About Lymphoma of the Skin

Overview and Types

If you have been diagnosed with lymphoma of the skin or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- **What Is Lymphoma of the Skin?**
- **Types of Lymphoma of the Skin**

Research and Statistics

See the latest estimates for new cases of lymphoma of the skin in the US and what research is currently being done.

- **Key Statistics for Lymphoma of the Skin**
- **What’s New in Skin Lymphoma Research and Treatment?**

What Is Lymphoma of the Skin?

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see [What Is Cancer?](https://www.cancer.org/cancer/about-cancer/what-is-cancer.html).

Lymphoma is a cancer that starts in cells called lymphocytes, which are part of the body’s immune system. The main types of lymphomas are:

- **Hodgkin lymphoma** (also known as Hodgkin’s lymphoma, Hodgkin disease, or Hodgkin’s disease)
- **Non-Hodgkin lymphoma** (also known as non-Hodgkin’s lymphoma, NHL, or sometimes just lymphoma), which includes all other lymphomas, *including all skin*
Lymphomas

Lymphocytes are in the lymph nodes (small, bean-sized collections of immune cells throughout the body) and other lymphoid tissues (such as the spleen, bone marrow, and some other organs, including the skin). Lymphomas can start in any of these places.

When a non-Hodgkin lymphoma starts only in the skin (not in other organs or tissues) it is called a skin lymphoma (or cutaneous lymphoma). A lymphoma that starts in lymph nodes or another part of the body and then spreads to the skin is not a skin lymphoma (because it didn’t start there).

Hodgkin disease and other types of non-Hodgkin lymphoma are discussed in separate American Cancer Society documents. The rest of this document focuses only on lymphoma of the skin.

The lymph system and lymphoid tissue

To understand what lymphoma is, it helps to know about the body’s lymph system.

The lymph system (also known as the lymphatic system) is made up of lymphoid tissue (see below), lymph vessels, and a clear fluid called lymph. Lymphoid tissue is found throughout the body and contains several types of immune system cells that work together to help the body fight infections.

Lymphocytes

Most of the cells in lymphoid tissue are lymphocytes, a type of white blood cell. The main types of lymphocytes are:

- **B lymphocytes (B cells):** B cells normally help protect the body against germs (bacteria or viruses) by making proteins called antibodies. The antibodies attach to the germs, marking them for destruction by other parts of the immune system.
- **T lymphocytes (T cells):** There are several types of T cells, each with a special job. Some T cells help protect the body against viruses, fungi, and some bacteria. For example, they recognize virus-infected cells and destroy them. T cells can also release substances called cytokines that attract other types of white blood cells, which then digest the infected cells. Some types of T cells help boost or slow the activity of other immune system cells.

Both types of lymphocytes can develop into lymphoma cells. In the skin, T-cell lymphomas are more common than B-cell lymphomas.
Doctors can tell B-cells and T-cells apart using lab tests that detect certain proteins on their surfaces and certain features of their DNA. These lab tests also can recognize several stages of B-cell and T-cell development. This can help doctors figure out which type of lymphoma a person has, which can help determine their treatment options.

**Lymphoid tissue**

Most lymphocytes are in lymph nodes. Lymph nodes are connected to each other by narrow tubes similar to blood vessels called lymphatics (or lymph vessels). Lymph vessels carry a colorless, watery fluid (lymph) that contains lymphocytes.

Along with the lymph nodes, lymphocytes can be found in the blood and in lymphoid tissues in many other places in the body, including the:

- Spleen
- Bone marrow (the soft, inner parts of certain bones)
- Thymus
- Adenoids and tonsils
- Digestive tract
- Skin
- Other organs

Lymphomas can start in any part of the body that contains lymphoid tissue.

Some other types of cancer – lung or colon cancers, for example – can spread to lymph tissue such as the lymph nodes. But cancers that start in these places and then spread to the lymph tissue are not lymphomas.

- References
  
See all references for Lymphoma of the Skin

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**Types of Lymphoma of the Skin**
Classifying lymphoma of the skin can be confusing (even for many doctors) because there are many types and they are not very common.

The main system used to classify skin lymphoma is from the World Health Organization (WHO) and the European Organization for Research and Treatment of Cancer (EORTC) and is called the WHO-EORTC classification. It is based on:

- How the lymphoma looks under the microscope
- Whether there are certain proteins on the lymphoma cells (based on lab tests)

T-cell skin lymphomas

Most skin lymphomas are T-cell lymphomas.

**Mycosis fungoides:** About half of all skin lymphomas are mycosis fungoides (MF). MF can occur at any age, but most patients are in their 50s and 60s. Men are almost twice as likely as women to develop this lymphoma.

The first sign of this disease is one or more patchy, scaly, red lesions (abnormal areas) on the skin. MF lesions can be very itchy. Often these lesions are the only symptom of MF. But in some people the disease can progress to more solid, raised tumors on the skin (called plaques). Because MF can be confused with other skin problems, it can be hard to diagnose at first. Several biopsies of the lesions might be needed before the diagnosis is confirmed.

Over time, MF can spread across the skin or invade lymph nodes and organs like the liver. In many patients this disease grows slowly, but it can be faster growing in older patients. Some people with MF go on to develop Sezary syndrome.

**Sezary syndrome:** This disease is often thought of as an advanced form of mycosis fungoides, but these are actually 2 different diseases. In Sezary syndrome (SS), most or all of the skin is involved, instead of just patches of skin. The disease causes a very itchy, red rash that can look like a sunburn. This is called generalized erythroderma. The skin is often thickened. Lymphoma cells, called Sezary cells, can be found in the bloodstream (as well as in the lymph nodes).

Whereas MF is usually slow growing, SS tends to grow and spread faster, and is harder to treat. Patients with SS also often have further weakened immune systems, which increases their risk of serious infections.

**Primary cutaneous anaplastic large cell lymphoma (ALCL):** This lymphoma usually
starts as one or a few tumors on the skin. The tumors can vary in size, with some smaller than an inch across and others several inches across. Some of these may break open (ulcerate) in the middle.

Most people with this disease are in their 50s and 60s, but it can also occur in children. It is found at least twice as often in men as in women. In most cases it does not spread beyond the skin, and the prognosis (outlook) is very good.

**Lymphomatoid papulosis:** This is a benign, slow-growing disease that often comes and goes on its own, even without treatment. It often begins as several large pimple-like lesions that may break open in the middle. Under the microscope, lymphomatoid papulosis has features that look like primary cutaneous ALCL.

This disorder is seen in younger people (average age around 45) more often than other T-cell skin lymphomas. Men get this disease more often than women.

This disease often goes away without treatment, but it can take anywhere from a few months to many years to go away completely. Lymphomatoid papulosis doesn’t spread to internal organs and is not fatal. Rarely, some people with this skin disorder develop another, more serious type of lymphoma.

**Subcutaneous panniculitis-like T-cell lymphoma:** This rare lymphoma invades the deepest layers of the skin, where it causes nodules (lumps) to form. Most often these are on the legs, but they can occur anywhere on the body. This lymphoma affects all ages and both sexes equally. It usually grows slowly and tends to have a good prognosis.

**Primary cutaneous peripheral T-cell lymphoma, unspecified:** This is a group of rare skin lymphomas that don’t fit into any special category. Most of these lymphomas tend to grow and spread quickly. There are several types.

- **Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma** develops as widespread patches, nodules and tumors that often break open in the middle. This type of lymphoma can sometimes look like mycosis fungoides, but a biopsy can tell them apart.

- **Primary cutaneous gamma/delta T-cell lymphoma** develops as thickened plaques (raised lesions) or actual tumors, mainly on skin of the arms and legs, but sometimes in the intestines or lining of the nose.

- **Primary cutaneous CD4+ small/medium sized pleomorphic T-cell lymphoma** often starts as a single area of thickening of the skin or a tumor, but later there may be multiple tumors. This type of lymphoma tends to grow more slowly and to have a
better outlook than the others in this group.

- Skin lymphomas that don’t fall into any of these 3 categories are called simply primary cutaneous peripheral T-cell lymphoma, unspecified. People can have either single or multiple nodules.

Other rare T-cell lymphomas: Some other rare types of T-cell lymphomas are more likely to start in other parts of the body, but they can sometimes be confined to the skin.

- Adult T-cell leukemia/lymphoma is linked to infection with the HTLV-1 virus (although most people infected with this virus do not get lymphoma). It is much more common in Japan and the Caribbean islands than other parts of the world. This lymphoma often grows quickly, but in some cases it advances slowly, or even shrinks on its own for a time.

- Extranodal NK/T-cell lymphoma, nasal type can start in either T-cells or in other lymphocytes known as natural killer (NK) cells. This rare type of lymphoma typically starts in the nose or sinuses, but sometimes it can start in the skin. This lymphoma has been linked to infection with the Epstein-Barr virus (EBV), and is more common in Asia and Central and South America. It tends to grow quickly.

B-cell skin lymphomas

Primary cutaneous marginal-zone B-cell lymphoma: This is a very slow-growing lymphoma that is usually curable. In Europe (but not in the United States), it is sometimes linked to an infection with Borrelia, the germ that causes Lyme disease.

This lymphoma can occur at any age. It causes skin lesions that are red to purplish large pimples, plaques (raised or lowered, flat lesions), or nodules (bumps) on sun-exposed areas of skin, like the arms. There may be only a single lesion, but there can sometimes be a few.

Primary cutaneous follicle-center lymphoma: This is the most common B-cell lymphoma of the skin. It tends to grow slowly. The early lesions are groups of red pimples, nodules, or plaques that form on the scalp, forehead or trunk. They are seldom found on the legs. Sometimes the pimples change into nodules.

This type is typically found in middle-aged adults. It is very sensitive to radiation therapy, and most patients have an excellent outlook.

Primary cutaneous diffuse large B-cell lymphoma, leg type: This is a fast growing lymphoma that begins as large nodules, mainly on the lower legs. It occurs most often in older people, and is more common in women than men. In some patients, this
lymphoma spreads to lymph nodes and internal organs, causing serious problems.

These lymphomas often require more intensive treatment. The outlook is better if there is only one lesion at the time of diagnosis.

**Primary cutaneous diffuse large B-cell lymphoma, other (non-leg):** This rare skin lymphoma is similar to large B-cell lymphomas that appear on the legs, except it develops on other sites in the body. It can also develop inside blood vessels under the skin. It tends to require intensive treatment, and the outlook is better if it is limited to only the skin.

- References
  See all references for Lymphoma of the Skin

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**Key Statistics for Lymphoma of the Skin**

The American Cancer Society’s most recent estimates for all types of non-Hodgkin lymphoma (NHL) in the United States for 2018 are:

- 74,680 new cases of NHL (41,730 in men; 32,950 in women)
- 19,910 deaths from NHL (11,510 in men; 8,400 in women)

Lymphomas of the skin are uncommon. The rate of skin lymphomas has been rising over the past few decades, although it seems to have leveled off in recent years. The reasons for this are not known.

- References
  See all references for Lymphoma of the Skin


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What’s New in Skin Lymphoma Research and Treatment?

Research into the causes, prevention, and treatment of lymphoma of the skin is being done in many medical centers throughout the world.

Genetics

As noted in Do We Know What Causes Lymphoma of the Skin? scientists are making progress in learning how changes in DNA can cause normal lymphocytes to develop into lymphoma cells. Understanding the gene changes that occur in lymphoma cells provides insight into why these cells grow too quickly, live too long, and don’t develop into normal mature cells. It might also lead to new drugs that specifically target these processes.

Our understanding of these DNA changes has already led to highly sensitive lab tests for detecting this disease. These tests can identify lymphoma cells based on their gene changes. For example, polymerase chain reaction (PCR) is a very sensitive test that can help tell if a lymphoma has been destroyed by treatment and whether a relapse is likely. These types of tests could help doctors pick out those patients who need early and more intensive treatment.

Skin-directed treatments

Several newer types of skin-directed treatments are now being studied for the treatment of early stage skin lymphomas.

Photodynamic therapy (PDT)

For this treatment, a light-activated drug called aminolevulinic acid (ALA) is applied to the skin lesions. A special type of laser light is then focused on the lesions. This light changes the drug that has collected inside the lymphoma cells, which kills them.
The advantage of PDT is that it can kill cancer cells with very little harm to normal cells. But because the chemical must be activated by light, it can only kill cancer cells near the surface of the skin. This limits its use to early stage skin lymphomas that have not grown deeply into the skin. Even then, PDT might only be used if other types of skin-directed therapies are not effective. You can find out more about PDT in Photodynamic Therapy.

**Topical sirolimus and tacrolimus**

These drugs affect immune system cells such as lymphocytes, the cells that develop into lymphoma cells. Applying them to skin lymphomas seems to work as well as using topical corticosteroids, but more research is needed to help determine their safety and effectiveness.

**Chemotherapy**

Many clinical trials are studying newer chemotherapy drugs. One example is pralatrexate (Folotyn), a drug that is already used to treat some T-cell lymphomas and has shown early promise in treating some skin lymphomas. Another drug that has shown some promise in early clinical trials is forodesine. Research on these and other new drugs continues.

Other studies are looking at ways to use drugs already known to be effective by combining them in new ways or using different doses or different sequences of these drugs.

**Targeted drugs**

Newer drugs known as targeted therapies have shown clear benefit in certain kinds of skin lymphoma. The drugs vorinostat (Zolinza) and romidepsin (Istodax) are forms of targeted therapy that can help treat some skin lymphomas. Doctors are now studying how to use these drugs most effectively.

Other targeted drugs are also being studied. One example is crizotinib (Xalkori), which has been shown help some patients with non-skin forms of anaplastic large cell lymphoma (ALCL). Others being studied for skin lymphomas include everolimus (Afinitor), lenalidomide (Revlimid), bortezomib (Velcade), and carfilzomib (Kyprolis).

**Monoclonal antibodies**
Lymphoma cells have certain chemicals on their surface. Special man-made antibodies that recognize these substances can be targeted to destroy the lymphoma cells while causing little damage to normal body tissues.

Several such drugs, including rituximab (Rituxan) and alemtuzumab (Campath), are already used to treat some skin lymphomas and are discussed in Whole Body (Systemic) Treatments for Skin Lymphomas.

New monoclonal antibodies are also being developed. One example is mogamulizumab (KW-0761), an antibody that has shown promise in early clinical trials.

Another is brentuximab vedotin (Adcetris), an antibody that is linked with a chemotherapy drug. The antibody attaches to a substance on the surface of some lymphoma cells, bringing the chemo drug directly to these cells. This drug is already used to treat some other types of lymphomas and is now being studied for certain skin lymphomas.

**Stem cell transplant**

*High-dose chemotherapy followed by a stem cell transplant* is sometimes used to treat lymphomas that no longer respond to other treatments. Researchers continue to improve stem cell transplant methods, including new ways to harvest these cells before transplantation.

A lot of research is focusing on reducing graft-versus-host disease in allogeneic transplants (using stem cells from a donor). This work involves altering the transplanted T-cells so that they won’t react with the patient’s normal cells but will still kill the lymphoma cells.

**Lymphoma vaccines**

Doctors know it is possible for people with cancer to develop immune responses to their cancer. In rare instances, people’s immune systems have rejected their cancers, and they have been cured. Scientists are now studying ways to boost this immune reaction using vaccines.

Unlike vaccines used to prevent infections, the purpose of these vaccines is to create an immune reaction against the lymphoma cells in patients who have very early disease or whose disease is in remission but could come back or relapse. This is a major area of research in lymphoma treatment, but it is still being tested in clinical trials. You may
want to consider enrolling in one of these studies.

- References
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