

CUTANEOUS LYMPHOMA

What is lymphoma?

Lymphomas are cancers that originate in a lymphocyte, which is a cell found principally in lymph nodes and other lymphatic tissue sites, such as the skin, spleen and the wall of the intestines. The transformation of a lymphocyte to a malignant cell gives it a growth and survival advantage over normal cells. The malignant cell multiplies and enlarges the lymph node so that it may be felt or observed if it is in a location near the surface of the body. The malignant lymphocytes may travel to other lymph nodes and those nodes may enlarge from uncontrolled malignant cell multiplication.



**The Leukemia &
Lymphoma Society**SM

Fighting Blood-Related Cancers

800.955.4572

www.leukemia-lymphoma.org

What is the derivation of word lymphoma?

Lymph is the fluid that is present in the small tubular channels, called lymphatics, that connect lymph nodes one to another, permitting lymphocytes to circulate through the lymph nodes. Thus, the lymphatics contain lymphocytes suspended in a watery fluid, the lymph, that circulates throughout the body from one lymph node to another. The lymphatic channels collect into larger lymphatic vessels that ultimately enter into the blood and this connection permits a small proportion of lymphocytes to be present in the blood, also.

The term lymph comes from the Greek for colorless fluid or sap, highlighting its difference from the red or bluish-red color of blood in arteries or veins. The lymph nodes are collections of lymphocytes the size of beans in which new lymphocytes are made. Lymphoma is a shortened version of lymphocytoma. The latter term is composed from the name of the cell type involved, the lymphocyte, which has undergone a malignant transformation and the Greek for tumorous affliction –oma. Hence, the shortened term lymphoma for a malignant tumor of lymphocytes.

Lymphomas are divided into two major categories: Hodgkin's disease and all other lymphomas (referred to as non-Hodgkin's lymphomas). In Hodgkin's disease, specific types of cells are present that are not found in the non-Hodgkin's lymphomas. Further information on the lymphocytes and lymphomas can be obtained in The Leukemia & Lymphoma Society booklet "The Lymphomas."



**The Leukemia &
Lymphoma Society** SM
Fighting Blood-Related Cancers

Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

What is skin (or cutaneous) lymphoma?

Although most lymphomas originate in lymph nodes, some may start and for extended periods be localized to other parts of the lymphatic system. The most common of these sites are the gastrointestinal tract and the skin. The word cutis is skin in Latin and the medical term for the organ, the skin, is the cutaneous tissue or system. Thus, the name cutaneous lymphoma for lymphomas that originate in the lymphocytes of the skin. It could just as well be referred to as skin lymphoma and often is in common speech.

There are three types of lymphocytes, T lymphocytes, B lymphocytes, and natural killer cells. Lymphomas in the skin arise most commonly from the malignant change in a T lymphocyte and these types of skin lymphomas are referred to as cutaneous T cell lymphomas. A smaller proportion of skin lymphomas result from the malignant change in B lymphocytes and are referred to as cutaneous B lymphocyte lymphomas. Before much was known about the origin of skin lymphomas, they were referred to descriptively. The earliest name for skin lymphoma was mycosis fungoides, first described early in the 19th century, but it was not known that the affected cells were lymphocytes until the middle of the 20th century. The disease was initially called mycosis fungoides because the first patient diagnosed had skin tumors that looked like mushrooms.

A second form of skin lymphoma was later recognized and it was characterized by a wide-spread red skin rash and sometimes sloughing of the exterior layers of the skin. It was found that in this form of skin lymphoma, malignant lymphocytes were usually present in the blood. The relationship of this type of skin lymphoma with a blood picture that looked somewhat like chronic lymphocytic leukemia was called Sézary syndrome after the French dermatologist who described the unusual lymphocytes in the blood. These terms, mycosis fungoides and Sézary syndrome, along with some less common forms of skin lymphoma are now collectively referred to as cutaneous T cell lymphoma, as they each originate in a T lymphocyte in the skin that has undergone a malignant change.

When the disease starts, the skin may have red patches or crops of small bumps covering only small parts or more extensive parts of the skin surface. These bumps may be circumscribed or quite broad, referred to as plaques. Sometimes quite large bumps or tumors are present or they may develop later. Sometimes a red rash is the principal change in the skin. Most cases start with dry skin, rash, and itching. For some patients, the initial sign is skin redness, or dark patches may develop on the skin. Itching may be severe, especially for patients with skin redness. Patients may have difficulty sleeping because of itching. Breaks in the skin may form. These do not heal well and often become infected.



**The Leukemia &
Lymphoma Society** SM
Fighting Blood-Related Cancers

Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

The skin changes may be similar to several other skin disorders and it often requires a biopsy and other tests to arrive at a diagnosis. Some time may pass before one can be certain of the diagnosis.

In later stages, the skin tumors may become ulcerated and infected. Malignant lymphocytes may spread to the lymph nodes and to other parts of the body, including the gastrointestinal system, liver, spleen, and other locations.

How is cutaneous lymphoma diagnosed?

Diagnosis requires a biopsy of a small area of affected skin. The skin sample is examined under a microscope by a skin pathologist. The skin appearance may be diagnostic of cutaneous T cell lymphoma. Sometimes it resembles other common, non-cancerous skin conditions. This similarity may make the diagnosis difficult at an early phase. Special tests that can identify malignant changes in the skin lymphocytes may make the diagnosis possible at an early stage. As the rash progresses, biopsies may become confirmatory of a skin lymphoma.

Skin lymphomas may progress slowly. On the one hand this is good, on the other it prolongs the uncertainty about the specific diagnosis. Patients and doctors may be frustrated by the uncertainty. Newer diagnostic techniques have made this circumstance less common. Repeated skin biopsies for microscopic, immunologic and molecular analysis may be required



**The Leukemia &
Lymphoma Society**SM
Fighting Blood-Related Cancers

Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

before a definite diagnosis is made. Examination of the blood lymphocytes may detect skin lymphoma cells in the blood and assist in making the diagnosis.

Since the disease can spread to lymph nodes or to other organs in the body, such as the spleen, lungs, or liver (tumor phase), careful repeated examination of the lymph nodes and the selective use of computed tomography or magnetic resonance imaging may be required to determine the extent of the disease.

In advanced stages, the malignant cells may progress to a different type of lymphoma. The lymphoma cells of patients may start to produce an cell protein called Ki-1, which is also associated with Hodgkin's disease, and cells resembling those in Hodgkin's disease may be present. Patients who undergo this sort of transformation become more resistant to treatment.

How common is skin lymphoma?

Between 1973 and 1984, the annual incidence of skin lymphoma in the United States doubled from about 2 to 4 cases per million persons. This represents about 1000 new cases per year. Men are twice as likely as women to have the disease, and it is several times more common in those of African as compared to European or Asian descent. The average age at diagnosis is 50 years, and children are rarely affected.



**The Leukemia &
Lymphoma Society** SM
Fighting Blood-Related Cancers

Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

How did I get skin lymphoma?

Like most lymphomas, the exact cause of skin lymphomas is not known. The lymphomas (like all cancers) result from acquired injury (mutation) to the DNA in a single cell, which becomes malignant as a result. The change confers a growth or survival advantage on the cell.

In certain geographic areas, a virus appears to be the cause of some lymphomas and the virus was first isolated from the cells of a patient with skin lymphoma. This relationship is not evident in most patients in the United States. Speculation about other environmental exposures has been present because of the increase in lymphomas over the last 35 years or longer but definitive associations have not yet been established. They are under study at the National Cancer Institute and other centers around the world.

How will I be treated for cutaneous lymphoma?

In the early stages, patients with stable disease are usually treated with creams and skin-softening agents, anti-itch agents, and gradual exposure to sunlight or ultraviolet light. Four types of specific treatment are available:

Photochemotherapy. Psoralen is a drug that binds to the DNA in malignant cells. Patients take the drug orally and then are exposed to ultraviolet light, which activates the drug, damaging the DNA of the malignant cells. This



Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

treatment often is referred to as PUVA, an acronym for Pсорalen and UltraViolet A light. Treatment is usually given several times a week for one or two months, and less frequently thereafter. Maintenance treatment is usually continued for a year or more. Patients in the early phase of disease have the best response to treatment.

Topical Nitrogen Mustard. Nitrogen mustard or mustargen is a chemotherapy agent that is administered as an ointment and applied daily either to affected areas of skin or to the entire body skin. Early stage patients respond best but relapses after therapy is stopped are common.

Electron beam radiation. Conventional radiation therapy penetrates the skin and reaches into areas inside the body. Electron beam therapy can be applied to the entire skin surface without affecting internal organs. This type of radiation has been helpful for patients who have skin tumors. The tumors often heal after treatment and the dead tissue heals, reducing the risk of infection. Treatment leads to complete clearing of lesions in several months without further treatment. Some patients appear to have long-standing regression of their skin lesions following this type of treatment.

Chemotherapy. Several combinations of chemotherapeutic agents have been used in patients with skin lymphoma, especially those with disease that involves the lymph nodes or other organs. The results have not been as good as they are in managing other types of lymphoma. The most commonly used drug



**The Leukemia &
Lymphoma Society** SM
Fighting Blood-Related Cancers

Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

combinations include cyclophosphamide, doxorubicin, vincristine, and prednisone. Other effective agents include VP-16 and methotrexate. Chemotherapy has not been able to cure widespread skin lymphoma and early studies of chemotherapy combined with radiation therapy in patients with early stages of disease have not been very successful.

Supportive therapy. The itching which accompanies the skin lesions can be difficult to control. Antihistamines, particularly Benadryl or Atarax, may relieve itching to some extent, but the major side effect of these drugs is drowsiness, and patients may develop a resistance (tolerance) to their effectiveness, requiring the use of larger doses.

Application of skin softeners or steroid ointments may also help relieve symptoms. Antibiotics are given if lesions become infected. Patients with long-standing, troublesome disease may require treatment for depression or insomnia.

What are the newest treatments for cutaneous lymphoma?

An “orphan” drug is one that has so small a potential number of users that high-cost research and development is hard for businesses to justify if profitability is the only consideration. In order to help encourage development, certain inducements may be given to industry to permit them to pursue research and clinical trials. Since skin lymphomas are uncommon, new treatments are classified as “orphan drugs or treatments” in order to reduce the costs of development.



**The Leukemia &
Lymphoma Society** SM
Fighting Blood-Related Cancers

Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

Alpha-interferon, combined with PUVA therapy, has shown promising preliminary results for patients with early-stage disease.

Bexarotene is an oral capsule now being investigated in patients with advanced and early-stage CTCL.

Drugs made from monoclonal antibodies target certain structures on the surface of cells. One new drug (Ontak[®], denileukin diftitox) attaches to the cell surface of T lymphocytes, the cells that most commonly cause skin lymphomas. Once attached to the T cell, the drug often kills the cell.

A family of drugs, that substitute for natural molecules that are building blocks for normal DNA may be effective for the treatment of skin lymphomas. The drug fools the cell into using it to make DNA which is functionless and will not support cell growth or survival, in this way killing the malignant cells. Drugs in this category, which have been tested, include fludarabine and pentostatin.

How successful is treatment for skin lymphoma?

The average (median) survival for patients with skin lymphomas is about 10 years. This means that half the affected patients live for more than 10 years. Survival is influenced by the extent of skin involvement and the presence of the disease in areas beyond the skin, such as lymph nodes. If areas other than skin are involved at the time of diagnosis, the outcome is less favorable



Cutaneous Lymphoma

800.955.4572

www.leukemia-lymphoma.org

than if only skin is involved. The less the area of skin involved the more favorable the outcome. New therapies are being developed continuously and patients may have the opportunity to have these applied in clinical trials if their physicians feel that such new approaches are warranted.

More information on cutaneous lymphoma:

To get more information, talk to your physician or call The Leukemia & Lymphoma Society, 1-800-955-4572. Web sites that discuss cutaneous lymphoma are:

- www.rarediseases.org
- The Leukemia & Lymphoma Society at www.leukemia-lymphoma.org

9/99
FS5



**The Leukemia &
Lymphoma Society**SM
Fighting Blood-Related Cancers

Cutaneous Lymphoma

800.955.4572
www.leukemia-lymphoma.org