugs that are given, an individual patient's tolerance, other medical conditions, and the length of time therapy is delivered. The same drug may cause no side effects in one patient, while in others it may cause very mild to very serious side effects. Other side effects do not occur until later and may become worse over time.

What Side Effects Are Caused by Chemotherapy?

Some of the most common side effects caused by chemotherapy used to treat patients with lymphoma include:

- Changes in taste
- Cognitive problems (trouble concentrating, impaired memory, sometimes called “chemo brain”)
- Constipation
- Decreased blood cell production (decreased red blood cells, hemoglobin, white blood cells, neutrophils, or platelets)
- Diarrhea
- Fatigue
- Hair loss
- Pain
- Heart damage (cardiotoxicity)
- Increased risk of infections
- Loss of appetite
- Lung toxicity (damage to the lungs)
- Mouth sores
- Nausea or vomiting
- Peripheral neuropathy (numbness or tingling in hands and feet)
- Problems with sexual function
- Sterility (inability to have children)

- Tumor Lysis Syndrome (TLS, a reaction to toxic substances released by dying cancer cells, which can damage the kidneys and other organs)
- Secondary cancers
- Change in skin and/or nails

Changes in Taste

Some patients receiving treatment experience a change in the way foods or beverages taste. Familiar foods may taste different (*dysgeusia*), or the flavors of foods may not taste as strong (*hypogeusia*). Some patients may also notice that foods have a metallic taste. These side effects are temporary and usually disappear after completion of chemotherapy.

Sometimes this side effect can be helped by dietary changes, such as eating foods that are frozen, cold, or at room temperature; adding extra seasonings or sugar to enhance taste and reduce bitterness; and avoiding metallic silverware.

Cognitive Problems

Chemotherapy can result in mild cognitive impairment, such as trouble concentrating, impaired memory, or issues with motor control (control over the body's movements) Some patients refer to these side effects as "chemo brain." Although these side effects can be stressful, they typically disappear over time.

Constipation

Constipation is a significant side effect observed in young and older patients with lymphoma. It can be severe in some of the regimens given to adolescents and young adults as a result of higher vincristine (Oncovin and others) doses. This can lead to nonadherence (not following directions) to regimens prescribed.

Decreased Blood Cell Production

Chemotherapy temporarily interferes with the ability of the bone marrow to produce enough red blood cells, white blood cells, and/or platelets (*myelosuppression*). Because of this, it is standard practice to space out the chemotherapy treatments and allow the bone marrow to restore its function.

To prevent and monitor myelosuppression, samples of a patient's blood are tested with a complete blood count (CBC) with differential, which measures the numbers of red blood cells and platelets, as well as all the different subtypes of white blood cells. These tests are usually done before and sometimes during the treatment process. Table 19.1 describes five of the most common conditions involving a decrease in blood cell production.

Table 19.1. Five Common Conditions Caused by Decreased Blood Cell Production

<p>Anemia</p>	<ul style="list-style-type: none"> ■ <i>Anemia</i> is a decrease in the number of red blood cells. ■ Many types of therapy cause mild or moderate anemia. ■ Anemia can make people feel tired and short of breath, especially when it is severe. ■ Drugs or red blood cell transfusions can be used in less common conditions where anemia is severe.
<p>Leukopenia</p>	<ul style="list-style-type: none"> ■ <i>Leukopenia</i> refers to a decrease in the number of leukocytes, or white blood cells. Leukocytes include lymphocytes (B-cells and T-cells), neutrophils, basophils, eosinophils, and monocytes. ■ Patients with low levels of neutrophils are at increased risk of infections.
<p>Lymphopenia</p>	<ul style="list-style-type: none"> ■ <i>Lymphopenia</i>, also called lymphocytopenia, refers to a decrease in the number of lymphocytes. Lymphocytes are white blood cells that produce antibodies and fight particular infections. About 20%-40% of white blood cells are lymphocytes. ■ Patients with low levels of lymphocytes are at increased risk of infections.

Neutropenia

- *Neutropenia* refers to a decrease in neutrophils, the primary type of white blood cells that fight bacterial infections.
- Patients with low neutrophil counts are at higher risk of serious and even life-threatening infections. Symptoms of infection often include fever and chills.
- During therapy, doctors regularly monitor the patient's absolute neutrophil count (ANC), the number of neutrophils in the peripheral blood. Because patients with an ANC below 500 cells per microliter are at particularly high risk for infections, doctors frequently modify or hold treatment in case of infection, until the ANC returns to 500 or greater.
- Some patients with neutropenia require treatment with antibiotics and hospitalization to prevent or treat infections.
- To avoid a patient missing a dose of therapy, doctors sometimes prescribe drugs like filgrastim (Neupogen, Granix, Zarxio) or pegfilgrastim (Neulasta, Fulphia) to reduce the duration and severity of neutropenia. These drugs can sometimes cause bone pain, which is usually temporary. Bone pain in the chest can mimic heart disease; patients experiencing unexplained chest pain should contact their doctor immediately.
- Unless contraindicated (not advised), bone pain can be managed with nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Advil and others) or naproxen (Aleve, Naprosyn), as well as the antihistamine loratadine (Claritin, Alavert). Acetaminophen (Tylenol) can also be used. Always ask your doctor about using NSAIDs, tylenol, or other medications.
- For patients with Hodgkin Lymphoma (HL), pegfilgrastim, filgrastim, and other white blood cell growth factors (substances that stimulate the growth of living cells) **SHOULD ALMOST NEVER BE GIVEN** to patients with early-stage HL receiving frontline ABVD. However, these substances can be given to patients with advanced HL who receive AVD-BV or AVD-nivolumab (Opdivo). Although these drugs can help to raise the ANC, they can also increase the chances that one of the chemotherapy drugs (for example, bleomycin) will cause lung problems. However, these growth factors can be given to patients who do not receive or who stop receiving bleomycin. Note that this is not generally a problem in the treatment of pediatric classical HL.

Thrombocytopenia

- *Thrombocytopenia* refers to a decrease in the number of platelets in the blood. Platelets help start the clotting process when bleeding occurs.
- Patients with low platelet counts may bruise easily; have cuts that bleed more or longer than usual; have nosebleeds or bleeding gums; or bleed from places that have not been injured.
- A platelet transfusion (the patient receives platelets from a donor through IV infusion) or certain medications may be needed if thrombocytopenia is severe or if the patient develops bleeding.

Diarrhea

Some types of chemotherapy may cause diarrhea. While most patients do not experience severe diarrhea, the most important point to remember is to stay hydrated. Signs of dehydration include dry mouth or skin, passing urine less often than usual, and feeling dizzy or lightheaded after standing up. The doctor should be contacted if the patient has bloody diarrhea, fever with diarrhea, or if the diarrhea lasts for a long time. Patients may follow the tips below.

PATIENT TIP

Avoiding Dehydration From Diarrhea or Vomiting

- Drink plenty of liquids (eight glasses a day), such as electrolyte replacement drinks like Gatorade, Pedialyte, and Powerade.
- Sometimes it helps to sip small amounts very frequently rather than to drink a full glass at once.
- Soup, especially broth, is a good source of both water and nutrients.
- Do not drink or eat dairy products because they can worsen diarrhea.
- Do not eat foods that are high in fiber or hard to digest because they can worsen diarrhea.
- Eat plenty of bananas and other high-potassium foods (after checking with your doctor or dietitian to make sure these foods will not interfere with your chemotherapy or other medications).
- Talk to your doctor before taking any over the counter anti-diarrheal medication. Take the medicines that your doctor recommends to control diarrhea or vomiting, and call your doctor if symptoms persist.

Fatigue

Fatigue is a common side effect of many therapies for lymphoma. Fatigue usually decreases after patients have completed their lymphoma treatment, but it can take weeks or months for patients' energy levels to return to normal. Patients may use the tips below to help them cope with fatigue.

PATIENT TIP

Coping With Fatigue

- Keep a diary to help keep track of when you have the most energy and which activities make you feel tired or give you energy. Use this to plan your activities for the times when you have the most energy.
- Ask for help with housework and other daily activities that are tiring.
- Exercise if your doctor says to do so, but do not overdo it. Try simple stretching and range-of-motion exercises or a short walk; these activities may energize you without tiring you out. Start slowly and build up to the level that is right for you. Ask your doctor, nurse, or physical therapist to help you create a personalized exercise plan.
- Rest and sleep during therapy are very important, but too much rest may decrease your energy levels. An afternoon nap helps some patients feel less tired for the rest of the day, but other patients cannot sleep at night if they nap during the day. If you have trouble sleeping, talk to your healthcare team to find out what you can do to get more rest.
- These symptoms usually improve once treatment is completed.

Hair Loss

Certain drugs can cause *alopecia* (thinning or loss of hair) anywhere on the body, including the scalp, eyebrows, eyelashes, arms, legs, and pelvis. The amount of hair loss varies.

When hair loss occurs, it usually starts two to six weeks after the first chemotherapy treatment. Remember that hair loss caused by chemotherapy is usually temporary; hair will most likely grow back after the end of treatment. When the hair first grows back, it may have a slightly

different texture or color than it had before treatment. Over time, the texture and color often return to how they looked before treatment started.

Loss of hair in the nose and nasal passages may lead to *rhinorrhea* (runny nose). Loss of eyelashes may make eyes more irritated and dry.

Patients may follow the tips below for managing chemotherapy-induced hair loss. However, it is important to understand that none of these measures have been shown to prevent hair loss.

PATIENT TIP

Managing Chemotherapy-Induced Hair Loss

- After washing your hair, pat it dry instead of rubbing it with a towel.
- Brush your hair with a soft-bristle brush or a wide-tooth comb.
- Do not use curlers or hair dryers
- Do not color or perm your hair or treat it with other chemicals.
- Use a hat or scarf to protect your scalp when you are out in the sun and to help keep you warm when you are indoors or outside in the cold.
- Many patients choose to wear a wig, scarf, turban, soft cotton hat, or head wrap to disguise hair loss. Some health insurance companies cover the cost of wigs with a doctor's prescription. Check your policy to see if it covers this cost.
- Some patients use caps to cool their scalp, before, during, or after chemotherapy to minimize hair loss during treatment. Discuss with your doctor the potential benefits and risks of using this approach as it may impact the effectiveness of treatment.

Pain

Patients may occasionally experience pain from the lymphoma itself or from the treatments and procedures. Pain is very treatable, and there is no reason for a patient to endure it without help. Patients should tell their doctors, nurses, nurse practitioners or physician assistants if they have any pain, because the healthcare team can help determine whether pain

is related to lymphoma, and potentially offer advice regarding medications and other ways to reduce and manage the pain.

Different types of pain are best controlled by different types of pain relievers, and some medications may not be appropriate for patients with lymphoma. The tips below may help for managing pain.

PATIENT TIP

Managing Pain

- Be specific when you describe your pain to the doctor or nurse
 - Where do you feel the pain?
 - When did the pain start?
 - What type of pain is it (sharp, dull, throbbing)?
 - Does the pain come and go, or is it steady? How long does it last?
 - How strong is it? Does the intensity change at different times?
 - Does anything make the pain feel better or worse?
 - Which drugs have you taken for the pain? Do they help? If so, for how long?
- Take your pain medication on a regular schedule, even if the pain seems to be better. Do not skip doses.
- Tell your family and friends about your pain so they can help you and understand why you may be acting differently.
- Try deep breathing, yoga, or other ways to relax.
- Ask to meet with a pain specialist or palliative care (special medical care for patients that aims to improve the quality of life and alleviate the suffering of patients with serious illnesses) specialist to help you find better ways to control your pain.
- Tell your doctor or nurse of any changes in your pain.

Heart Damage (Cardiotoxicity)

Cardiotoxicity refers to damage to cells in the heart or heart muscle. Long-term use of certain chemotherapy agents such as doxorubicin can cause cardiotoxicity in a small number of patients.

In general, most patients with lymphoma treated with potentially cardiotoxic chemotherapy, such as doxorubicin, receive these drugs at dosages that are not likely to cause cardiotoxicity. In addition, patients only generally receive doxorubicin during frontline chemotherapy and not later during treatment. This helps reduce their risk for developing chemotherapy-related cardiovascular disease.

A patient's history of heart disease, high cholesterol, or high blood pressure, as well as obesity and smoking and lack of exercise), may increase the chance of developing chemotherapy-related cardiotoxicity.

Careful monitoring by the healthcare team can reduce the chances of patients developing cardiotoxicity. Before deciding to treat patients with a cardiotoxic drug, most doctors order either an echocardiogram (ECHO, test that uses ultrasounds to check how the heart and nearby blood vessels are working) or a multigated acquisition (MUGA, test that looks at how well the heart is pumping blood by following a special marker injected into the bloodstream) scan to measure the patient's cardiac function (the ability of the heart to meet the demands of the body). These tests ensure that patients are prescribed a safe chemotherapy dosage given their current heart function. Patients with underlying conditions that put them at high risk of cardiotoxicity may also have their heart function monitored more intensively during the course of treatment for lymphoma.

Infections

Some lymphoma treatments can lower a patient's ability to fight infections, especially when they cause myelosuppression. Patients with a fever of 100.5°F or greater should contact the doctor or their healthcare team. Chills or a chilly sensation often comes before a fever. Patients should ask their provider what to do if they have a sore throat, rash, diarrhea, cough, or redness, swelling, or pain around a wound. The doctor should also be contacted if the patient experiences any painful local rash with or without blisters, as this could indicate an infection with shingles (herpes zoster).

To reduce the risk of infections, patients may be prescribed antibiotic, antiviral, or antifungal medications. Patients may be at increased risk for viral infections such as shingles, and sometimes doctors prescribe medication to prevent a shingles outbreak during therapy. If a patient has recurrent infections, the doctor may consider the prescription of gamma immunoglobulins, to boost the patient's immunity and help to fight the invading microbes (small living organisms such as bacteria and viruses). Other ways to reduce the risk of infections are included below.

PATIENT TIP

Reducing Infection Risk During Chemotherapy

- Check with your doctor to make sure your vaccinations are up to date before starting treatment.
- Wash your hands diligently and regularly.
- Avoid crowds, especially during influenza season (October–May in North America) and other outbreaks.
- Make sure all foods are thoroughly washed and/or cooked; avoid raw foods that may carry germs.
- Do not sleep with pets.
- Consider wearing a mask in certain situations

Generally, it is not recommended to receive a vaccine while undergoing chemotherapy although your doctor may recommend it in certain situations. Vaccines generate an immune response to provide long-lasting protection against a disease. During treatment for lymphoma, the immune system may be unable to generate an appropriate response to provide that protection.

However, infection with influenza (also called the flu) can be serious and life-threatening. To protect against influenza, a flu shot with inactive (dead) flu virus is recommended. Talk with your doctor and healthcare team to receive their specific recommendations for vaccination and timing, particularly for the flu and COVID-19 vaccines.

Loss of Appetite

Loss of appetite is sometimes a symptom of lymphoma itself, but it can also be a side effect of chemotherapy. Patients may eat less than normal, not feel hungry, or feel full after eating only a small amount of food. Ongoing loss of appetite can lead to weight loss and poor nutrition, which can become serious. Side effects from chemotherapy and other treatments, such as nausea and vomiting, mouth sores or pain, fatigue, depression, dry mouth, and difficulty swallowing can all contribute to a patient's loss of appetite.

The patient's healthcare team should be notified about lack of appetite to determine the underlying cause. Loss of appetite can sometimes be treated with drugs or by changing eating habits, such as eating several small meals each day and making nutritious food choices. Patients may wish to visit a nutritionist for additional tips. For more information about nutrition, please view the Nutrition fact sheet on Lymphoma Research Foundation's website at www.lymphoma.org/publications.

Lung (Pulmonary) Toxicity

Damage to the lungs is a serious side effect of the chemotherapy drug bleomycin (Blenoxane). Patients who are receiving ABVD, escalated BEACOPP, Stanford V, ABVE-PC or any other chemotherapy regimen that contains bleomycin should tell their doctor immediately if they experience cough, chest pain, or shortness of breath. Some doctors monitor patients' lung health by regularly performing pulmonary (lung) function tests (PFTs) during the course of any chemotherapy regimen that contains bleomycin. In addition to bleomycin, other treatments may have a risk of inflammation of the lungs and if your doctor informs you this is a risk of your treatment, it is important to notify them immediately of any these symptoms.

Mouth Sores

Some chemotherapy drugs can cause a patient's mouth to become red, sore, or irritated, which is called *mucositis*. Additionally, some patients undergoing chemotherapy become more susceptible to viral or fungal infections of the mouth and throat. Mouth sores can be due to herpes simplex virus and your doctor may recommend a swab testing.

The doctor should be informed if the patient develops a sore throat. The doctor may examine the patient's throat and take a swab that is sent to a laboratory to check for infection. Several medications are available to treat different types of infections. To help decrease chances of mouth infections, patients should have a complete dental checkup and cleaning before starting therapy. Other tips for preventing and caring for mouth sores are listed below.



PATIENT TIP

Preventing and Caring for Mouth Sores

- Clean your mouth and teeth regularly. Use a soft-bristle toothbrush, a nonabrasive toothpaste, and lip moisturizer.
- Do not use mouthwashes that contain alcohol. Your doctor may prescribe a mouth rinse that cleans mouth sores without irritating them.
- Do not eat citrus fruits (such as oranges, grapefruit, lemons, or clementines) or drink citrus juices, and avoid other acidic foods and sodas. The acids in these foods and drinks can further damage the lining of the mouth.
- Swish and spit warm salt water (1/4 teaspoon of salt mixed in a coffee cup of warm water) four to six times per day to soothe mouth irritation.
- Eat soft foods to avoid bruising your gums and other soft tissues in your mouth. Do not eat spicy foods.
- Do not floss your teeth if your blood counts are low, as this may cause your gums to bleed.
- Viral infections (such as herpes) can be prevented or managed with acyclovir (Zovirax), valacyclovir (Valtrex), and other anti-viral medications.
- Fungal infections (such as Candida and Monilia) can be managed with miconazole (Monistat) or nystatin (Mycostatin). If severe, fungal infections can be treated with the oral treatment fluconazole (Diflucan).

Nausea or Vomiting

Many chemotherapy drugs can cause nausea or vomiting. This typically occurs on the day chemotherapy is administered, but it may also occur one or two days later. Doctors prescribe an antiemetic (a drug that prevents nausea and vomiting) before chemotherapy. Examples of antiemetics include aprepitant (Emend), ondansetron (Zofran, Zuplenz), granisetron (Kytril), metoclopramide (Reglan), prochlorperazine (Compazine, Procomp, Compro), dolasetron (Anzemet), and a variety of corticosteroids such as prednisone and dexamethasone. In most cases, these antiemetics can partially or completely prevent nausea and vomiting. Tips for controlling or minimizing nausea and vomiting are listed below.

PATIENT TIP

Controlling or Minimizing Nausea and Vomiting

- Before chemotherapy, drink a liquid diet consisting of water-based items such as broth, gelatin, ice pops, tea, and water. Do not drink milk or have a meal in which the main ingredients are dairy products.
- Do not eat foods that are too hot or too cold, greasy or fatty, sweet or spicy.
- Eat smaller, more frequent meals instead of fewer large meals each day.
- Avoid strong or offensive smells. Get plenty of fresh air.
- Take prescribed antiemetics before chemotherapy to prevent nausea.
- If you vomit, avoid becoming dehydrated (see tips on page 185).
- Try different approaches to determine what works best for you.

Peripheral Neuropathy

Some drugs may damage the nervous system, causing *peripheral neuropathy* (nerve damage) in the hands and feet (sometimes extending to the arms and legs). Symptoms of peripheral neuropathy include pain, numbness, a tingling or prickling sensation, sensitivity to cold and touch, and muscle weakness that can impair fine motor skills such as buttoning a shirt or picking up small objects.

Peripheral neuropathy can be a difficult side effect for patients to manage, and it is a common cause of dose reduction. Furthermore, while neuropathy improves or resolves in most patients after completion of therapy, the symptoms can last beyond the end of the treatment period. Patients should notify their doctor as soon as symptoms begin to develop so the treatment regimen and dosing can be modified appropriately or even discontinued to prevent further complications.

Although no medications have been specifically approved by the U.S. Food and Drug Administration (FDA) to treat chemotherapy-induced peripheral neuropathy, there are several different classes of drugs that doctors may prescribe to help alleviate patients' symptoms. These include antiepileptic agents (drugs used to treat seizures) such as pregabalin (Lyrica) and gabapentin (Gralise, Horizant, Neurontin, and others); local anesthetics such as lidocaine patches; opioid pain relievers; and antidepressants that also target pain such as duloxetine (Cymbalta, Irenka) and amitriptyline (Elavil). Complementary therapy techniques such as acupuncture and massage may also help with neuropathy symptoms (see page 66 in Part 1 of this guide). Finally, patients should avoid tight-fitting shoes or clothes and exposure to cold, as these may worsen neuropathy symptoms in the hands and feet.

A specific type of neuropathy called Raynaud phenomenon may occur in some patients receiving treatment for lymphoma, particularly bleomycin (Blenoxane). This condition is characterized by signs of poor red blood cell circulation in the blood vessels near the nose, ears, fingers, and toes in response to cold temperatures (including cool weather); symptoms include feelings of cold, numbness, tingling, discoloration of affected areas, and pain in the hands and feet in cool temperatures. Raynaud phenomenon may be managed with a class of medications called calcium channel blockers.

Problems With Sexual Function

Psychological factors such as fear about illness, altered body image due to hair loss and depression, and the physical side effects of treatment on the body and the brain, often cause a drop in *libido* (sex drive). However, a normal libido usually returns after treatment is finished. Patients should not be embarrassed to talk with their doctor about any problems or concerns they have about changes in their libido or sexual function. The doctor might order tests to track hormone levels or recommend seeing

a specialist. Doctors can also prescribe medications to restore erectile function in men, or hormone therapy to alleviate vaginal dryness and other menopausal symptoms in women. It is important for patients to discuss this issue openly with their spouses or partners.

Sterility

Chemotherapy may damage sperm and egg cells and cause temporary or permanent *sterility* (the inability to have children) in both men and women. The potential for developing sterility depends on the treatment type and dosage, the number of therapies given, and the patient's age at the time of treatment. Options for preserving fertility both before and during treatment include protection of the ovaries or testes, freezing of sperm cells and egg cells, and *in vitro* creation (egg cells are fertilized by sperm in a laboratory) and freezing of fertilized embryos. Patients should speak with their doctor about fertility preservation before beginning treatment.

Despite these risks, it is still possible for female patients with lymphoma to become pregnant and for male patients with lymphoma to father children during and after treatment. Because some treatments can cause severe birth defects and other pregnancy complications, it is critical that patients receiving these treatments always use reliable birth control methods during treatment and for several months after completion of therapy. The period of time during which a woman should use birth control methods depends in part on the treatment regimen administered. Patients should discuss fertility concerns and pregnancy prevention with their doctor and, if needed, with a fertility specialist.

Tumor Lysis Syndrome (TLS)

Patients who have large, rapidly growing, or multiple tumors such as those associated with Burkitt lymphoma may experience *tumor lysis syndrome* (TLS) during treatment. This condition occurs when a drug triggers the quick death of a large number of lymphoma cells, causing the dying cells to release cellular breakdown products (substances that are stored inside the cell or that result from the decomposing of cellular materials), such uric acid, potassium, and phosphorus into the blood in high concentrations that can damage the kidneys and other organs. Certain chemotherapy agents are known to have the potential to cause TLS. If not promptly treated, TLS may lead to kidney failure.

Patients who are receiving medications that commonly cause TLS have frequent blood tests to detect any signs of organ damage or abnormal levels of chemicals in the blood from TLS. Patients may receive extra oral and IV fluids and medications such as allopurinol (Aloprim, Lopurin, Zyloprim) or febuxostat (Uloric), which reduce high blood levels of uric acid. In patients at high risk of TLS or if TLS develops, it can be treated with rasburicase (Elitek) which affects uric acid levels in the blood.

Secondary Cancers

There is a risk of developing a secondary cancer (a second type of cancer that develops due to the toxicity of the treatment) as a late effect (happens a long time after the initial treatment) following chemotherapy treatment. In particular, alkylating chemotherapy drugs such as cyclophosphamide (Cytoxan, Neosar) in combination with etoposide (VePesid, Toposar, Etopophos) may have an increased risk of secondary cancer. Chemotherapy regimens have shifted to lower chemotherapy doses when possible, to potentially reduce the risk. Regular doctor visits following the completion of lymphoma treatment can help monitor for the appearance of a secondary cancer. In certain cases, your doctor may recommend additional testing such as initiation of routine cancer screening at an earlier age that may include laboratory or imaging follow up.

Other Possible Side Effects

Chemotherapy can cause other side effects, such as skin rashes, general weakness, and loss of balance or coordination. Many of these side effects are temporary, but some may last for an extended period. The doctor should be contacted immediately if the patient experiences any painful local rash with or without blisters, as this may be a sign of shingles (herpes zoster).

What Side Effects Are Caused by Steroids?

Corticosteroids (often simply called “steroids”) are commonly given along with chemotherapy. Steroids can serve several purposes including helping to treat the lymphoma, reducing inflammation, relieving nausea, and stimulating appetite. However, corticosteroid drugs can cause insomnia (the inability to fall or stay asleep), increased appetite, mood or personality changes, anxiety, high blood pressure, fluid retention, and weight gain. Prednisone can also trigger diabetes in patients prone to that disease or

worsen diabetes in patients who already have it. Long-term steroid use can also cause osteoporosis, cataracts, and changes in appearance.

If personality changes do occur, the doctor should be informed right away, as the steroid dosage may need to be reduced.

What Side Effects Are Caused by Immunotherapy?

Monoclonal Antibodies

The monoclonal antibodies used to treat lymphoma —obinutuzumab (Gazyva), ofatumumab (Arzerra), rituximab (Rituxan), rituximab and hyaluronidase human (Rituxan Hycela), tafasitamab (Monjuvi), mogamulizumab (Poteligeo), alemtuzumab (Campath)—may cause side effects such as low blood cell counts and infusion reactions, although monoclonal antibodies are less likely than chemotherapy to cause low blood cell counts. These side effects are usually mild, but they can sometimes be severe. Other rare but potentially very serious side effects include infections, TLS, and reactivation of past infections such as hepatitis. Other important side effects that may occur while receiving monoclonal antibodies include:

■ Infusion/Injection Reactions

- An infusion/injection reaction is a reaction that typically occurs during or within 24 hours after IV infusion or administration of a subcutaneous injection. Symptoms include dizziness, fainting, headache, feeling warm or flushed, fever or chills, hives, itching, shortness of breath, changes in heart rate and blood pressure, pain in the back or abdomen, and swelling of the face, tongue, or throat. Some infusion/injection reactions are true allergic reactions that can cause low blood pressure, difficulty breathing, and anaphylactic shock (severe allergic reaction).
- To prevent infusion/injection reactions, patients are given an antihistamine such as diphenhydramine (Benadryl), as well as acetaminophen (Tylenol) and sometimes corticosteroids before or during the antibody infusion/ injection. Nurses closely monitor patients during the infusions/injections for signs of an infusion/ injection reaction. Patients should immediately report any symptom they experience during or after an infusion/injection.

■ Infections

- Treatment with CD20-directed monoclonal antibodies (i.e., obinutuzumab, ofatumumab, and rituximab) can trigger immune system changes that reactivate HBV (infection comes back), which can cause acute liver failure. To prevent HBV from reactivating, patients are screened for HBV infection before treatment. Patients who have the virus are closely monitored during and after treatment and may be given antiviral medications to control HBV infection. Patients should be mindful of signs of an active HBV infection, such as increasing fatigue, yellowing of the skin or eyes, and dark urine.
- Very rare cases of a serious and usually fatal central nervous system infection called JC virus infection or progressive multifocal leukoencephalopathy (PML) can occur with any of the monoclonal antibodies. Patients should be mindful of neurological symptoms, such as difficulty thinking, loss of balance, changes in speech or walking, weakness on one side of the body, or blurred or lost vision.

Antibody-Drug Conjugates

The most common side effects reported in patients treated with brentuximab vedotin (Adcetris) include low blood counts, peripheral neuropathy (usually not until the third or fourth cycle of treatment), fatigue, nausea, upper respiratory tract infection, diarrhea, fever, weight loss, mouth sores, constipation, and vomiting. Patients may also experience reactions at the site of the treatment infusion. Hair loss is possible. Rarely, brentuximab vedotin (Adcetris) can be associated with inflammation of the pancreas, and patients with severe abdominal pain or diarrhea should seek medical attention immediately. Polatuzumab vedotin-piiq (Polivy) and loncastuximab tesirine-lpyl (Zynlonta) have similar side effects.

Immune Checkpoint Inhibitors

In patients with lymphoma who are treated with the checkpoint inhibitors nivolumab (Opdivo) or pembrolizumab (Keytruda), the most common side effects include fatigue, upper respiratory tract infection, urinary tract infection, headache, fever, diarrhea, cough, itching, decreased appetite, rash, shortness of breath, muscle, joint and bone pain, constipation, vomiting and nausea.

Immune-mediated adverse reactions can occur in any organ system. The most common immune-mediated adverse reaction is *hypothyroidism* (a condition where the thyroid gland does not create and release thyroid hormone into the blood). Other immune-mediated reactions include *pneumonitis* (infection of the lungs), *colitis* (swelling and/or inflammation of the large intestine), hepatitis, *endocrinopathies* (hormonal diseases), *nephritis* (inflammation of the kidneys) with renal dysfunction, and skin reaction. For patients who receive pembrolizumab (Keytruda), there is an additional risk of solid organ transplant rejection.

Immunomodulators

The most common side effects of the immunomodulatory drug lenalidomide (Revlimid) are decreased red blood cells, white blood cell, and platelet counts. Other common side effects include rash, diarrhea, constipation, muscle cramping, and fatigue. Increased clotting of the blood may occur, and patients are usually advised to take aspirin or another type of blood thinner while taking lenalidomide.

Radioimmunotherapy

The only currently available radioimmunotherapy that is FDA-approved for lymphoma is ibritumomab tiuxetan (Zevalin). The most common side effects are *cytopenias* (low level of blood cells and platelets), fatigue, nasopharyngitis (inflammation of the throat and nasal passages), nausea, abdominal pain, cough, diarrhea and fever, and weakness or loss of energy.

What Side Effects Are Caused by Targeted Therapies?

Many targeted therapies have similar common side effects. These include but are not limited to low blood cell counts, nausea, diarrhea, bleeding, peripheral neuropathy (numbness and pain in the hands and feet), fatigue, *neuralgia* (a type of nerve pain), constipation, vomiting, cough, rash, fever, pain, upper respiratory tract infection, or loss of appetite.

Less commonly, secondary cancers may also arise from the use of targeted therapies. There is also a risk of harm in developing embryos or fetus when using targeted therapies. There are other less common side effects that are specific for each drug or class of targeted therapy.

Keep in mind that no two patients are alike and that statistics can only predict how a large group of patients will do and cannot predict what will happen to an individual patient. The doctor most familiar with the patient's situation is in the best position to interpret these statistics and understand how well they apply to a patient's particular situation.

Bruton tyrosine kinase (BTK) inhibitors

Ibrutinib (Imbruvica) and acalabrutinib (Calquence) must be held before and after surgeries or biopsies to prevent significant bleeding complications. Atrial fibrillation (irregular and very rapid heart beat) may occur with ibrutinib (Imbruvica), acalabrutinib (Calquence), zanubrutinib (Brukinsa) and pirtobrutinib (Jaypirca). TLS may occur with ibrutinib (Imbruvica).

Histone deacetylase (HDAC) inhibitors

Patients with rapidly progressing tumors or a large number of tumors who are treated with HDAC inhibitors may also be at risk for TLS. Apart from the common side effects mentioned above, romidepsin (Istodax) may also cause changes in the patients' electrocardiogram (an exam that records the heart's electrical activity), while vorinostat (Zolinza) requires monitoring for high blood sugar and blocked lungs and veins caused by blood clots (*thromboembolism*).

Proteasome inhibitors

Patients treated with bortezomib (Velcade) may experience side effects like TLS, hypotension (low blood pressure), cardiac failure, acute respiratory disease, and acute liver failure.

Phosphatidylinositol-3-kinase (PI3K) inhibitors

Patients receiving idelalisib (Zydelig) can develop severe cutaneous (skin) reactions and elevated liver enzymes. Copanlisib (Aliqopa) may cause low blood sugar, severe cutaneous reactions and high blood pressure. Patients treated with PI3K inhibitors also reported *colitis* (inflammation of the colon) that typically appears later than other events and is serious in most cases (grade 3 or higher).

Tyrosine kinase inhibitors

Crizotinib (Xalkori) may cause cardiac changes, liver failure and severe visual loss.

BCL2 inhibitors

TLS may occur with venetoclax (Venclexta).

Nuclear export inhibitors

Selinexor (Xpovio) may cause low sodium concentrations in the blood (*hyponatremia*) and visual problems like cataracts.

What Side Effects Are Caused by Radiation Therapy?

Radiation therapy itself is painless, but it can cause short-term (immediate) and long-term (occurring over a long period of time) side effects that vary depending on the type of radiation, the dosage, and the area of the body treated. Side effects are usually worse when radiation therapy and chemotherapy are given at the same time. It is important to remember that radiation only affects the area that is treated, much like a flashlight only illuminates the area it shines upon.

Some of the side effects caused by radiation therapy used to treat patients with lymphoma include:

- Dry mouth
- Fatigue
- Loss of appetite and taste
- Nausea
- Skin reactions
- Sterility
- Throat irritation
- Cardiovascular damage
- Secondary cancers

Dry Mouth

Patients who receive radiation therapy to the mouth may experience a temporary decrease in saliva production causing *xerostomia* (dry mouth). Dry mouth may result in difficulty swallowing foods or thick liquids. It can also cause food particles to stick to the teeth and gums.

Because saliva helps prevent cavities, doctors may advise patients to visit the dentist for fluoride treatments before they start radiation therapy to reduce the risk of tooth decay.

Fatigue

The likelihood of patients experiencing fatigue as a result of radiation therapy depends on their disease and their specific radiation plan. Patient tips for coping with fatigue are included on page 186.

Loss of Appetite and Taste

During radiation treatment, patients might lose their appetite for foods they normally enjoy, or their sense of taste may become diminished. Patient tips for coping with these side effects are included on pages 182 and 191.

Nausea

Radiation treatment can cause nausea, especially in patients who receive radiation to the abdomen. Not eating a few hours before radiation therapy may help patients avoid nausea. The doctor may also prescribe an antiemetic medication to be taken before each radiation therapy session. Patient tips for coping with nausea are included on page 193.

Skin Reactions

Radiation therapy can cause redness, itchiness, dry and peeling skin, sores or ulcers, swelling, and puffiness to the affected area. These skin changes usually decrease and disappear over a few weeks after the radiation therapy ends. However, some skin changes, such as darker and blotchy skin, very dry skin, or thicker skin, may last much longer or be permanent. The radiated area can also sunburn more easily than other parts of the body. Patients should avoid tanning beds and protect their skin from sunlight with a wide-brimmed hat, long sleeves, long pants, and sunscreen with an SPF of at least 30.

Patients should speak with their doctor, nurse, or physician assistant if they experience any skin changes. A list of tips to help patients care for their skin during and after radiation therapy is provided below.

PATIENT TIP

Skin Care During and After Radiation Therapy

- Be gentle with your skin; do not rub, scrub, or scratch.
- Use only lotions and other skin products that your doctor prescribes, or your nurse suggests.
- Do not put anything on your skin that is very hot or cold.
- Shower or bathe in lukewarm water and limit your bathing to less than 30 minutes every other day. Use a mild, unscented soap and pat your skin dry after bathing. Be sure not to wash off the ink markings needed for radiation therapy.
- Check with your doctor or nurse before using bubble bath, cornstarch, cream, deodorant, hair removers, makeup, oil, ointment, perfume, powder, and sunscreen.
- Wear soft, loose clothes that allow your skin to breathe.
- Use soft sheets, such as those made with cotton.
- Add moisture (humidity) to the rooms in your home by placing a bowl of water on the radiator or using a properly cleaned and maintained humidifier.
- Do not use tanning beds and protect your skin from the sun every day.
- Do not put adhesive tape or bandages on your skin. Ask your nurse about ways to bandage without tape.
- Ask your doctor or nurse if you may shave the affected area. Shave only with an electric razor, and do not use pre-shave lotion.
- Report any skin changes you notice to your doctor or nurse.

Sterility

Like chemotherapy, radiation may also damage sperm and egg cells, and cause temporary or permanent *sterility* in both men and women. Patients should speak with their doctor about fertility preservation as early as possible before beginning treatment.

Throat Irritation

Radiation therapy to the neck, throat, or chest may cause sore throat, dry mouth, nausea, and/or cough. Patients may have difficulty eating or swallowing, especially toward the end of their treatment regimen. Patients should tell their doctor if swallowing becomes difficult, as there are treatments for the discomfort. Patients should take precautions to avoid becoming dehydrated during treatment (see page 185 for tips on avoiding dehydration). Difficulty swallowing usually goes away a few weeks after treatment is completed. Sometimes a viral infection such as oral herpes or a fungal infection such as thrush can contribute to throat irritation. Patients should notify their doctor if they are experiencing throat irritation.

The tips listed below may help ease throat irritation during radiation therapy.

PATIENT TIP

Easing Throat Irritation During Radiation Therapy

- Eat bland foods that are soft, smooth, and easy to digest, such as pudding, yogurt, and milkshakes.
- Take small bites and swallow each bite completely before taking another one.
- Puree foods in a blender to make them easier to swallow.
- Avoid citrus fruits and citrus juices.
- Ask your doctor whether lidocaine hydrochloride solution (Xylocaine Viscous, a liquid used to relieve the pain and discomfort from a sore throat or mouth) or Magic Mouthwash may be appropriate.

Cardiovascular Damage

Radiation therapy has three major effects on the heart: it damages arteries, most commonly those in the neck (carotid arteries) and the heart (coronary arteries), which can increase the risk of heart attack and stroke; it damages the valves of the heart; and it causes *pericarditis* (inflammation of the membrane that surrounds the heart). Radiation therapy can also damage the conduction system of the heart, which is the muscles and fibers that provide the electrical signals that make the heartbeat regularly. At least every five years, patients who have been treated with radiation therapy to the chest should undergo a complete cardiovascular examination that includes a Doppler ultrasound to examine the carotid arteries, an echocardiogram (ECHO) to measure valve function, and a stress test to assess coronary artery disease. Statin drugs (used to manage cholesterol) are strongly recommended for patients who have received radiation therapy to prevent coronary artery disease.

Secondary Cancers

The risk of developing secondary cancers from radiation therapy depends on the amount of radiation given and the part of the body treated. Newer methods of radiation therapy limit the amount of healthy tissue exposed to radiation, which reduces but does not eliminate the risk of secondary cancers after these treatments. It is imperative that patients protect irradiated skin from direct sun exposure, no matter how long ago the radiation was administered.

What Side Effects Are Caused by CAR T-cell Therapies?

Axicabtagene ciloleucel (Yescarta), tisagenlecleucel (Kymriah), brexucabtagene autoleucel (Tecartus) and lisocabtagene maraleucel (Breyanzi) are the only CAR T-cell therapies approved by FDA to treat lymphoma. Many of the common side effects of these CAR T-cell therapies are similar to those experienced by patients taking other lymphoma therapies, such as fatigue, decreased appetite, chills, pain, diarrhea, *febrile neutropenia* (low levels of white blood cells called neutrophils, along with fever), infection, nausea, cough, vomiting, and constipation. Patients treated with these CAR T-cells therapies may also have prolonged cytopenias. Neurological symptoms may also occur during the first two to three days after receiving the CAR T-cells and include altered mental

state (encephalopathy), headache, tremor, dizziness, speech problems (aphasia), delirium, insomnia, and anxiety. CAR T-cells therapies may also temporarily affect the patients' ability to drive and use heavy equipment or machines after treatment.

Cytokine release syndrome (an intense systemic inflammatory response) is a unique side effect in response to the activation and growth of a patient's CAR T-cells and will be monitored. A medication called tocilizumab (Actemra) was approved by the FDA in 2017 for the treatment of CAR T-cell–induced severe cytokine release syndrome.

More recently, the FDA announced an investigation into several reported cases of secondary T-cell malignancies in patients previously treated with CAR T-cell therapy. Despite the preliminary investigation the FDA determined that the risk of secondary T-cell cancers applies to all currently approved CD19- and B-Cell maturation antigen (BCMA)-directed genetically modified autologous CAR T-cell immunotherapies including, lisocabtagene maraleucl (Breyanzi), axicabtagene ciloleucl (Yescarta), brexucabtagene autoleucl (Tecartus), and tisagenlecleucl (Kymriah).

While there is a potential risk, the development of any type of second cancer after treatment with CAR T-cell therapies is extremely rare and the cause of secondary cancers has not been confirmed in many cases, so it remains unclear whether the secondary T-cell malignancies were caused by CAR T-cell therapy.

In the event of secondary cancers following treatment with CAR T-cell therapy, contact the manufacturer to report the event and ask about the patient testing for the presence of CAR transgene (gene transferred from one organism to another) in the tumor. To report adverse events including T-cell malignancies, contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

What Side Effects Are Caused by Stem Cell Transplantation?

The type and frequency of the side effects associated with blood stem cell transplantation are quite different depending on whether the stem cells are autologous (from oneself) or allogeneic (from a donor). Patients treated with high doses of chemotherapy and/or radiation before undergoing a blood stem cell transplant are at increased risk for developing infection, bleeding,

and other side effects as described previously (see the section “What Side Effects Are Caused by Chemotherapy?” on page 181 and the section “What Side Effects Are Caused by Radiation Therapy?” on page 201).

Patients receiving high-dose chemotherapy with autologous stem cell transplantation are followed carefully for the first three to four weeks because of the risks of mouth sores, infection, anemia, and uncontrollable bleeding due to the inability of the blood to clot. Transfusions and antibiotics may be necessary, which are often administered in the hospital.

Additionally, patients undergoing allogeneic stem cell are also at risk of developing *graft-versus-host disease* (GVHD), a serious condition in which the donated stem cells attack the patient’s tissues and organs, resulting in symptoms such as diarrhea, abdominal pain, nausea, and vomiting. GVHD can occur at any time after the transplant, but acute GVHD occurs in the first 100 days after transplant. Drugs can be used to reduce the risk of developing GVHD or to treat the condition once it develops.

When Should a Patient’s Doctor Be Contacted?

Patients should talk with their doctor about which symptoms and side effects they should watch for. As a general rule, a patient’s doctor should be contacted if the patient experiences:

- A side effect that is unexpected or lasts longer than expected.
- A medical problem—such as fever/chills, shortness of breath, prolonged or constant nausea and vomiting, chest pain, and/or dizziness—that cannot wait for a regularly scheduled appointment.

Part 5 — Survivorship and Living with The Side Effects of Treatment

Chapter 20: Managing Life During and After Treatment

This chapter discusses some general issues that patients may encounter in their daily lives during and after treatment for lymphoma.

Survivorship

Following completion of treatment, patients should expect to receive a “survivorship care plan” which is a summary of the cancer type, date of diagnosis, date of ending treatment, all cancer treatments received, and cancer surgery performed. Monitoring for late effects following treatment is an important part of a survivorship care plan. If available, a specialized cancer survivorship clinic can provide a more in-depth evaluation for late effects, monitoring for late effects, and recommendations to reduce risk and improve quality of life.

Coping Strategies

Each person’s experience with cancer is different, and the way an individual copes with the physical and emotional impacts of lymphoma is unique to each patient’s personality and situation. Table 20.1 lists some suggestions for coping with common issues that patients may face.

Table 20.1. Coping Strategies

Build a Strong Support System

- Communicate your fears and concerns about your disease by talking to your family, friends, doctors, and counselors.
- Write down your concerns in a journal.
- Find a support group or a one-to-one peer support program such as the LRF’s *Lymphoma Support Network* or other individuals who are also coping with cancer.

Get Help for Depression	<ul style="list-style-type: none"> ■ Feeling sad or having a depressed mood from time to time is not unusual in patients living with cancer, but this is not the same as having a psychiatric diagnosis of depression, known as “Major Depressive Disorder.” ■ Watch for signs such as sleeping more or less than usual, a loss of interest in preferred activities, crying, or an inability to concentrate. ■ If these symptoms last more than two weeks, ask for a referral to a psychiatrist, social worker, psychologist, or counselor who can help you cope with your feelings through talk therapy, medications, or both.
Deal With Physical Changes	<ul style="list-style-type: none"> ■ Some patients with lymphoma may feel unattractive because of hair loss and other changes in appearance caused by their treatment. ■ If desired, plan ahead and buy a wig or head covering if hair loss is a possibility. ■ Seek advice from a beautician familiar with the side effects of cancer treatment about makeup if you are concerned about a blotchy complexion. ■ Ask your healthcare team for advice on how to manage other temporary changes in your skin and brittle nails.
Maintain a Healthy Lifestyle	<ul style="list-style-type: none"> ■ Eat a healthy diet that includes fruits, vegetables, proteins, and whole grains. ■ Engage in regular physical exercise, which can help improve mood and reduce anxiety, depression, and fatigue. ■ Get sufficient rest to help combat the stress and fatigue of your disease and its treatment. ■ Quit smoking and reduce alcohol consumption.
Undergo Routine Healthcare and Preventative Care	<ul style="list-style-type: none"> ■ Continue to visit your primary care physician, dentist, dermatologist (skin doctor) and optometrist (eye doctor), and your other regular healthcare providers throughout treatment and afterwards; however, let each one know about your current diagnosis and treatment in case adjustments in your care need to be made. ■ As directed by your healthcare team, continue to receive preventative care, such as vaccines and screenings.
Set Reasonable Goals	<ul style="list-style-type: none"> ■ Having goals for how you want to live your life during and after treatment can help you maintain a sense of purpose. ■ Avoid setting unreasonable goals, such as working full-time if you do not yet have the energy or stamina to do so. ■ Stay as active and involved as you can in work and other activities that interest you.

Maintain a Healthy Lifestyle

Regular physical activity helps keep the cardiovascular system strong and the body muscles flexible. Exercise can also help patients alleviate breathing problems, constipation, and mild depression. Additionally, it may help reduce stress and fatigue. Patients should talk to their doctor before starting an exercise program and consider visiting a physical therapist for advice. The most important point to remember is to avoid overexertion (the use of too much mental and physical effort).

Patients dealing with cancer do not need to perform activities at the same level of intensity that they did before their lymphoma diagnosis, and they should not push themselves to their limit.

Several types of exercise may be particularly helpful, including:

- General physical activity, such as swimming, dancing, household chores, and yard work
- Aerobic activity to improve cardiovascular fitness, such as walking, jogging, and bicycling
- Resistance training to strengthen muscles, protect joints, and help prevent osteoporosis by building bone mass
- Flexibility exercises such as stretching and yoga to improve range of motion, balance, and stability

A healthy diet is especially important during treatment for lymphoma because it helps patients keep up their strength and energy, tolerate treatment-related side effects, decrease the risk of infections, and heal and recover more quickly. Patients should aim for a diet high in fruits and vegetables, protein (such as poultry, fish, and eggs), and whole grains.

During or after treatments that can lower white blood cell counts, such as chemotherapy and stem cell transplantation, patients may be instructed to follow a *neutropenic diet*, which involves temporarily avoiding raw fruits and vegetables that may increase the risk of infection. The healthcare team can help develop an appropriate eating plan.

Patients should talk to their doctor before taking any dietary supplements, because they may interfere with treatments or have unexpected side effects.

Vaccines

Patients receiving chemotherapy for lymphoma need special consideration with regards to the timing of vaccine administration, since these treatments affect the immune system. If possible, all recommended vaccines should be administered before the start of chemotherapy or other immunosuppressive medications.

Vaccination during chemotherapy should generally be avoided because response to the vaccine may be decreased. If inactivated vaccines (containing dead microbes that cannot cause disease but stimulate the body's immune system) are administered during chemotherapy or stem cell transplant treatment, they should be readministered after immune system function returns to normal. If patients receive a vaccine within 14 days before starting therapies that affect the immune system, they should be revaccinated at least 3 months after the treatment has stopped and immune function has returned to normal. Patients receiving chemotherapy with anti-B-cell antibodies (e.g., rituximab) or stem cell transplant therapy should wait at least 6 months or longer after therapy before receiving inactivated vaccines.

Patients with altered immune system function should not receive live vaccines, and live vaccines should not be administered for at least 3 months after immunosuppressive treatments. Live vaccines can be administered to patients with leukemia, lymphoma, or other malignancies whose disease is in remission, who have restored immune system function, and whose chemotherapy has been discontinued for at least 3 months.

The currently FDA-approved or FDA-authorized coronavirus disease 2019 (COVID-19) vaccines can be safely administered to patients with compromised immune system function. When possible, COVID-19 vaccine doses should be completed at least 2 weeks before starting or resuming immunosuppressive therapies. An additional dose of an mRNA COVID-19 vaccine administered at least 28 days after completion

of an initial 2-dose primary mRNA COVID-19 vaccine series should be considered in patients with moderate to severe immune compromise. Immunocompromised patients are eligible for a third dose including those receiving active treatment for hematologic malignancies, patients who are recipients of CAR T-cell therapy or stem cell transplantation (within 2 years of transplantation or receiving immunosuppressive therapy), and active treatment with chemotherapy classified as severely immunosuppressive.

In addition, the CDC also recommends a booster dose of any of the three available vaccines for patients with cancers of the blood. It is important that lymphoma patients discuss this matter with their healthcare team to determine if and when they should receive a booster dose.

Patients who are immunocompromised should be aware of the potential for a reduced immune response to COVID-19 vaccines and the need to follow currently recommended preventive measures, like washing their hands regularly and wearing a mask, to protect themselves against COVID-19. The information on COVID-19 continues to evolve and vaccination guidelines may change. Please refer to the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) guidance for the most up-to-date information on COVID-19 vaccines for immunocompromised patients, located at: <https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>

Close contacts of patients with lessened immune function, like caregivers and family, should also receive all recommended vaccines, with the exception of smallpox vaccine.

The Importance of Follow-up Care

At the first visit following the completion of treatment, patients should discuss their follow-up schedule with the doctor. This schedule may be different for each patient depending on their disease stage, age, and overall health. It is critical that patients adhere to their schedule of follow-up visits—these are very important for monitoring disease recurrence, as well as detecting and treating any new health problems that might arise because of the treatment.

During these follow-up visits, the doctor asks about any medical changes since the last appointment and conducts a physical examination. The doctor may also prescribe blood tests and other laboratory tests, molecular diagnostic testing (laboratory tests that analyze the genetic material or other markers of the disease), or imaging.

It is very important to follow all scheduled appointments and to take all your treatments as prescribed, because this will ensure maximum treatment efficacy.

Be Proactive in Healthcare Decisions

To stay proactive in healthcare decisions, patients should write out their questions and bring them to their appointments and take notes during their visits. Patients should also obtain and save the following information from their medical team:

- Copies of all medical records and a written summary of their treatments in case the patient switches doctors or needs to see a physician who is not familiar with the patient's lymphoma history and treatment. LRF's mobile app, *Focus On Lymphoma*, can keep track of the details to share with the healthcare team
- A list of things to watch for, including signs of disease recurrence and late side effects from treatment

At the follow-up care appointments, patients should inform their doctor of:

- Any new symptoms
- Pain or any physical problems that disrupt their daily life, such as fatigue, insomnia, sexual dysfunction, and weight gain or loss
- Any new health problems, such as heart disease, diabetes, and high blood pressure
- Any new medications and vitamins they are taking, including over-the-counter medications
- Emotional problems, such as anxiety and depression
- Whether they have a medical alert system (particularly for patients over 70 who live alone)
- Any other questions or concerns

Psychological Impact on Survivors

Emotional Effects and Fear of Recurrence

Survivors often report that they entered a very different world once treatment ended. While it may be a time to rejoice and recover from the experience, this “new normal” period often comes with mixed emotions. You may have a hard time trying to return to your routine as it was before you were diagnosed with lymphoma and some things you once did easily may now be challenging, or you may not have the same energy.

It is also very common for survivors to feel anxious about the future. This feeling stem out of the fear that the lymphoma will return (*fear of recurrence*) and can be triggered by simple things like birthdays, a visit to a doctor’s office or an unexpected symptom. You can be proactive and take the following steps to cope with fear of recurrence:

- Be informed about the signs of recurrence for your type of lymphoma.
- Keep track of any questions and symptoms you have and discuss them with your healthcare team.
- Stay up-to-date with your medical appointments and follow your doctor’s recommendations.
- Be patient and allow yourself time to process your feelings.
- Take control of what you can and make a follow-up care plan (see the *When Treatment is Over* fact sheet on LRF’s website at lymphoma.org/publications).

Fear of recurrence can be associated with conditions such as depression and anxiety, which may linger for years. This can manifest in different ways, like trouble sleeping, changes in appetite, lack of interest in activities you previously enjoyed and inability to handle daily chores. Mental health professionals can help you develop skills to reduce stress levels and cope with anxiety and depression. Complementary therapies such as acupuncture, meditation, and massage can also be beneficial in the management of the emotional effects of treatment.

Taking Care of Yourself

As a cancer survivor, it is important that you practice self-care regularly to reset your physical and emotional well-being. Adopting routines of self-care will help you recharge your batteries and stay healthy. Talk with your healthcare team about developing a wellness plan to help you stay physically and emotionally healthy and improve your mood. Consider the following suggestions:

- Stay active with short periods of daily exercise. (30 minutes of power walking, jogging or biking). If not possible, take the stairs instead of the elevator or park farther away than usual.
- Maintain a balanced diet and eat fruits and vegetables.
- Cut down on risk factors. Quit smoking and reduce alcohol intake.
- Try to get 7 hours of sleep per night or take naps when needed.
- Meditation, deep breathing and stretching can help you relax.
- Keeping a journal with thoughts and feelings may help you to let go of worries and fears.

Finding Support

Identify at least one person with whom you feel you can be honest about your feelings. You can open up to friends and family or join a support group for cancer survivors. Having a reliable support network can provide a means to work through your negative emotions and help you cope with physical effects of treatment or deal with aspects of daily life.

The LRF's one-to-one peer support programs - Lymphoma Support Network – 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. For more information about this program, please contact the LRF Helpline or visit lymphoma.org/resources/supportservices/lasn.

You can also find assistance online with support-oriented patient organizations such as Cancer Care (call 800-813-4673 or visit cancercare.org/support_groups) and the Cancer Support Community (call (888) 793-9355 or visit cancersupportcommunity.org).

For some individuals, faith and spirituality is the best route to find comfort. Some members of your place of worship may help you cope with your concerns, such as feeling alone, fear of death, searching for meaning, and doubts about faith.

There are many options available, and it is important that you choose the one that is right for you. Follow-up care can also include home care, occupational or vocational therapy, pain management or physical therapy.

LYMPHOMA

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**Lymphoma Research Foundation
(LRF) Helpline and Clinical Trials
Information Service**

CONTACT THE LRF HELPLINE

Trained staff are available to answer questions and provide support to patients, caregivers and healthcare professionals in any language.

Our support services include:

- Information on lymphoma, treatment options, side effect management and current research findings
- Financial assistance for eligible patients and referrals for additional financial, legal and insurance help
- Clinical trial searches based on patient's diagnosis and treatment history
- Support through LRF's Lymphoma Support Network, a national one-to one volunteer patient peer program

Monday through Friday
9:30 am – 7:30 pm Eastern Standard Time (EST)
Toll-Free (800) 500-9976
or email helpline@lymphoma.org

