

Cutaneous T-Cell Lymphoma



A six-word narrative about living with blood cancer from patients in our LLS Community

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, nutrition and optimism. Finding the joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.



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- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care.

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Acknowledgement

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Introduction

Cutaneous T-cell lymphoma (CTCL) is a term for a group of rare blood cancers that affect the skin. CTCL is a type of non-Hodgkin lymphoma that starts in lymphocytes (white blood cells) that reside in the skin.

CTCL is a chronic condition. While some people with CTCL may live without symptoms for years, it requires ongoing care and management.

This booklet provides information about the diagnosis, staging and treatment of CTCL with a focus on the two most common types: mycosis fungoides (MF) and Sézary syndrome (SS). It also includes brief descriptions of normal blood, bone marrow and the lymphatic system, as well as a glossary of health terms related to CTCL.

We hope that you will keep this booklet handy and that, should you ever feel alone in confronting problems, you will turn to it for information and guidance to find the support and resources you need.

We are here to help.

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Lymphoma Basics

“Lymphoma” is the general name for many different types of blood cancer that start in lymphocytes in the lymphatic system. A lymphocyte is a type of white blood cell. The lymphatic system is a part of the body’s immune system. It is a network of organs and tissues that protects the body against disease and infection and removes waste and toxins. The lymphatic system includes the lymph nodes, spleen, thymus, tonsils and bone marrow. Lymphoma is the most common type of blood cancer. For more information on the lymphatic system, see page 41.

There are three main types of lymphocytes: B lymphocytes (B cells), T lymphocytes (T cells) and natural killer (NK) cells. B cells make antibodies to fight infection; T cells help fight infections and attack cancer cells; and NK cells attack cancer cells and eliminate viruses. B-cell lymphomas are more common than T-cell and NK-cell lymphomas.

Changes in the genetic material of a lymphocyte cause it to become an abnormal cancer cell (often called a “lymphoma cell”). The lymphoma cell divides again and again, making more and more abnormal cells. These abnormal cells eventually crowd out healthy cells and form tumors, generally in the lymph nodes or in the lymphatic tissue found in organs such as the stomach, intestines, skin or spleen. Lymphoma can develop in any part of the body where there are lymphocytes. While some lymphomas can be detected through routine bloodwork, most are diagnosed through the examination of a biopsy sample (lymph node biopsy, skin biopsy, tumor biopsy, etc.).

Lymphomas are grouped into two major categories: Hodgkin lymphoma and non-Hodgkin lymphoma. Hodgkin lymphomas contain Reed-Sternberg cells, which have a particular appearance when viewed under a microscope. They are unusually large, abnormal lymphocytes that may contain more than one nucleus. Non-Hodgkin lymphomas are a varied group of lymphomas that do not have the characteristic Reed-Sternberg cells seen in Hodgkin lymphoma.

There are more than 90 different subtypes of non-Hodgkin lymphoma (NHL). Non-Hodgkin lymphomas can start in any of the three types of lymphocytes: B lymphocytes (B cells), T lymphocytes (T cells) and natural killer (NK) cells, and are broadly classified as B-cell NHL and T/NKT-cell NHL depending on the type of lymphocyte that becomes cancerous.

Non-Hodgkin lymphomas are also grouped according to the rate of disease progression, either indolent (slow growing) or aggressive (fast growing). When indolent lymphomas are first diagnosed, most patients have fewer symptoms than patients with aggressive lymphomas.

Treatment for NHL is based on the subtype and biological behaviors (whether it is aggressive or indolent) of the lymphoma. It is important to get an accurate diagnosis and know your specific subtype. This information will help you understand your prognosis and your treatment options.

For more information about non-Hodgkin lymphoma, view the free LLS booklets *Non-Hodgkin Lymphoma* and *The Lymphoma Guide*.

About Cutaneous T-Cell Lymphoma

The skin is the body’s largest organ. One of the main functions of skin is to keep bacteria and other germs from entering the body and bloodstream. In addition to providing a physical barrier against infection, skin also contains a wide variety of immune cells. These include lymphocytes (B cells, T cells and NK cells), which act as a defense against germs.

Cutaneous (skin) lymphomas make up a rare group of non-Hodgkin lymphomas

that start in the skin. They happen when a mutation (change) or a series of mutations in the genetic material of a healthy lymphocyte in the skin causes it to turn into a lymphoma cell that multiplies uncontrollably. These lymphoma cells accumulate in the skin and cause abnormalities called “skin lesions.” Skin lesions are areas of the skin that are different than the surrounding skin. They may appear red, purple or brown, and they are often itchy. A lymphoma that begins in the lymph nodes or another part of the lymphatic system and then spreads to the skin is not considered a cutaneous lymphoma because it did not start in the skin. Cutaneous lymphoma is also not a type of skin cancer. Skin cancer develops in skin cells. Cutaneous lymphoma develops in lymphocytes in the skin.

There are two main types of cutaneous lymphoma:

- Cutaneous T-cell lymphoma (CTCL), which starts in T cells or NK cells
- Cutaneous B-cell lymphoma (CBCL), which starts in B cells

Cutaneous T-cell lymphoma is more common than cutaneous B-cell lymphoma. Cutaneous T-cell lymphoma starts in T cells that are at home and reside in the skin. Genetic changes cause a normal, healthy T cell to grow and divide uncontrollably, leading to skin lesions made up of abnormal T cells. In certain CTCLs, cancerous T cells may also circulate in the bloodstream (as they do in Sézary syndrome) or they may accumulate in the lymph nodes or other areas of the body.

Cutaneous T-cell lymphomas have various signs and symptoms, treatment options and outcomes. Most CTCLs are indolent (slow-growing) lymphomas and are often not life-threatening. They are treatable, but they cannot be cured.

The two most common types of CTCL are:

- Mycosis fungoides (MF)
- Sézary syndrome (SS)

Other less common CTCL subtypes include:

- Primary cutaneous CD30-positive T-cell lymphoproliferative disorder
- Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous gamma/delta T-cell lymphoma
- Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma
- Primary cutaneous gamma/delta T-cell lymphoma
- Primary cutaneous acral CD8-positive lymphoproliferative disorder
- Primary cutaneous CD4-positive small or medium T-cell lymphoproliferative disorder

Mycosis fungoides (MF) is the most common CTCL subtype. It accounts for approximately 50 to 70 percent of CTCL cases. The name comes from the mushroom-like skin tumors that may appear in the advanced stages of the disease, although the disease is not related to a fungus. For most patients, MF is indolent. It may start with dry skin and a red rash, either with or without itching.

In its earliest stage, MF can be difficult to diagnose because it resembles other skin conditions like eczema or psoriasis. There may be red patches or raised areas of the skin that often have scaling on the surface and cover either small or large portions of the skin. Large bumps or tumor nodules with significant thickness may develop initially or later in disease progression. For most patients, MF remains confined to the skin and does not spread to the lymph nodes or internal organs. In advanced stages, MF can spread to the lymph nodes, blood or other organs such as the spleen or liver. In rare cases MF can transform into a more aggressive form called “transformed MF.” Transformed MF occurs when the MF lymphoma cells undergo genetic changes that cause them to become larger.

Sézary syndrome (SS) is a fast-growing CTCL that affects the skin and blood. It is the second most common type of CTCL, after MF. It accounts for about 3 to 5 percent of cases of CTCL. Sézary syndrome is a leukemic form of CTCL. People with SS, like leukemia patients, often have very high white blood cell counts. This type of CTCL tends to have more aggressive features than the typically slower-growing MF, and it can result in reduced survival in affected patients. People with SS develop a red, very itchy rash that covers large portions of their body. Sézary cells are found in the rash and the blood. They may also be found in the lymph nodes. Sézary cells are cancerous T cells. Under a microscope Sézary cells have an abnormally shaped nucleus and look larger than normal T cells.

Signs and Symptoms

Signs and symptoms are changes in the body that may indicate the presence of disease. A “sign” is a change that the doctor sees during an examination or in a laboratory test result. A “symptom” is a change that a patient can see and/or feel.

The signs and symptoms of CTCL vary depending on the type. Cutaneous T cell lymphoma causes skin lesions that are often itchy. Some CTCLs appear as a rash. They can look a lot like other common skin conditions such as psoriasis or eczema. Patients with advanced CTCL may have thicker skin tumors that are widespread. The tumors may develop ulcers (open sores) and become infected and painful.

CTCL is not contagious. It is not an infection and cannot be passed to another person.

Signs and symptoms of mycosis fungoides (MF) include:

- Skin lesions. Skin lesions can appear anywhere on the body, but they tend to start in areas of the skin protected from the sun by clothing. They may vary from either a single or a few lesions to extensive skin involvement. A combination of lesions is possible. The lesions may come and go, sometimes making MF difficult to diagnose.

Types of lesions seen in people with MF include:

- Patches—flat, scaly, pink or red areas on the skin. Patches are flat but may be scaly. They can disappear and reappear or remain stable. They may be hypopigmented (lighter in color than the surrounding skin).
- Papules—small, solid, raised bumps on the skin by hair follicles. Papules may be red, pink, purple or brown.
- Plaques—abnormal, thickened patches of skin that are raised or hard. They can be smooth, scaly, crusted or ulcerated (having open sores). They are typically red, purple or brown in color.
- Tumors—solid dome-shaped masses at least 1 cm in size. They are raised nodules that are thicker and deeper than plaques. Some tumors may be ulcerated.
- Erythroderma—redness of the skin covering more than 80 percent of the skin surface. This condition may lack distinct skin lesions.
- Pruritus (severe itching)
- Enlarged lymph node(s)

Sézary syndrome (SS) is associated with more severe symptoms. It is characterized by erythroderma, an extensive red, severely itchy rash that covers more than 80 percent of the skin surface. There may also be patches, plaques or tumors on the skin.

Other common signs and symptoms of SS may include:

- Thickened skin on the palms of the hands and the soles of the feet
- Abnormalities of the fingernails and toenails
- Swelling of the skin
- Alopecia (hair loss)
- Edema (skin swelling)
- Lower eyelids that turn outward
- Enlarged lymph nodes
- Less ability to control body temperature
- A high white blood cell count

Testing for CTCL

While certain signs and/or symptoms may indicate that a person has a CTCL, laboratory tests are needed to confirm the diagnosis. It is important to have an accurate diagnosis because it helps the doctor to:

- Estimate how the disease will progress
- Determine the appropriate treatment

Talk to your doctor about:

- The diagnostic tests that are being done
- What the results mean
- Getting copies of the results

Many CTCLs can be difficult to diagnose, especially in early stages. The symptoms and skin biopsy findings are similar to other skin conditions like eczema and psoriasis.

A biopsy is the removal of cells or tissues for examination by a pathologist, a doctor who has special training in identifying diseases by studying the biopsy sample under a microscope and performing other specialized tests on the sample.

Sometimes several skin biopsies are taken over many months and years in order to come to a correct diagnosis. It is very important to have a pathologist who has experience and expertise in diagnosing CTCL confirm any CTCL diagnosis. Pathologists in large medical centers often have more expertise and experience in diagnosing CTCL.

The following tests and procedures are used to diagnose MF or SS:

Medical History. Because CTCL causes skin lesions and rashes, many people often first see a dermatologist to find out what is causing their skin problems. A dermatologist is a doctor who has special training in diagnosing and treating skin problems.

Your doctor will take a thorough medical history. The history may include information about past illnesses, injuries, allergies, treatments and medications, including any supplements that you may be taking. Some illnesses run in families, so the doctor may also ask about the health of your blood relatives. It is important to tell your doctor about any skin lesions or rashes that you have had in the past. Often, people with MF have had skin lesions for months or even years before being diagnosed with the disease.

Physical Examination. The physical examination should involve a complete skin examination of the entire body including the scalp, between the legs, and between the fingers and toes. Your doctor will observe the type of skin lesions and determine the percentage of your skin that is affected. Lymphoma cells can sometimes be found in lymph nodes and other organs in the body such as the liver and spleen. Your doctor may check the lymph nodes in your neck, armpits and groin (top inner part of the thigh) and feel your abdomen to see if you have an enlarged liver or spleen.

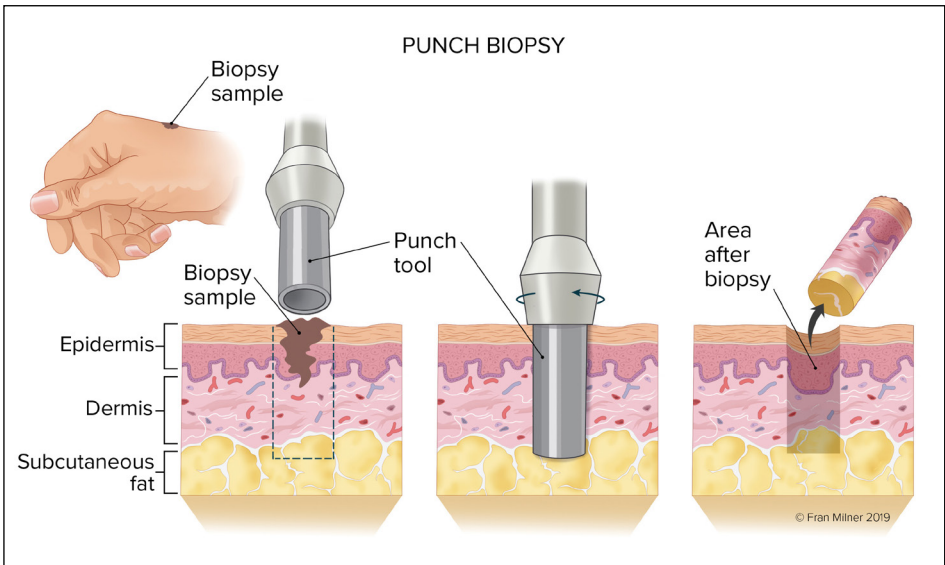
Skin Biopsy. A skin biopsy is a procedure to remove a small amount of skin so it can be tested in a laboratory. A diagnosis of CTCL is based primarily on a skin biopsy of an involved lesion, and multiple biopsies are often needed to confirm the diagnosis.

Before a skin biopsy, the doctor will wipe the area with rubbing alcohol or another antiseptic to reduce the risk of infection. Then you will be given an injection to numb the area so you do not feel pain during the biopsy.

Skin biopsy procedures may include:

- **Punch biopsy.** The doctor uses a circular tool to remove a small but deep circle of tissue from all of the skin layers: epidermis (outermost layer of the skin), dermis (inner layer of the skin) and subcutaneous fat. Stitches are often used to close the opening in the skin. See **Figure 1**.

Figure 1. Punch Biopsy



- **Excisional biopsy.** The doctor uses a scalpel (small knife) to remove the entire skin lesion, usually with some healthy skin around it. The sample of removed tissue may include the skin's deeper layer, the "dermis," along with the fat below the skin. If the skin lesion is large, the doctor may remove only a piece of it. This is called an "incisional" biopsy. Stitches are often required after excisional and incisional biopsies.
- **Shave biopsy.** The doctor uses a tool similar to a razor to remove the epidermis, the outermost layer of skin, and part of the dermis, the second layer of skin. Stitches are usually not needed after this procedure. This type of biopsy may not be recommended to diagnose CTCL. It only removes the top layers of the skin and may not remove abnormal T cells that are often found under the surface of the skin, which may be needed to confirm a diagnosis.

Depending on the number and type of lesions, multiple biopsies may be taken at the time of diagnosis. Samples are then sent to a laboratory for examination and testing.

Cell Assessment. At the laboratory, a pathologist examines the skin sample. It is recommended that a pathologist with expertise in CTCL evaluate the skin sample.

The review under the microscope is often referred to as "histology." The pathologist examines the cells to determine their size, shape and type, and how they are arranged in the layers of skin and around other structures such as hair follicles.

The pathologist will perform additional tests on the sample to help diagnose CTCL and the CTCL subtype.

Biomarker Testing. These laboratory tests look for biomarkers (molecules found in the blood, other body fluids or tissues that are signs of a normal or abnormal process, or of a condition or disease) to provide information about a person's cancer. Each person's cancer has a unique pattern of biomarkers.

Biomarker testing is used to help diagnose some types of cancer. It may also be used to help plan treatment, make a prognosis or predict whether cancer will come back or spread to other parts of the body. Biomarker tests may include:

- **Immunophenotyping (flow cytometry).** This lab test identifies cancer cells based on markers called "antigens." Antigens are proteins found either on the surface of or within white blood cells. Finding (or not finding) certain antigens can help determine the type of lymphoma. The pattern of the surface proteins is called the "immunophenotype."

Immunophenotyping is done with an instrument called a "flow cytometer."

A flow cytometry test can measure the number of cells in a sample, as well as specific characteristics of the cells including their size and shape, and identify specific markers on the cell surfaces. A sample of cells is tagged

with a panel of antibodies that are specific to the markers (usually different proteins) on the cell surfaces. The cells are stained with a light-sensitive dye and are passed through a laser beam in the flow cytometer. If they have an antibody-specific surface marker, the cells light up and are counted. Flow cytometry is used to determine the type of lymphocytes (B cells or T cells) and to assess the maturity of the cells.

Lymphoma cells have different markers on their surface, depending on the type of lymphoma. MF and SS cells have characteristic surface protein patterns that allow them to be differentiated from healthy T cells and other types of leukemia and lymphoma. Typically, patients with MF or SS have T cells that test positive for specific proteins called cluster of differentiation (CD). Their T cells have the markers known as CD2, CD3, CD4 and CD5, and they lack certain T-cell markers, including CD7 and CD26. However, patients with some subtypes of MF test positive for CD8 (especially the hypopigmented variant). In most MF cases, CD30 is found on at least a few cells but it can be more heavily expressed in the large transformed cells.

- **Molecular testing.** Molecular testing refers to a number of different laboratory tests that examine the exact sequence (order) of DNA or RNA. This makes it possible to identify a variety of genetic changes in a patient's cancer cells. These changes are important in diagnosing the subtype of lymphoma and determining treatment options. Often patients with MF and SS have rearrangements in the clonal *TCR* (T-cell receptor) gene. In gene rearrangements, part of a gene has broken off and attached to another gene. This test may be valuable to confirm a diagnosis of CTCL when histology and immunophenotyping cannot clearly confirm a diagnosis. This test may use a sample from the skin biopsy or the blood.

Blood Tests. These tests require a sample of blood, which is removed through a needle placed into a vein. Blood tests measure the amount of certain substances in the blood or count different types of blood cells. Blood tests may be done to look for signs of disease, to check for biomarkers and to see how well your treatment is working.

- **Complete blood count (CBC).** This test is used to measure the number of red blood cells, white blood cells and platelets in a sample of your blood. The CBC should include a “differential,” which measures the numbers of the different types of white blood cells in the sample.
- **Sézary screen.** In this test, a sample of blood is viewed under a microscope to identify and count the number of abnormally shaped Sézary cells in the blood. A Sézary cell is a cancerous T cell that has an abnormally shaped nucleus, and it looks larger than normal T cells.
- **Blood chemistry profile.** This blood test measures the levels of certain substances released into the blood by organs and tissues in the body. These substances include electrolytes (such as sodium, potassium and chloride),

fats, proteins, glucose (blood sugar), uric acid and enzymes. A blood chemistry test indicates how well a person's kidneys, liver and other organs are working. It also provides helpful information about any potential organ damage caused by cancer cells or cancer treatments.

- **Lactate dehydrogenase (LDH) test.** This test measures the level of lactate dehydrogenase (LDH) in the blood. LDH is a protein found in most cells. When a cell is damaged, LDH is released into the bloodstream. High levels of LDH in the blood may be caused by cancer and may also be a sign that the cancer is widespread. LDH may be elevated in cases of transformed or advanced-stage MF.

Lymph Node Biopsy. In this procedure, all or part of a lymph node is removed and checked under a microscope for signs of infection or disease. If you have one or more swollen or enlarged lymph nodes, your doctor will perform a lymph node biopsy to examine whether there are lymphoma cells in the lymph nodes. This is important for diagnosing lymphoma and confirming the subtype.

To ensure that there is enough tissue to make an accurate diagnosis, the preferred method for a lymph node biopsy is usually an excisional biopsy (removal of a whole lymph node) or an incisional biopsy (removal of part of the lymph node). If the lymph node is just under the skin, the biopsy procedure is usually simple and can sometimes be done with a local anesthetic (numbing medication) under guidance from imaging with ultrasound or computed tomography (CT) scans to locate the abnormal node. If the lymph node is deep inside the chest or abdomen (stomach area), you may be sedated or receive general anesthesia for a surgical procedure.

A core needle biopsy may be necessary in certain situations, if the lymph node is too difficult to reach. In this method, a wide needle is used to remove a column of tissue from the lymph node. It is done with local anesthesia to numb the area. Another type of needle biopsy, called fine-needle aspiration, is generally not suitable for diagnosing lymphoma. This is because the long, thin needle that is used to draw out fluid and cells often does not collect enough cells to make an accurate diagnosis.

Once an adequate tissue sample has been obtained, a pathologist reviews it under a microscope to look at the size, shape and type of cells in the lymph node. In addition, the cells will be analyzed for biomarkers.

Bone Marrow Aspiration and Biopsy. These two tests are used to collect and examine bone marrow, the spongy tissue found inside bones where blood cells are formed. Generally, a bone marrow aspiration and biopsy are not needed in the care of patients with CTCL, especially in early stages. In some patients with CTCL, bone marrow aspiration and biopsy may be necessary to see whether the lymphoma has spread to the bone marrow. It is also done to show whether the bone marrow is healthy and making normal amounts of blood cells, especially if a bone marrow transplant is being considered as a treatment

option. Bone marrow aspiration and biopsy are generally done at the same visit, either at the doctor's office or in a hospital, under local anesthesia.

Bone marrow has both a solid and a liquid component. For a bone marrow aspiration, a special, hollow needle is inserted through the hip bone and into the bone marrow to aspirate (remove) a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of solid bone that contains bone marrow. Both samples are sent to the lab where they are examined under a microscope and analyzed for biomarkers.

Imaging Tests. These tests create detailed images of areas inside the body. In CTCL, imaging tests are done to determine if the cancer has spread to lymph nodes or other organs. This helps the doctor determine the stage of the cancer (for more information on staging, see page 14) and plan appropriate treatment. Not all patients who have cutaneous lymphomas need imaging with scans. Your doctor will determine whether imaging tests are needed.

Ultrasound. This procedure uses high-energy sound waves to look at tissues and organs inside the body. The sound waves make echoes that form pictures of the tissues and organs, which are viewed on a computer screen.

Computed tomography (CT) scan. In this type of imaging test, a computer linked to an x-ray machine is used to take a series of detailed pictures of areas inside the body. A CT scan may be used to see whether lymphoma cells are accumulating in lymph nodes in the chest or abdomen, or in organs such as the spleen and liver.

Positron emission tomography (PET) scan. For this type of imaging test, a small amount of radioactive glucose (sugar) is injected into a patient's vein. The PET scanner detects areas in the body where large amounts of glucose are being used. In the images, the cancer cells appear brighter than the normal cells because they use glucose more quickly than normal cells. A PET scan may be done to see if there are lymphoma cells in the lymph nodes or organs.

Positron emission tomography–computed tomography (PET–CT) scan. This procedure combines images from a PET scan and a CT scan. The combined scans give a more detailed image of areas inside the body than either scan can by itself.

Magnetic resonance imaging (MRI) scan. This imaging test uses magnetic fields and radio waves to create images of the body's organs and tissues, as well as the brain and spinal cord.

See the free LLS booklets *Understanding Genetics, Biomarker Testing for Cancer Treatment* and *Understanding Lab and Imaging Tests* for more information about these tests.

To view interactive 3D illustrations of some lab and imaging tests, visit www.LLS.org/3D.

Treatment Planning

Choosing a Hospital and Doctor. When you find out that you have cancer, you want to get the best possible medical care and treatment. CTCL can be difficult to diagnose and treat. It is essential to seek treatment in a center with hematologist-oncologists who have significant experience in care of patients with CTCL. A hematologist-oncologist is a doctor who has special training in diagnosing and treating blood disorders and blood cancers such as leukemia, lymphoma and myeloma.

If time allows, you may want to seek a second opinion from another doctor, as it may help you feel more confident about the recommended treatment plan. The second opinion should come from another hematologist-oncologist, preferably one who treats CTCL. These doctors usually have the most knowledge and experience about the latest treatment options for CTCL.

If you are unsure about getting a second opinion or feel uncomfortable about how to tell your current doctor that you are seeking one, call our Information Specialists at (800) 955-4572 to discuss a way to do so that makes you feel comfortable. You may also want to check in advance with your insurance company to be sure that your plan covers the cost of getting a second opinion and to see if specific doctors or centers are recommended.

See the free LLS booklet *Choosing a Specialist or Treatment Center* for more information.

Fertility and Pregnancy. If you are of child-bearing age, you should be aware that some cancer treatments for CTCL can affect your fertility (the ability to have children in the future). Before you begin treatment, it is important to talk with your doctor about whether the treatment could affect your fertility. You may also want to speak with a fertility specialist, a doctor who has special training helping people who have trouble conceiving or carrying a pregnancy to term. This specialist can talk to you about possible options for preserving your fertility. You may be able to take steps to preserve your fertility. However, delaying treatment to address fertility options may not always be recommended.

Some therapies for CTCL can be harmful to an unborn child conceived during treatment. This is because some treatments can cause malformations, abnormalities or death to an unborn child. Females may be advised not to become pregnant while taking certain therapies for CTCL. In that case, your doctor will explain what birth control method you should use and how long you should remain on it. Tell your doctor if you are pregnant, or become pregnant, during CTCL treatment.

Some males may be advised not to father a child while taking certain therapies. Some CTCL drugs may be present in semen. You may need to use either a latex or a synthetic condom or avoid any sexual contact with a female who

is pregnant or may become pregnant while you are taking these medications. Tell your doctor if you have had unprotected sex with a partner who is pregnant or can become pregnant.

View the free LLS booklet *Fertility and Cancer* for more information about fertility preservation.

Staging. When CTCL is diagnosed, your doctor will perform tests to determine the stage of your lymphoma. This process is called “staging.” Staging provides important information about how far the disease has spread in the body and helps in determining the best treatment. Doctors may use the findings from physical examinations, laboratory tests and imaging tests to determine the stage of CTCL.

The International Society for Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC) have developed the TNBM staging system for MF and SS (see **Table 1** on page 15) based on the classification of the following four factors:

- T (tumor)—refers to how much of the skin is affected by the lymphoma and the number, type and size of skin lesions
- N (node)—describes if the lymphoma cells have spread to the lymph nodes
- M (visceral)—refers to if the lymphoma cells have spread to other organs (called “metastasis”)
- B (blood)—refers to the number of lymphoma cells (Sézary cells) in the blood

Table 1. TNMB Classification and Staging of Mycosis Fungoides and Sézary Syndrome

T (skin)

- T0** Absence of clinically suspicious lesions
- T1** Limited patches, papules and/or plaques covering less than 10% of the skin surface
- T2** Patches, papules and/or plaques covering 10% or more of the skin surface
- T3** One or more tumors that are 1cm or more in size
- T4** Erythema covering 80% or more of the body surface area

N (lymph node)

- N0** No abnormal lymph nodes; biopsy not required
- N1** Enlarged lymph nodes, but the cells look normal or close to normal under the microscope
- N2** Enlarged lymph nodes in which many abnormal T cells are found when viewed under a microscope
- N3** Enlarged lymph nodes in which abnormal T cells have altered the structure of the lymph node when viewed under a microscope
- NX** Enlarged lymph nodes that have not been removed for a biopsy.

M (visceral)

- M0** Lymphoma cells have not spread to other organs
- M1** Lymphoma cells have spread to other organs (must have pathology confirmation and organ involved should be specified)

B (blood)

- B0** Absence of significant blood involvement (no blood involvement or very small amounts of Sézary cells in the blood)
- B1** Low blood tumor burden (low numbers of Sézary cells in the blood)
- B2** High blood tumor burden (high numbers of Sézary cells in the blood)

Source: NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines in Oncology. Primary cutaneous lymphomas. 2023.

The physical examination, laboratory and imaging data are used to determine the T, N, M and B status (disease classification) of a patient, and then T, N, M and B are grouped together and assigned a stage that ranges from one (I) through four (IV). See **Table 2**, on page 17. A higher stage indicates more extensive disease. Each stage may further be divided into categories using letters “A” and “B.” Within a stage, “A” refers to a lower stage while “B” refers to a higher stage.

Stage I

- Stage IA (T1, N0, M0, B0 or B1)—less than 10 percent of the skin surface is covered with patches, papules and/or plaques but no skin tumors. The lymph nodes are not enlarged, lymphoma cells have not spread to other organs. There may be low numbers of Sézary cells in the blood.
- Stage IB (T2, N0, M0, B0 or B1)—10 percent or more of the skin surface is covered with patches, papules and/or plaques but no skin tumors. The lymph nodes are not enlarged, lymphoma cells have not spread to other organs. There may be low numbers of Sézary cells in the blood.

Stage II

- Stage IIA (T1 or T2, N1 or N2, M0, B0 or B1)—up to 80 percent of the skin surface is covered with patches, papules and/or plaques but no skin tumors. Lymph nodes are enlarged and may contain lymphoma cells. Lymphoma cells have not spread to other organs. There may be low numbers of Sézary cells in the blood.
- Stage IIB (T3, N0 to N2, M0, B0 or B1)—at least one of the skin lesions is a tumor that is 1 cm across or larger. Lymph nodes may be enlarged and may contain lymphoma cells. Lymphoma cells have not spread to other organs. There may be low numbers of Sézary cells in the blood.

Stage III

- Stage IIIA (T4, N0 to N2, M0, B0)—skin lesions cover at least 80 percent of the skin. The lymph nodes are either normal or are enlarged which may contain abnormal T cells. Lymphoma cells have not spread to other organs, and there is no blood involvement.
- Stage IIIB (T4, N0 to N2, M0, B1)—skin lesions cover at least 80 percent of the skin. Lymph nodes are either normal or enlarged which may contain abnormal T cells. Lymphoma cells have not spread to other organs, and there are low numbers of Sézary cells in the blood.

Stage IV

- Stage IVA₁ (T1 to T4, N0 to N2, M0, B2)—skin lesions can cover any amount of skin. The lymph nodes are either normal or are enlarged which may contain abnormal T cells. The lymphoma cells have not spread to other organs. The number of Sézary cells in the blood is high.

- Stage IVA₂ (T1 to T4, N3, M0, B0 to B2)—skin lesions can cover any amount of the skin. Abnormal T cells have altered the structure of the lymph nodes. Lymphoma cells have not spread to other organs. There may be either high or low numbers of Sézary cells in the blood.
- Stage IVB (T1 to T4, any N, M1, B0 to B2)—skin lesions can cover any amount of the skin. The lymph nodes may be either normal or abnormal. The lymphoma cells have spread to other organs. There may be either high or low numbers of Sézary cells in the blood.

Table 2. Clinical Staging of Mycosis Fungoides and Sézary Syndrome

Clinical Stage	T (skin)	N (node)	M (visceral)	B (blood)
IA (Limited skin involvement)	T1 (Patches, papules and/or plaques covering less than 10% of the skin)	N0	M0	B0 or B1
IB (Skin disease only)	T2 (Patches, papules and/or plaques covering 10% or more of the skin)	N0	M0	B0 or B1
IIA	T1-2	N1-2	M0	B0 or B1
IIB (Tumor stage disease)	T3 (One or more tumors equal to or greater than 1 cm in diameter)	N0-2	M0	B0 or B1
IIIA (Erythrodermic disease)	T4 (Confluence of erythema 80% or more of the skin)	N0-2	M0	B0
IIIB (Erythrodermic disease)	T4 (Confluence of erythema 80% or more of the skin)	N0-2	M0	B1
IVA ₁ (Sézary syndrome)	T1-4	N0-2	M0	B2
IVA ₂ (Sézary syndrome or Non-Sézary)	T1-4	N3	M0	B0 or B1 or B2
IVB (Visceral disease)	T1-4	N0-3	M1	B0 or B1 or B2

Source: NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines in Oncology. Primary cutaneous lymphomas. 2023.

Prognosis. A prognosis is a prediction of the outcome of the patient's disease. It is an educated guess on how well a person will respond to treatment. It is a consideration when planning treatment.

The prognosis for an individual with MF or SS may depend on the following factors:

- Stage of the cancer
- Patient's age and health before diagnosis
- Extent of skin involvement and type of lesions
- Presence of extracutaneous disease (whether the disease has spread from the skin to the lymph nodes or other organs in the body)
- Extent of peripheral blood involvement (amount of Sézary cells in the blood)
- Level of lactate dehydrogenase (LDH) in the bloodstream

Doctors estimate prognosis by using statistics that researchers have collected over many years about patients with the same type of cancer. These statistics are based on large groups of patients, so they cannot predict precisely what will happen to any individual patient. Every person is different. Treatments, and patients' responses to treatments, vary significantly.

Treatment

New treatments may have been approved since this booklet was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Before you begin treatment, you and your doctor will discuss your treatment options. One option may be a clinical trial. Like all treatment options, clinical trials have possible risks and benefits. By considering all your treatment options, including clinical trials, you will be taking an active role in a very important decision that affects you. For more information on clinical trials, see page 28.

Talk to your doctor about:

- Your treatment options and the results you can expect from treatment
- The possibility of participating in a clinical trial

CTCLs are chronic conditions that are generally considered incurable; however, these diseases are treatable and are not life threatening in most cases.

Treatment may put CTCL in remission. This means that the patient has fewer or no signs and symptoms of CTCL. In order to maintain a remission, maintenance therapy is often given with the same treatment at lower doses. Often people

with CTCL require several types of treatment in their lifetime, and they often have good quality of life for years after receiving additional treatment.

Typically, the goals of treatment are to relieve symptoms, induce remission and slow disease progression. The most common and challenging symptom is itching, which can affect a person's quality of life. Severe itching can cause problems sleeping, anxiety and depression.

Specific treatments include watch and wait, skin-directed therapies (treatments that are applied or work externally on the skin) and systemic therapies (treatments that travel through the blood to cells all over the body). While patients with early-stage disease may respond well to skin-directed therapies alone, patients with more advanced disease may require a combination of skin-directed therapies and systemic therapies. For an overview of treatment options, see **Table 3** on page 26. Doctors will consider the side effects of medications and tailor treatments for each individual patient.

For a list of drug classes and drug mechanisms as well as list of drugs to treat CTCL see **Table 4** and **Table 5** on pages 34-37. Some of the treatments are approved by the Food and Drug Administration (FDA). Other treatments are used off-label. "Off-label" prescribing is when a doctor gives a drug that is FDA approved to treat one condition for another condition.

Watch and Wait. Patients with MF stage IA disease have a low risk of disease progression. For some of these patients "watch and wait" may be a reasonable first option. This means that treatment is deferred or delayed until there are signs of disease progression. Frequent and careful observation by a doctor is required so that effective treatment can be started if the disease begins to progress.

See the free LLS booklet *Watch and Wait* for more information.

Skin-Directed Therapies. Skin-directed therapies are treatments that are applied or work externally on the skin. These are often the first treatments used in people with CTCL, especially if the condition does not cover large areas of the body. This is often the case in early stages of MF. Skin-directed therapy may also be used in combination with systemic therapy, which aims to kill cancer cells throughout the body. People with more advanced stages of CTCL often receive both skin-directed and systemic therapies.

Topical Therapies. Topical therapies are treatments that are applied directly to the lesions on the skin. They can be lotions, ointments, creams or gels.

- Topical corticosteroids. Corticosteroids are part of treatment regimens for some lymphomas and can temporarily reduce symptoms such as itching. For CTCLs, topical corticosteroids may be used in the treatment of individual lesions to help alleviate red, swollen and inflamed skin. They may be prescribed in a cream, lotion, foam, gel or ointment formulation. Long-term use of topical corticosteroids can have side effects such as thinning of the skin and stretch marks.

- Topical chemotherapy. **Nitrogen mustard (mechlorethamine HCl, Valchlor gel®)** is a chemotherapy drug that can be applied directly to skin lesions. It is a gel that is in a class of medications called “alkylating agents.” It works by slowing or stopping the growth of cancer cells. The most common side effects include redness, swelling, itching, skin ulcers or blisters, skin infection and darkening of areas of the skin. Get medical help right away if the gel gets in your eyes, mouth or nose. Caregivers or family members who accidentally come into contact with the medication should wash the affected area with soap and water right away for at least 15 minutes and remove any contaminated clothing. Females should avoid becoming pregnant during treatment as it may harm their unborn baby. Males who are using topical chemotherapy, and who have female partners who are able to become pregnant, should use a barrier method of birth control such as a condom.
- Topical retinoids. Retinoids are drugs related to vitamin A that can slow the growth of certain types of cancer cells. **Bexarotene gel (Targretin®)** and **tazarotene (Avage®, Tazorac®)** are topical retinoids that can be applied directly to skin lesions. Bexarotene is the only topical retinoid approved by the FDA for the treatment of CTCL, but some doctors use tazarotene off-label to treat skin lymphomas. Topical retinoids frequently cause skin irritation, but this side effect typically disappears once the drugs are stopped. Retinoids can cause severe harm to unborn babies and should never be used by pregnant females or females who plan to become pregnant. If you are male and have a partner who is pregnant or can become pregnant, talk to your doctor about precautions you should take during treatment with a retinoid.
- Topical immunotherapy. Immunotherapy modifies the activity of your immune system. By doing so, it improves your body’s ability to find and destroy cancer cells. **Imiquimod (Aldara®)** cream is a type of immunotherapy that is applied to skin lesions. Some doctors use it off-label to treat skin lymphomas. Several research groups have reported the effectiveness of imiquimod in early-stage MF. Side effects may include redness, itching, flaking, scaling or thickening of the skin.

Phototherapy. This treatment uses ultraviolet (UV) light, the same type of light that comes from the sun. It is used to treat CTCL that does not respond to topical medications or that covers large areas of skin. The ultraviolet light damages the abnormal T cells found in the skin.

There are two main types of phototherapy used to treat CTCL—ultraviolet A (UVA) and ultraviolet B (UVB). Both UVA and UVB therapy are given using special lamps that direct the radiation beam to the target area on the skin. Phototherapy can be given to a specific area of the body or to the entire body, and it can be used with topical therapies.

- Ultraviolet B phototherapy. UVB phototherapy uses UVB light to treat patches and thin plaques. It can be either broadband or the more commonly

used narrowband. The patient will stand undressed in a “cabinet” or “box” that is fitted with fluorescent light tubes for up to 30 minutes. Some parts of the body, such as the eyes, will be covered. The dose of UVB is usually increased at each visit. Patients typically have 3 to 5 treatments a week. Skin lesions often begin to fade after 20 to 40 visits. Once the lesions are gone, the number of visits is reduced and then eventually stopped. Side effects may include red, painful skin that resembles a sunburn.

- Psoralen plus ultraviolet A (PUVA). This type of therapy uses UVA light and an oral medication called “psoralen.” For patients who have skin plaques, PUVA is often recommended instead of UVB. Ultraviolet A is able to penetrate deeper into the skin than UVB, so PUVA may be more effective for the treatment of thick lesions. Approximately 1 to 2 hours before a PUVA treatment, the patient will receive the medication psoralen. Typically, it is given in pill form. The patient waits for the psoralen to be absorbed. Patients then remove their clothing and wear goggles to protect the eyes and a visor if their faces are unaffected. They stand in a “cabinet” that has many UVA bulbs. Patients are usually exposed to the UVA for up to 30 minutes. This therapy is often given 2 to 3 times a week until the lesions are gone. This can often take 4 to 6 months.

After treatment, a patient’s skin may appear red and blistered. It may also feel dry and itchy. Psoralen makes the skin more sensitive to light so patients may burn more easily than usual in the sun. Patients should protect their skin from the sun for at least 24 hours after treatment.

Long-term phototherapy is associated with an increased risk of skin cancer (basal cell and squamous cell cancers and melanoma). Patients who have a strong personal or family history of these skin cancers should discuss the risks and benefits of phototherapy with their doctor.

Radiation Therapy. This type of treatment uses high-energy x-rays or other types of radiation to kill cancer cells. Radiation therapy can be used to treat individual CTCL lesions or the entire skin surface. It is very effective in treating lesions. It may be used alone for patients with single lesions, but it is often used along with other systemic treatments.

“Electron beam therapy” is a form of radiation therapy that is most frequently used to treat skin lesions. Electrons do not penetrate deeply into the body, so they are less likely to harm the tissue and organs beneath the skin. Patients with one lesion or a few lesions can be treated with localized electron beam therapy. For patients with widespread lesions, total skin electron beam therapy can treat the entire skin surface. Typically treatment is given up to 5 times a week over a period of 3 to 4 weeks.

- Localized electron beam therapy. This type of therapy has been helpful for patients who have a few lesions. Prior to treatment, the patient undergoes

a treatment planning procedure called a “simulation.” The simulation ensures that the treatment site is mapped out correctly on the patient’s body. During the simulation, the radiation therapist takes pictures of the patient’s skin and uses a felt marker to outline the area(s) of the skin that need to be treated.

During an actual treatment, the patient is positioned on the table in exactly the same way as in the simulation. Once the patient is in the correct position, the radiation therapist leaves the room and begins the treatment. Patients will neither see nor feel the radiation, although they may hear the machine as it turns on and off and moves around them. Patients who receive spot treatment usually have minor side effects that involve the skin, hair and nails in the treated areas.

- Total skin electron beam therapy. This type of therapy is appropriate for patients with widespread thick plaques, either with or without skin tumors. During treatment, the patient stands on a platform that rotates so that the entire surface of the patient’s skin can be treated from different angles. Receiving the radiation usually takes just a few minutes. Side effects typically involve the skin, hair, fingernails and toenails. The skin may become red, dry and irritated over the entire body. The redness and irritation typically improve after the treatment is finished. A patient may lose body hair including on the head (scalp), eyebrows and pubic area. This loss is usually temporary, and hair will begin to grow back 3 to 6 months after treatment is completed. A patient’s fingernails and toenails may also fall out, but new ones eventually begin to grow.

Systemic Therapies. These therapies travel through the blood to reach cells all over the body including the skin. Systemic therapies are most useful for more advanced or quickly growing CTCL. In some patients with CTCL, a systemic treatment is combined with a skin-directed therapy or with another systemic treatment.

Extracorporeal Photopheresis. This treatment is for people whose CTCL has traveled beyond the skin into the bloodstream. It is most effective in patients with blood involvement such as those who have Sézary syndrome.

Extracorporeal photopheresis is a method of treating T cells outside of the body. In this procedure, blood is removed through a patient’s vein. The photopheresis machine separates the white blood cells from the rest of the blood. The red blood cells and plasma are returned to the patient’s body. The white blood cells are then treated with a medication called “methoxsalen” and exposed to UVA light, which activates the methoxsalen. The treated white blood cells are subsequently returned to the body. This process injures the cancerous T cells and helps stimulate the immune system to fight the cancer. This procedure takes about 3 to 4 hours. Patients are treated on 2 consecutive

days. Treatment is typically repeated every 2 weeks until the full effect takes place. This treatment is very well tolerated and has no long-term side effects.

Oral Retinoids. Retinoid are drugs related to vitamin A and can slow the growth of certain cancers. While some retinoids are applied directly to the skin, other retinoids are formulated as pills and are used to treat CTCL that is more widespread on the skin. Doctors use oral retinoids **bexarotene (Targretin®)**, **acitretin (Soriatane®)**, **isotretinoin (Accutane®)** and **tretinoin (Vesanoid®)** to treat MF and SS, but only bexarotene is approved by the FDA for treating MF. Common side effects include hyperlipidemia (high numbers of fat particles in the bloodstream) and hypothyroidism (low levels of thyroid hormones). Patients may also develop dry skin, muscle and joint pain, headaches and light sensitivity. Most side effects of retinoids diminish once treatment has been completed. Retinoids can cause severe harm to unborn babies and should never be used by pregnant females or females who plan to become pregnant. If you are male and have a partner who is pregnant or can become pregnant, talk to your doctor about precautions you should take during treatment with a retinoid.

Histone Deacetylase (HDAC) Inhibitors. HDAC inhibitors are a class of anticancer agents that modify abnormal cancer genes and cause the cancer cells to stop dividing and die. **Vorinostat (Zolinza®)** and **Romidepsin (Istodax®)** are HDAC inhibitors that are used to treat CTCL. They are usually given after other treatments have been tried. Common side effects may include nausea, diarrhea, fatigue, dry mouth, hair loss, fever, headaches, changes in taste and low platelet counts.

Monoclonal Antibodies. These are immunotherapy drugs that are designed to target specific proteins in cancer cells while minimizing harm to healthy cells. Some of these drugs work by themselves while others are coupled with chemotherapy drugs, toxins or radioactive substances to target malignant cells. The anti-CC chemokine receptor 4 (CCR4) monoclonal antibody **mogamulizumab-kpkc (Poteligeo®)** targets the CCR4 protein, which is frequently found on the surface of cancer cells in patients with CTCL. Mogamulizumab is used in the treatment of people with relapsed or refractory MF or SS. **Pembrolizumab (Keytruda®)** is a monoclonal antibody that binds to the protein PD-1 on the surface of T cells. It works by keeping cancer cells from suppressing the immune system. This allows the immune system to attack and kill cancer cells. Pembrolizumab is being studied in clinical trials for the treatment of relapsed and refractory MF and SS. **Alemtuzumab (Lemtrada®)** is an anti-CD52 monoclonal antibody that is used for patients with advanced CTCL, mostly in patients with SS. While alemtuzumab is no longer commercially available it may be obtained for compassionate use for patients.

Antibody-Drug Conjugates. These drugs are designed to target specific proteins on the surface of cancer cells. CD30 is a protein that is sometimes expressed in MF, especially the aggressive transformed MF. This protein can be targeted with anticancer therapies. One such agent, **brentuximab vedotin (Adcetris®)**, attaches to cells that express CD30 antigens, penetrates the lymphoma cells and directly delivers chemotherapy to the lymphoma cells and kills them. The most common side effects include neutropenia (low white blood cell count), anemia (low red blood cell count), peripheral neuropathy, nausea, fatigue, constipation, diarrhea and vomiting.

Interferons. These drugs are a type of immunotherapy. Interferons are natural substances that help the body's immune system fight infection and other diseases such as cancer. Interferons are made in the body, but they can also be made in the laboratory to use as treatments. In cancer therapy, interferons may help keep cancer cells from growing and may help kill cancer cells. **Interferon (IFN)-alfa** and **interferon (IFN)-gamma** can cause some types of CTCL to shrink or stop growing. These treatments are given several times a week. Common side effects include neutropenia, flu-like symptoms, fatigue, nausea, vomiting, depression, hair thinning and heart and liver damage.

Chemotherapy. Chemotherapy works by either stopping or slowing the growth of cancer cells. Different types of chemotherapy drugs work in different ways to eliminate lymphoma cells or stop new lymphoma cells from forming. Mechlorethamine (nitrogen mustard, **Valchlor®**) is an example of a chemotherapy drug that can be applied directly to the skin, but most chemotherapy drugs for MF and SS are given as systemic therapy either intravenously or by mouth. These treatments travel in the bloodstream to treat cancer throughout the body. Systemic chemotherapy is generally used in patients with advanced-stage MF or SS whose disease has relapsed multiple times and who have few therapeutic options. Responses to chemotherapy are rarely durable in patients with MF and SS. As a result, eventually, MF and SS both relapse in most patients treated with chemotherapy.

Side effects of chemotherapy depend on many factors, including the type of treatment and dosage, the age of the patient and coexisting medical conditions. Therapy may cause fever or chills, fatigue, nausea, loss of appetite, mouth sores, peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet), changes in blood cell counts, infection, rash, vomiting, diarrhea, shortness of breath, swelling, temporary hair loss and other side effects.

Most side effects are temporary and resolve when treatment is completed. However, other side effects persist over the long term and may appear years after the treatment has been completed. Late side effects may include developing another type of cancer, heart disease, low levels of thyroid hormones (hypothyroidism), nerve damage and loss of fertility.

Some systemic chemotherapies for patients with MF and SS include:

- **Chlorambucil (Leukeran®)**
- **Cyclophosphamide (Cytoxan®)**
- **Etoposide (VP-16, VePesid®, Etopophos®)**
- **Gemcitabine (Gemzar®)**
- **Liposomal doxorubicin (Doxil®)**
- **Methotrexate (Trexall®)**
- **Pentostatin (Nipent®)**
- **Pralatrexate (Folotyn®)**

Table 3. Treatments for Cutaneous T-Cell Lymphoma

Skin-Directed Therapies	Systemic Therapies	Combination Therapies
<p>For limited/localized skin involvement</p> <ul style="list-style-type: none">• Topical corticosteroids• Topical chemotherapy• Topical retinoids• Topical imiquimod• Local radiation• Phototherapy <p>For generalized skin involvement</p> <ul style="list-style-type: none">• Topical corticosteroids• Topical chemotherapy• Phototherapy• Total skin electron beam therapy	<ul style="list-style-type: none">• Oral retinoids• Interferons• Histone deacetylase (HDAC) inhibitors• Extracorporeal photopheresis (ECP)• Monoclonal antibodies• Antibody-drug conjugates• Chemotherapy	<p>Skin-Directed + Systemic</p> <ul style="list-style-type: none">• Phototherapy + retinoid• Phototherapy + interferon• Phototherapy + ECP• Total skin electron beam + ECP <p>Systemic + Systemic</p> <ul style="list-style-type: none">• Retinoid + interferon• ECP + retinoid• ECP + interferon• ECP + retinoid + interferon

Source: NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines in Oncology. Primary cutaneous lymphomas. 2023.

New treatments may have been approved since this booklet was printed.
Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Relapsed and Refractory Disease

Some people with CTCL do not respond to initial therapy. When this occurs, it is called “refractory” disease. In other patients CTCL comes back after a remission. In these cases, it is called “relapsed disease.”

Many people with refractory CTCL can achieve a remission with different treatments, and many people with relapsed CTCL can obtain another period of remission with additional treatment. This approach can control CTCL for many years. Often people with CTCL will require several different treatments in their lifetime, and they often have a good quality of life for years after receiving additional treatment.

Allogeneic Stem Cell Transplantation. For some people, the doctor may recommend allogeneic stem cell transplantation to manage CTCL that is growing rapidly and not responding to skin-directed or systemic therapies.

The goal of allogeneic stem cell transplantation is to cure CTCL. Typically, the process involves administering intensive chemotherapy, followed by infusion of healthy stem cells from a donor.

Compared to other treatment options, allogeneic stem cell transplantation is associated with a higher rate of side effects and mortality. The decision to perform an allogeneic transplant also depends on many factors, including the patient’s age, physical fitness, comorbidities (other coexisting medical conditions) and social supports (from family members, caregivers, friends, etc.), as well as the patient’s understanding of the potential benefits and risks. Allogeneic stem cell transplantation may be an appropriate therapy for carefully selected younger people with CTCL who have an available donor. Talk to your doctor to see if this is a treatment option for you.

Reduced-Intensity Allogeneic Stem Cell Transplantation. This type of transplantation may be a treatment option for older patients who cannot tolerate the high doses of chemotherapy used in preparation for a standard allogeneic stem cell transplant. The conditioning therapy in a reduced-intensity transplant uses lower doses of chemotherapy and/or radiation. With a reduced-intensity conditioning regimen, the patient’s blood cell counts may not fall as low as they would with high-dose chemotherapy. Additionally, the less toxic regimens put less strain on the patient’s organs, making this regimen safer and more tolerable.

For more information, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called clinical trials and they are used to find better ways to care for and treat people with cancer.

In the United States, the FDA (U.S. Food and Drug Administration) requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer.

Researchers use cancer clinical trials to study new ways to:

- Treat cancer using
 - A new drug
 - An approved drug to treat a different kind of cancer
 - A new combination of drugs
 - A new way of giving a drug—by mouth (pill), intravenously (IV)
- Manage cancer symptoms and ease treatment side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients being willing to join clinical trials. Anyone interested in being part of a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/WhatToAsk for lists of suggested questions).
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes.

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **LLS Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome barriers to enrollment and provide support throughout the entire clinical trial process.

Our Clinical Trial Nurse Navigators are registered nurses who are experts in adult and pediatric blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (like past treatments, treatment responses, and your cancer genetic profile), your current health, and your medical history—because these might impact whether you can take part in certain clinical trials
- Help you understand how your finances, insurance coverage, support network, and ability and willingness to travel might impact your choice of clinical trials
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you enroll in a trial
- Support you throughout the clinical trial process

Please call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.

Also, visit www.LLS.org/booklets to view *Understanding Clinical Trials for Blood Cancers*.

Side Effects of Treatment

The side effects of treatment will depend on many factors including the type of treatment, the drug dosage, the age of the patient and any coexisting medical conditions. Therapy may induce fatigue, nausea, fever, chills, dizziness, blood clots, infertility and other effects.

Managing the side effects of treatment is important. Patients should discuss side effects with their doctors to get help. Most side effects can be managed without compromising the effectiveness of treatment. In fact, aggressive management of side effects often leads to better treatment outcomes. Most side effects are temporary and resolve when treatment is completed. However, some side effects are long term and may appear years after the treatment has been completed. Late side effects may include developing another type of cancer, heart disease, low levels of thyroid hormones (hypothyroidism) and loss of fertility.

Visit www.LLS.org/booklets to view the free LLS series *Side Effect Management* (filter for Side Effect Management) for more information.

Supportive Care

Supportive care refers to specialized medical care focused on providing relief from symptoms and the stresses of a serious illness. The goal of supportive care is to improve the patient's quality of life and to relieve discomfort as much as possible. Supportive care is an important part of CTCL treatment. It can help relieve or prevent symptoms of CTCL such as itching and skin infections, but it does not treat the disease itself.

To protect the skin, it is important for MF and SS patients to keep their skin well moisturized. Dry, cracked skin can intensify itching and can allow infectious agents to penetrate the skin. To protect the skin, patients should:

- Take shorter showers or baths (5 to 10 minutes maximum) in warm, not hot, water. Showering or bathing too long can dry out your skin.
- Use a mild cleanser that is scent-free and dye-free.
- Wash your skin gently and avoid rubbing your skin with a washcloth or sponge.
- Pat off water gently and apply a thick ointment or moisturizer after showering or bathing.
- Apply moisturizers frequently, at least two to three times a day.
- Use fragrance-free laundry detergents and fabric softeners. The fragrances in these products can come in contact with the skin and cause irritation.
- Keep your skin comfortable by wearing loose-fitting clothes made of fabrics that “breathe” such as cotton.
- Avoid becoming over-heated. Sweating can worsen the itch.

Most people with MF and SS suffer from severe itching that may be difficult to control. Patients should be evaluated for itching at each visit to the doctor. Supportive therapies that may help manage itching include:

- Placing ice packs on itchy area
- Soaking in an oatmeal bath
- Using topical corticosteroids, with or without occlusion. Occlusion involves covering the treated area with a dry, protective dressing (wrapping it in cloth).
- Taking oral medications:
 - Antihistamines, such as diphenhydramine (Benadryl®) or hydroxyzine (Atarax®), may relieve itching. The major side effect of these drugs is drowsiness, so they are frequently prescribed for use at night. Nonsedating antihistamines such as loratadine (Claritin®), cetirizine (Zyrtec®), and fexofenadine (Allegra®) can be prescribed for daytime use, but these drugs are generally less effective.

- Antidepressants doxepin (Zonalon®) and mirtazapine (Remeron®) may help manage itching.
- Aprepitant (Emend®) is a prescription medication used for preventing chemotherapy-induced nausea that has been shown to reduce itching.
- Gabapentin (Neurontin®), an anticonvulsant prescribed to individuals prone to seizures, has been effective in treating severe itching.

Because people with MF and SS frequently have cracked and ulcerated skin, they are susceptible to bacterial skin infections and viral herpes skin infections. Patients should consider taking the following preventive measures to reduce infections:

- Routinely use skin moisturizers to protect the skin.
- Wash skin gently with an antibacterial soap and apply an antibiotic ointment to skin lesions.
- Take bleach baths or soaks. This can help with skin irritation and help lower the risk of skin infections, especially if you have any open sores. To make a bleach bath, add ½ cup of liquid bleach to every ¼ full bathtub of warm water. Avoid getting the water with bleach in your face, eyes or hair. Do not sit in the bath for longer than 10 minutes. Ask your doctor how often you should take a bleach bath. If you do not have a bathtub, you can make your own bleach-based spray (talk to your doctor for directions).

It is important to recognize the signs of skin infections. Signs of skin infection may include redness, swelling, increased pain or pus (weeping fluid). Patients with infections may need aggressive antibiotic treatment.

Follow-Up Care

Your doctor will continue to monitor your lymphoma and manage your side effects of treatment. This is called follow-up care.

Monitoring for Recurrence. After a patient completes treatment and is in remission, follow-up tests are done to check how well the treatment worked and to look for signs of relapse. Tests are also done to see how well the patient's organs are working.

You are encouraged to:

- Maintain regular follow-up appointments with your doctors. They will monitor you for signs of relapse and will also be able to detect any treatment side effects or the onset of other medical problems.
- Keep a record of your cancer diagnosis, treatment and follow-up care needs. This record, often called a “survivorship care plan,” should be provided to you in writing so you can share it with any new healthcare providers you see. Ask the doctor for this information. The plan should include the following information:
 - List of all healthcare providers
 - Diagnosis summary with specifics such as subtype and/or genetic markers
 - Treatment summary with specifics such as the names, dates, and dosages of chemotherapy or other drugs, the area treated with radiation therapy, surgery and/or transplantation information, as well as treatment response and side effects
 - Maintenance treatment information, if applicable
 - List of possible late effects
 - Schedule for ongoing monitoring with recommended tests, frequency and coordinating provider
 - Health and wellness recommendations, such as nutrition, exercise and other disease screenings
- Receive periodic screening and monitoring for other types of cancer, including skin, gastrointestinal, kidney, blood, bladder, prostate, breast, lung, head and neck cancer, if you have received treatments that increase the risk of developing a second cancer.
- Seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.
- Consider ways to reduce your risks for cancer, such as quitting smoking and vaping, protecting your skin from prolonged sun exposure, maintaining adequate nutrition and exercising.

Vaccines. People with non-Hodgkin lymphoma are advised to receive certain vaccinations. For adult patients, these include vaccinations for influenza and pneumococcal pneumonia and the inactivated (or killed) vaccine for the herpes virus, called **Shingrix**. Patients should not be given vaccines that use live organisms or those with high viral loads. Current COVID-19 vaccines are also recommended. Speak to your doctor for more information on vaccines.

Visit [LLS.org/SurvivorshipWorkbook](https://lls.org/SurvivorshipWorkbook) to view the free LLS survivorship publications *Navigating Life During and After a Blood Cancer Diagnosis* with versions for Adults, Young Adults and Children and Adolescents.

Financial Concerns

Paying for healthcare is a major concern for many people who are living with blood cancer. The high cost of cancer treatment can lead to significant financial and emotional stress for both patients and their families. Even if you have health insurance, cancer can still take a toll on your finances. You may have new expenses such as co-payments or travel for treatment. You may also have less income if you need to take time off from work.

Speak with your healthcare team if you have any concerns about being able to afford your treatment. They may be able to provide information and resources that can help. Health insurance plans may not cover all of the costs of cancer care, but there are many resources available to help with prescription drug payment. In addition, several major drug manufacturers currently provide patient assistance or prescription assistance programs. These programs can provide both insured and uninsured patients free or reduced-cost medications.

LLS offers financial assistance programs for eligible patients. Other organizations also offer financial assistance programs. You can call an LLS Information Specialist at (800) 955-4572 for more information about our financial assistance programs.

For more information and resources to help cope with the financial costs of cancer care, please see the free LLS booklet *Cancer and Your Finances*.

Treatment Outcomes

The prognosis for patients with mycosis fungoides (MF) and Sézary syndrome (SS) depends on a number of factors, including patient age, disease type and stage, rate of disease progression and response to therapy. Some patients may have stable or slowly progressive disease, while others may have a more rapidly progressive disease. Many MF patients will have disease limited to the skin. These patients may live normal lives for many years while being treated for their disease, and some are able to remain in remission for long periods of time.

For these patients, a normal life span can be expected. A minority of patients will experience a more rapidly progressive disease that spreads to the lymph nodes and/or other organs. It is important to emphasize that outcomes for patients with advanced disease are improving as a result of new treatment options.

Drug Information

The two following tables include information about drug classification and treatments for CTCL.

Table 4. Drug Classes and Drug Mechanisms

Alkylating Agents (DNA-Damaging Drugs)	These drugs work by either stopping or slowing the growth of cancer cells in the body.
Antibody-Drug Conjugates	These drugs are made up of a monoclonal antibody chemically linked to a drug. The monoclonal antibody binds to specific proteins or receptors on certain types of cells, including cancer cells. The linked drug enters these cells and kills them without harming other cells.
Antifolates	Antifolates stop cells from using folic acid to make DNA and may kill cancer cells.
Antimetabolites	These drugs mimic the building blocks of DNA or RNA that cancer cells need to survive and grow. When the cancer cell uses an antimetabolite instead of the natural substances, it cannot produce normal DNA or RNA and the cell dies.
Antitumor Antibiotics	Anticancer drugs that block cell growth by interfering with DNA.
Corticosteroids	Certain hormones (corticosteroids) can kill lymphocytes. They are believed to work by blocking cell metabolism through their effect on specific genes. In high doses, these synthetic hormones—relatives of the natural hormone cortisol—can kill malignant lymphocytes.
DNA Repair Enzyme Inhibitors	These drugs selectively kill cancer cells that have a defect in the DNA damage response or DNA repair.
Histone Deacetylase (HDAC) Inhibitors	Histone deacetylase inhibitors are substances that cause a chemical change that stops cancer cells from dividing.
Immunomodulator	A type of therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection and other diseases.
Monoclonal Antibodies	Monoclonal antibodies are laboratory-produced proteins that target specific antigens on the cancer cell's surface to interfere with the cell's function and destroy it. Once the antibody finds and attaches to its target, it can “recruit” (harness) other parts of the immune system to destroy cells that contain the antigen.

Table 4. Drug Classes and Drug Mechanisms (continued)

Purine Analogs	These drugs are similar to a natural chemical compound called purine. Cells use purine to make the chemical building blocks of DNA and RNA. Purine analogs may kill cells, including cancer cells, by blocking important enzymes needed to make DNA and RNA and by damaging DNA.
Retinoids	These are vitamin A or vitamin A-like compounds that may stop the growth of cancer cells.

Table 5. Some Drugs Used in the Treatment of Cutaneous T-cell Lymphoma (CTCL)

For more information, see the package insert and/or the full prescribing information for each medication (available on the internet).

Drug Name Type of Drug Administration	Indications
Acitretin (Soriatane®) Retinoid Oral	Off-label treatment for CTCL.
Alemtuzumab (Lemtrada®) Monoclonal Antibody Intravenous (IV)	While alemtuzumab is no longer commercially available, it may be obtained for compassionate use for the treatment of Sézary syndrome.
Bexarotene (Targretin®) Retinoid Oral	Indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma in patients who are refractory to at least one prior systemic therapy.
Bexarotene gel (Targretin®) Retinoid Topical	Indicated for the topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.
Brentuximab vedotin (Adcetris®) Antibody-Drug Conjugate Intravenous (IV)	Indicated for the treatment of adult patients with primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy.
Chlorambucil (Leukeran®) Alkylating Agent Oral	Indicated for the treatment of untreated and relapsed/refractory non-Hodgkin lymphoma.

Drug Name Type of Drug Administration	Indications
Cyclophosphamide (Cytoxan®) Alkylating Agent Intravenous (IV) or Oral	Indicated for the treatment of non-Hodgkin lymphoma.
Etoposide (Etopophos®, VePesid®, VP-16) DNA Repair Enzyme Inhibitor Intravenous (IV) or Oral	Off-label treatment for non-Hodgkin lymphoma.
Gemcitabine (Gemzar®) Antimetabolite Intravenous (IV)	Off-label treatment for CTCL.
Imiquimod (Aldara®) Immunomodulator Topical	Off-label treatment for CTCL.
Interferon-alfa (Roferon-A®) and interferon-gamma (Actimmune®) Immunomodulator Subcutaneous Injection	Off-label treatment for CTCL.
Isotretinoin (Accutane®) Retinoid Oral	Off-label treatment for CTCL.
Liposomal Doxorubicin (Doxil®) Antitumor Antibiotic Intravenous (IV)	Off-label treatment for CTCL.
Methotrexate (Trexall®) Antimetabolite Oral	Indicated for the treatment of adults with mycosis fungoides (cutaneous T-cell lymphoma) as a single agent or as part of a combination chemotherapy regimen.
Mogamulizumab-kpkc (Poteligeo®) Monoclonal Antibody IV Injection	Indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy.

Drug Name Type of Drug Administration	Indications
Nitrogen mustard (mechlorethamine HCl, Valchlor gel®) Alkylating agent Topical	Indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.
Pembrolizumab (Keytruda®) Monoclonal Antibody Intravenous (IV)	Off-label treatment being studied for advanced mycosis fungoides and Sézary syndrome.
Pentostatin (Nipent®) Purine Analog Intravenous (IV)	Off-label treatment for CTCL.
Pralatrexate (Folotyn®) Antifolate Intravenous (IV)	Off-label treatment for CTCL.
Romidepsin (Istodax®) Histone Deacetylase (HDAC) Inhibitor Intravenous (IV)	Indicated for the treatment of cutaneous T-cell lymphoma (CTCL) in adult patients who have received at least one prior systemic therapy.
Tazarotene (Avage®, Tazorac®) Retinoid Topical	Off-label treatment for CTCL.
Tretinoin (Vesanoid®) Retinoid Oral	Off-label treatment for CTCL.
Vorinostat (Zolinza®) Histone Deacetylase (HDAC) Inhibitor Oral	Indicated for the treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma (CTCL) who have progressive, persistent or recurrent disease on or following two systemic therapies.

Normal Blood and Bone Marrow

Blood. Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

Plasma. Plasma is largely made up of water, in which many chemicals are dissolved. These chemicals each have a special role. They include:

- Proteins
 - Albumin, the most common blood protein
 - Blood-clotting proteins (coagulation factors) made by the liver
 - Erythropoietin, a protein made by the kidneys that stimulates red blood cell production
 - Immunoglobulins, proteins that help the body fight infection
- Hormones, such as thyroid hormone and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate (B9) and vitamin B12
- Electrolytes, such as calcium, potassium and sodium

Blood Cells. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis." See **Figure 2** on page 40. The blood cells are suspended in the plasma.

Stem cells in the bone marrow develop into three types of mature blood cells:

1. Red blood cells are the cells that carry oxygen; they

- Make up a little less than half of the body's total blood volume
- Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO₂) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO₂ is removed from the lungs.

2. Platelets are cells that help blood clot; they

- Are small cells (one-tenth the size of red blood cells)
- Help stop bleeding from an injury or cut
- Stick to the torn surface of the vessel, clump together, and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.

3. White blood cells (WBCs) are cells that fight infections. The several types of WBCs include:

- Neutrophils and monocytes. These are “phagocytes” (eating cells) that ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
- Eosinophils and basophils. These WBCs respond to allergens or parasites.
- Lymphocytes. WBCs found mostly in the lymph nodes, spleen and lymphatic channels, lymphocytes are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
 - T lymphocytes (T cells)
 - B lymphocytes (B cells)
 - Natural killer (NK cells)

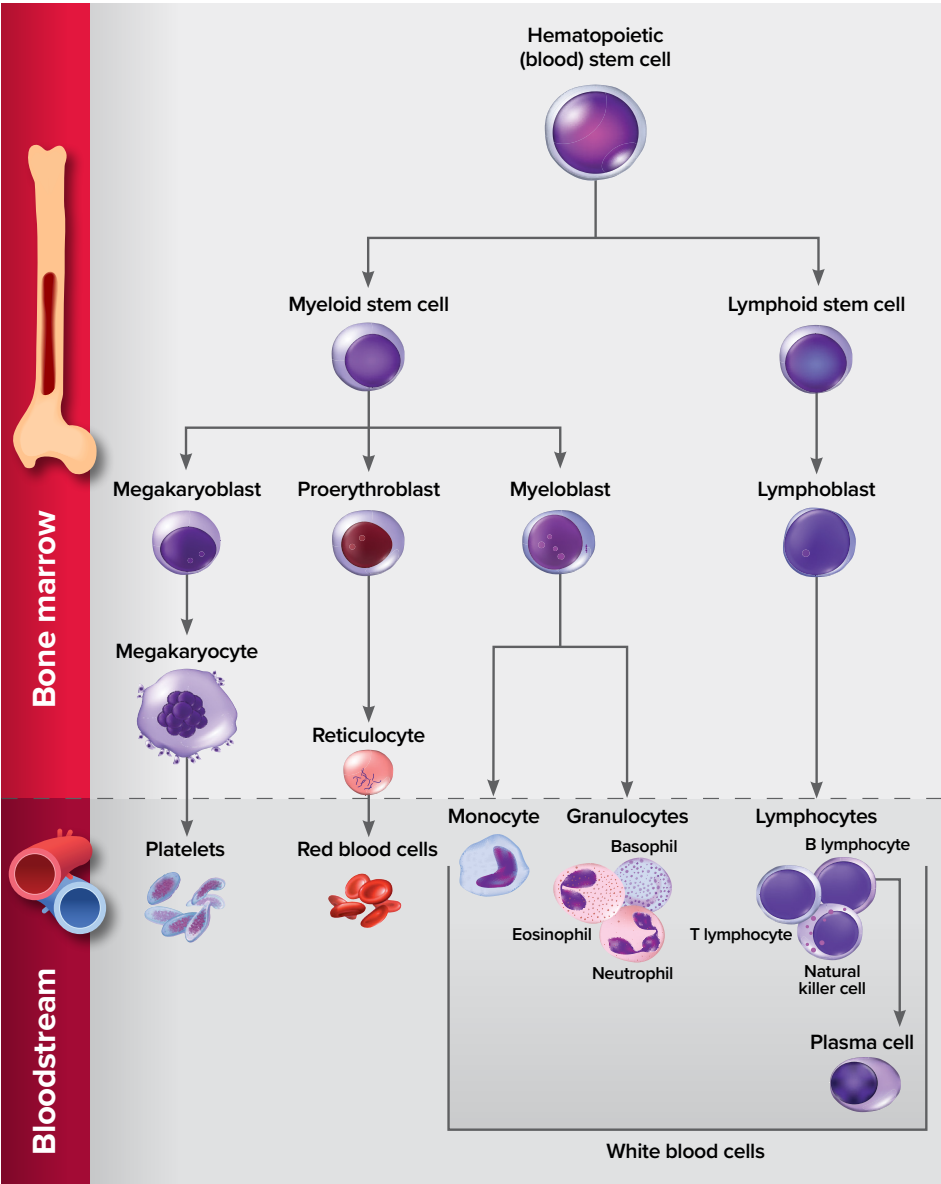
Bone Marrow. In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the bone marrow and then circulates throughout the body.

In babies, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have blood-forming marrow. In adults, bone marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull.

Hematopoietic stem cells are found in the bone marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the bone marrow and have them migrate into the bloodstream. Then a special technique called “apheresis” is used to separate them from the circulating blood so they can be collected and stored. Stem cells can also be collected from the placenta and umbilical cords of newborn infants. The cells are stored and later used for transplantation.

Figure 2. Blood Cell and Lymphocyte Development

Most blood cells start as hematopoietic (blood) stem cells in the bone marrow. Hematopoietic stem cells are the most immature blood-forming cells. They must mature (go through many stages) to become a red blood cell, white blood cell or platelet. Some blood cells mature in the bone marrow. Other blood cells leave the bone marrow and travel to other parts of the body to develop into mature blood cells.



The Lymphatic System

The lymphatic system is the tissues and organs that produce, store and carry lymphocytes (a type of white blood cell) that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and lymphatic vessels (a network of thin tubes that carry lymph and white blood cells). See **Figure 3** on page 42.

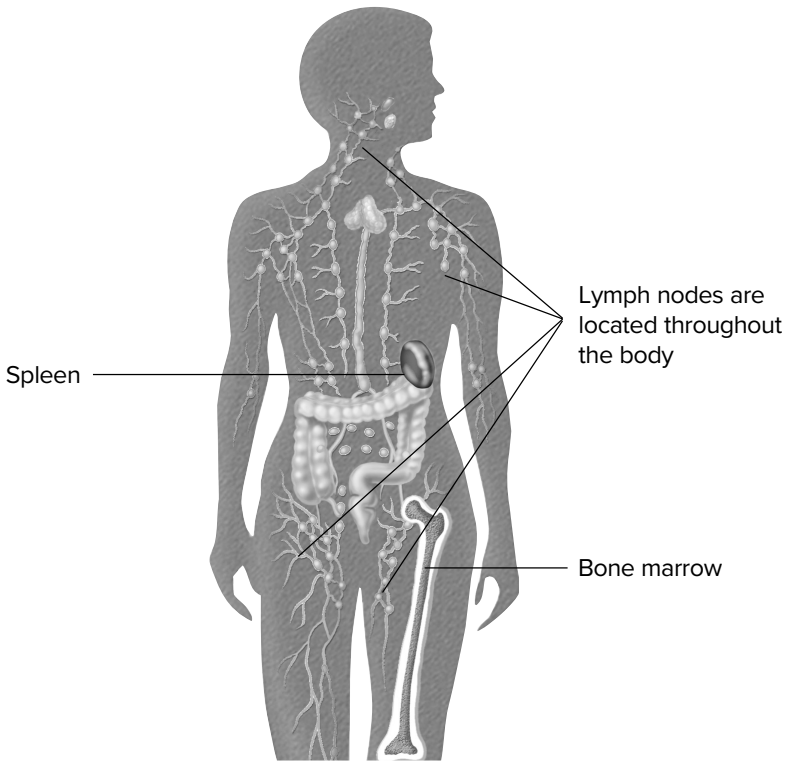
The bone marrow is really two organs in one. It is the organ that forms blood cells, and it is also the organ that forms lymphocytes, which make up part of the immune system.

The marrow produces three main types of lymphocytes. They are:

- B lymphocytes (B cells), which make antibodies in response to foreign antigens, especially microbes
- T lymphocytes (T cells), which mature in the thymus. The T lymphocytes have several functions, including assisting B lymphocytes to make antibodies against invading bacteria, viruses or other microbes. The antibody attaches to the microbe, making it possible for other white blood cells to recognize the antibody and pull it into the cell (ingest it) along with its attached microbe. The white blood cell then kills and ingests the microbe.
- Natural killer (NK) cells, which attack virus-infected cells or tumor cells without requiring an antibody or other mediation. T cells and NK cells have other functions as well, and are important elements in research efforts to design immunotherapies to treat lymphoma and other cancers.

The lymphocytes circulate through channels called “lymphatics,” which connect the lymph nodes to each other throughout the body. The lymphatic channels collect into large ducts that empty into blood vessels. Lymphocytes enter the blood via these ducts. Most lymphocytes are found in the lymph nodes and other parts of the lymphatic system, such as the skin, spleen, tonsils and adenoids, intestinal lining, and (in young people) the thymus.

Figure 3. The Lymphatic System



The lymphatic system is part of the immune system. The normal immune system helps to protect the body from infection. The marrow, lymph nodes and spleen are parts of the immune system. There are about 600 lymph nodes throughout the body.

Lymph nodes and other lymphoid tissues that are commonly involved in lymphoma are those around the ears and jaw, in the tonsils and adenoids, in the front and back of the neck, above and below the collar bone, in the armpit, near the elbow, in the chest, in the abdomen, in the pelvis and in the groin. The spleen contains many clusters of lymphocytes that can become malignant and grow, leading to the enlargement of the spleen. The gut-associated (intestinal) lymph tissue may also be the site of lymphoma development.

Resources and Information

LLS offers free information and services for patients and families affected by blood cancers. This section lists various resources you may find helpful.

For Help and Information

Consult with an Information Specialist. Information Specialists can assist you through cancer treatment, financial and social challenges and give accurate, up-to-date disease, treatment and support information. Our Information Specialists are highly trained oncology social workers and nurses. Language services are available. For more information, please

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. ET)
- Email and Live chat: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Pediatric and adult patients and caregivers can work with our Clinical Trial Nurse Navigators who will help find clinical trials and provide personalized support throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Nutrition Consultations. Schedule a free one-on-one nutrition consultation with one of our registered dietitians who have expertise in oncology nutrition. Consultations are available to patients and caregivers of all cancer types. Dietitians can assist with information about healthy eating strategies, side effect management and more. Please visit www.LLS.org/nutrition for more information.

Free Information Booklets. LLS offers free education and support booklets for patients, caregivers and healthcare professionals that can either be read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial support to eligible individuals with blood cancer for insurance premiums, co-pays, and non-medical expenses like travel, food, utilities, housing, etc.

For more information, please:

- Call: (877) 557-2672
- Visit: www.LLS.org/finances

Resources for Families. Blood cancer occurs in a small number of children. Families face new challenges, and the child, parents and siblings may all need support. LLS has many materials for families including a caregiver workbook, a children's book series, an emotion flipbook, a dry erase calendar, coloring books and a coloring app, a school re-entry program, and other resources.

For more information, please:

- Call: (800) 955-4572
- Visit: www.LLS.org/FamilyWorkbook

Podcast. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit www.LLS.org/TheBloodline for more information and to subscribe to access exclusive content, submit ideas and topics, and connect with other listeners.

3D Models. LLS offers interactive 3D images to help visualize and better understand blood cell development, intrathecal therapy, leukemia, lymphoma, myeloma, MDS, MPNs, and lab and imaging tests. Visit www.LLS.org/3D for more.

Free Mobile Apps.

- LLS Coloring For Kids™—Allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. Visit www.LLS.org/ColoringApp to download for free.
- LLS Health Manager™—Helps you track side effects, medication, food and hydration, questions for your doctor, and more. Visit www.LLS.org/HealthManager to download for free.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Visit www.LLS.org/SuggestedReading to find out more.

Connecting with Patients, Caregivers and Community Resources

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients and caregivers reach out and share information. Please visit www.LLS.org/chat for more information.

Local Programs. LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection*® Program (a peer-to-peer support program), local support groups and other great resources. For more information about these programs or to contact your region, please:

- Call: (800) 955-4572
- Visit: www.LLS.org/LocalPrograms

Advocacy and Public Policy. Working closely with dedicated volunteer advocates, LLS's Office of Public Policy elevates the voices of patients to state and federal elected officials, the White House, governors and even courts. Together, we advocate for safe and effective treatments. We pursue policies that would make care more accessible to all patients. And, most of all, we advocate for the hope for a cure. Want to join our work? Visit www.LLS.org/advocacy for more information.

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to view the directory.

Additional Help for Specific Populations

Información en Español (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

Language Services. Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. For more information, please:

- Call: the VA (800) 749-8387
- Visit: www.publichealth.va.gov/exposures/AgentOrange

Information for Firefighters. Firefighters are at an increased risk of developing cancer. There are steps that firefighters can take to reduce the risk. Please visit www.LLS.org/Firefighters for resources and information.

World Trade Center Health Program. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please:

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

People With Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a two-week period. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov and enter “depression” in the search box

Health Terms

Allogeneic Stem Cell Transplantation. A treatment that replaces a person's damaged or diseased bone marrow with healthy blood-forming stem cells from a donor. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**

Biomarker. A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.

Biopsy. A procedure to remove a sample of cells or tissue from or examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissues.

Chronic Condition. A long-lasting disease or illness that usually can be controlled but not cured.

Compassionate Use. A way to provide an investigational treatment to a patient who is not eligible to receive the treatment in a clinical trial but who has a serious or life-threatening condition for which other treatments are not available.

Computed Tomography (CT) Scan. A procedure that uses a computer linked to an x-ray machine to make a series of detailed pictures inside the body.

Cutaneous. Having to do with the skin.

Dermatologist. A doctor who has special training to diagnose and treat skin problems.

DNA. Abbreviation for deoxyribonucleic acid, the material found inside cells that carries genetic information. DNA is passed to new cells during the process of cell division. A mutation (change) in the DNA can lead to cell death, changes in cell function and, in some cases, cancer.

Erythema. Redness of the skin.

Erythrodermic Disease. Widespread redness of the skin. It may be accompanied by scaling, peeling and flaking of the skin, and may include itching and hair loss.

Food and Drug Administration (FDA). An agency in the United States federal government that ensures that drugs, medical devices and equipment are safe and effective.

Hematology. The branch of medicine dealing with blood and blood disorders.

Hematologist-Oncologist. A doctor with advanced training in diagnosing and treating both blood diseases and cancer, and who specializes in treating people with blood cancers.

Histology. The study of tissues and cells under a microscope.

Imaging Test. A test that makes images (pictures) of organs, bones, blood vessels or other structures inside the body. Imaging tests use different forms of energy, such as x-rays, radio waves and ultrasound.

Immune System. A complex network of cells, tissues and organs that work together to defend the body against infections and other diseases.

Immunophenotyping. A laboratory test that detects the presence of markers, called “antigens,” on white blood cells. Normal white blood cells have antigen patterns that are unique to specific cell types and stages of development. Abnormal cells seen in leukemias and lymphomas also have specific antigen patterns that can be used to identify them. This test can help diagnose specific types of leukemia and lymphoma.

Immunotherapy. A type of therapy that uses a person’s immune system to help fight cancer.

Intravenous. Refers to a way of giving a drug through a needle or tube inserted into a vein.

Indolent Lymphoma. A type of lymphoma that typically grows and spreads slowly.

Lymph Node. A bean-sized structure that is part of the body’s immune system. Lymph nodes are distributed throughout the body. They contain lymphocytes, a type of white blood cell that helps the body fight infections and other diseases. In patients with lymphoma and some types of lymphocytic leukemia, cancerous lymphocytes multiply and cause the lymph nodes to become enlarged.

Lymphatic System. The tissue and organs that make, store and carry lymphocytes (a type of white blood cell), which fight infections and other diseases.

Lymphocyte. A type of white blood cell that is essential to the body's immune system. There are three major types of lymphocytes: B lymphocytes (B cells), which produce antibodies to help combat infectious agents like bacteria, viruses and fungi; T lymphocytes (T cells), which have several functions, including assisting B lymphocytes to make antibodies; and natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

Malignant. A term used to describe cancer.

Monoclonal Antibody. A type of synthetic protein that can bind to substances in the body, including cancer cells. Monoclonal antibodies are used in cancer treatment to target cancer cells; they can be used alone or modified and attached to chemotherapy drugs.

Neutropenia. A condition in which there is a lower-than-normal number of neutrophils (a type of white blood cell) in the blood.

Off-Label. The legal use of a prescription drug to treat a disease when it has not been approved by the FDA for that disease.

Oncologist. A doctor who has special training in diagnosing and treating cancer.

Oral Medication. Medicine that is taken by mouth. It can be a pill, capsule, or liquid such as drops and syrups.

Papule. A small, solid, raised bump on the skin that has a border with edges that are easy to see. Papules may be red, purple, brown or pink.

Peripheral Neuropathy. A nerve problem that causes pain, numbness, tingling, swelling or muscle weakness in different parts of the body. It may be caused by cancer or cancer treatment, such as chemotherapy.

Pathologist. A doctor who has special training in identifying and diagnosing diseases by studying cells and tissues under a microscope.

Platelet. A small, colorless piece of a cell that helps control bleeding. Platelets are produced from large cells in the bone marrow, called "megakaryocytes." Platelets travel to and then collect at the site of a wound. The platelets' sticky surface helps them form clots at the site of the wound and stop bleeding. Also called "thrombocyte."

Prognosis. The likely outcome or expected course of a disease; the chance of recovery or recurrence.

Radiation Oncologist. A doctor who has special training in using radiation to treat cancer.

Radiation Therapy. The use of x-rays and other forms of radiation to kill cancer cells and shrink tumors.

Remission. A decrease or disappearance of signs and symptoms of cancer.

RNA. Abbreviation for ribonucleic acid, a molecule in cells that carries out the instructions in DNA (deoxyribonucleic acid) for making proteins.

Staging. The use of exams and tests to determine if and how far a cancer has spread throughout the body. Staging provides important information for treatment planning.

Subcutaneous. Beneath the skin.

Systemic Therapy. Treatment with drugs that travel through the blood to cells all over the body.

Tumor Burden. Refers to the number of cancer cells, the size of a tumor or the amount of cancer in the body.

Ulcer. A skin ulcer is an open sore on the skin.

Ultrasound. A procedure that uses high-energy sound waves to look at tissues and organs inside the body. The sound waves make echoes that form pictures of the tissues and organs, which are viewed on a computer screen.

Visceral. Having to do with the viscera, which are the soft internal organs of the body, including the lungs, the heart and the organs of the digestive, excretory, reproductive and circulatory systems.

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NOTES

Get support.
Reach out to our
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The Leukemia & Lymphoma Society® team consists of highly trained oncology social workers and nurses who are available by phone, email and live chat Monday through Friday, 9 a.m. to 9 p.m. (ET).

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- Know the questions to ask your doctor
- Discuss financial resources
- Receive individualized clinical-trial searches
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Contact us at
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or **www.LLS.org/**
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(Language interpreters
can be requested.)



For more information, please
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The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. Find out more at www.LLS.org.