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# 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?](#)

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# What Is Lymphoma of the Skin?

Cancer starts when cells begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas. To learn more about how cancers start and spread, see [What Is Cancer?](#)<sup>1</sup>

Lymphoma is a cancer that starts in white blood cells called **lymphocytes**, which are part of the 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 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 lymphoma](#)<sup>2</sup> and other types of [non-Hodgkin lymphoma](#)<sup>3</sup> are discussed on separate pages.

## The lymph system and lymphoid tissue

To understand what lymphoma is, it helps to know something about the lymph system (also known as the lymphatic system). The lymph system is part of the immune system, which helps fight infections and some other diseases. The lymph system also helps fluids move around the body.

### Lymphocytes

The lymph system is made up mainly of 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 destroy germs or abnormal cells in the body. Other 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 with [lab tests](#)<sup>4</sup> that detect certain proteins on their surfaces and certain features of their DNA. These 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](#)<sup>5</sup> options.

## Lymph tissue

Most lymphocytes are in **lymph nodes**, which are bean-sized collections of lymphocytes and other immune system cells throughout the body. Lymph nodes are connected to each other by narrow tubes like blood vessels called **lymphatics** (or lymph vessels), which 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 lymph tissue.

Some other types of cancer, such as lung cancer or colon cancer, 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.

## Hyperlinks

1. [www.cancer.org/cancer/cancer-basics/what-is-cancer.html](http://www.cancer.org/cancer/cancer-basics/what-is-cancer.html)
2. [www.cancer.org/cancer/hodgkin-lymphoma.html](http://www.cancer.org/cancer/hodgkin-lymphoma.html)
3. [www.cancer.org/cancer/non-hodgkin-lymphoma.html](http://www.cancer.org/cancer/non-hodgkin-lymphoma.html)
4. [www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/how-diagnosed.html)
5. [www.cancer.org/cancer/skin-lymphoma/treating.html](http://www.cancer.org/cancer/skin-lymphoma/treating.html)

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# Types of Lymphoma of the Skin

There are many types of skin lymphomas. Classifying them can be confusing (even for many doctors) because many of them are not very common.

The main system used to classify skin lymphoma is from the World Health Organization (WHO), which was last updated in 2016. It is based mainly on:

- Whether the lymphoma starts in T lymphocytes (T cells) or B lymphocytes (B cells)
- How the lymphoma looks under the microscope
- Whether certain proteins are on the lymphoma cells (based on lab tests)

## T-cell skin lymphomas

Most skin lymphomas are T-cell lymphomas. These are sometimes called **cutaneous T-cell lymphomas (CTCLs)**.

**Mycosis fungoides:** Nearly half of all skin lymphomas are mycosis fungoides (MF). MF can occur in people of any age, but most who get it are in their 50s or 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](#)<sup>1</sup> 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 people this disease grows slowly, but it can sometimes grow more quickly, especially in older people. Some people with MF go on to develop Sezary syndrome.

Rare variants of MF include **folliculotropic MF**, **pagetoid reticulosis**, and **granulomatous slack skin**.

**Sezary syndrome (SS):** This is often thought of as an advanced form of mycosis fungoides, but these are actually different diseases. In SS, most or all of the skin is affected, instead of just patches of skin. People with SS typically have a very itchy, scaly red rash that can look like a severe sunburn. This is called **generalized erythroderma**. The skin is often thickened. Lymphoma cells, called **Sezary cells**, can be found in the blood (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. People with SS also often have further weakened immune systems, which increases their risk of serious infections.

**Adult T cell leukemia-lymphoma (ATLL):** This rare type of T-cell lymphoma is more likely to start in other parts of the body, but it can sometimes be confined to the skin. It 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.

**Primary cutaneous anaplastic large cell lymphoma (C-ALCL):** This lymphoma usually starts as one or a few tumors on the skin, which can vary in size. Some of these may break open (ulcerate).

Most people with this disease are in their 50s or 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. In fact, some doctors think of it not as a lymphoma, but rather as an inflammatory disease that might progress to a lymphoma.

But under a microscope, it has features that look like primary cutaneous ALCL.

Lymphomatoid papulosis often begins as several large pimple-like lesions that may break open in the middle.

This disorder is seen in younger people more often than other T-cell skin lymphomas, with an average age of around 45. 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 outlook.

**Extranodal NK/T-cell lymphoma, nasal type:** This rare type of lymphoma can start in T-cells or in other lymphocytes known as natural killer (NK) cells. It 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.

**Primary cutaneous peripheral T-cell lymphoma, rare subtypes:** This is a group of rare skin lymphomas that don't fit into any of the above categories. There are several types.

- **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. This type of lymphoma tends to grow and spread quickly.
- **Primary cutaneous CD8+ aggressive epidermotropic 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](#)<sup>2</sup> can tell them apart. This lymphoma tends to grow and spread quickly.
- **Primary cutaneous acral CD8+ T-cell lymphoma** is very rare, and typically starts as a nodule on the ear, although it can also start on other parts of the body, such as the nose, hand, or foot. It tends to grow slowly and can often be cured with treatment.

- **Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder** often starts as a single area of thickening of the skin or a tumor on the head, neck, or upper body. This disease tends to grow slowly and can often be cured with treatment.

## B-cell skin lymphomas

These lymphomas are sometimes referred to as **cutaneous B-cell lymphomas (CBCLs)**.

**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, although it tends to occur more often in older adults. It appears as skin lesions that are red to purplish large pimples, plaques (raised or lowered, flat lesions), or nodules (bumps) on the arms or upper body. 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 upper body. Less often they are found on the legs. Sometimes the pimples grow into nodules.

This type of lymphoma is typically found in middle-aged adults. It tends to respond well 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 people, 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.

## Hyperlinks

1. [www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/how-diagnosed.html)
2. [www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/how-](http://www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/how-)

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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 2020 are:

- 77,240 new cases of NHL (42,380 in men and 34,860 in women)
- 19,940 deaths from NHL (11,460 in men and 8,480 in women)

However, lymphomas of the skin are uncommon, accounting for only about 4% of all non-Hodgkin lymphomas. 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.

Survival rates for skin lymphomas can vary a great deal, depending on the [type of lymphoma](#), how [advanced](#)<sup>1</sup> it is, and how well it responds to [treatment](#)<sup>2</sup>.

## Hyperlinks

1. [www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/staging.html](http://www.cancer.org/cancer/skin-lymphoma/detection-diagnosis-staging/staging.html)
2. [www.cancer.org/cancer/skin-lymphoma/treating.html](http://www.cancer.org/cancer/skin-lymphoma/treating.html)

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## What's New in Skin Lymphoma

# Research?

Research into the [causes](#)<sup>1</sup>, [prevention](#)<sup>2</sup>, and [treatment](#)<sup>3</sup> of lymphoma of the skin is being done in many medical centers throughout the world.

## Genetics

As noted in [What Causes Lymphoma of the Skin?](#)<sup>4</sup> scientists are making progress in learning how changes in the DNA inside normal lymphocytes can cause them to develop into lymphoma cells. Understanding these changes can provide 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 the development of highly sensitive [lab tests](#)<sup>5</sup> for detecting this disease. For example, polymerase chain reaction (PCR) is a very sensitive test that can help tell if a lymphoma has been destroyed by treatment or if a relapse is likely. These types of tests could help doctors pick out those patients who need 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](#)<sup>6</sup>.

### Topical imiquimod and resiquimod

These drugs affect a protein called TLR7. When applied to a skin lesion as a cream or gel, they can cause a local immune reaction, which can kill skin lymphoma cells. More research is needed to help determine their safety and effectiveness, although imiquimod is already available to treat some other skin conditions, so doctors can use it [off-label](#)<sup>7</sup> to treat skin lymphomas.

## Chemotherapy

Many clinical trials are studying newer chemotherapy drugs. One that has shown some promise in early [clinical trials](#)<sup>8</sup> is forodesine. Research on this and other new drugs continues.

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

## Targeted drugs

Newer drugs known as [targeted therapies](#)<sup>9</sup> 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 for skin lymphomas, including everolimus (Afinitor), lenalidomide (Revlimid), and bortezomib (Velcade).

## Monoclonal antibodies

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

Several such drugs, including rituximab (Rituxan), brentuximab vedotin (Adcetris), and mogamulizumab (Poteligeo), are now being used to treat some skin lymphomas. These are discussed in [Whole Body \(Systemic\) Treatments for Skin Lymphomas](#)<sup>10</sup>.

Many new monoclonal antibodies are now being developed as well.

## Immune checkpoint inhibitors

A promising newer area of cancer treatment is [immunotherapy](#)<sup>11</sup>, which helps a

person's own immune system attack cancer cells in the body. Immunotherapy drugs called [checkpoint inhibitors](#)<sup>12</sup> are monoclonal antibodies that help boost the immune response. These drugs have been found to be helpful in treating many types of cancer, and some of them are now being studied for use against skin lymphomas. Examples include pembrolizumab (Keytruda), durvalumab (Imfinzi), and atezolizumab (Tecentriq). Some studies are testing these drugs along with other treatments such as radiation therapy, which might help them work better.

## Stem cell transplant

[High-dose chemotherapy followed by a stem cell transplant](#)<sup>13</sup> 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.

## Hyperlinks

1. [www.cancer.org/cancer/skin-lymphoma/causes-risks-prevention/what-causes.html](http://www.cancer.org/cancer/skin-lymphoma/causes-risks-prevention/what-causes.html)
2. [www.cancer.org/cancer/skin-lymphoma/causes-risks-prevention/prevention.html](http://www.cancer.org/cancer/skin-lymphoma/causes-risks-prevention/prevention.html)
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8. [www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html](http://www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html)
9. [www.cancer.org/cancer/skin-lymphoma/treating/whole-body-treatments.html](http://www.cancer.org/cancer/skin-lymphoma/treating/whole-body-treatments.html)
10. [www.cancer.org/cancer/skin-lymphoma/treating/whole-body-treatments.html](http://www.cancer.org/cancer/skin-lymphoma/treating/whole-body-treatments.html)
11. [www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html](http://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html)
12. [www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/immune-checkpoint-inhibitors.html](http://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/immune-checkpoint-inhibitors.html)

13. [www.cancer.org/cancer/skin-lymphoma/treating/whole-body-treatments.html](http://www.cancer.org/cancer/skin-lymphoma/treating/whole-body-treatments.html)

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