

## Peripheral T-Cell Lymphoma

*Expert review by:*

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### Lymphoma Overview

Lymphoma is a cancer of the white blood cells, namely lymphocytes, that constitute the lymphatic system. The two main types of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma. Lymphoma is the most common blood cancer and the third most common cancer of childhood. Lymphoma occurs when lymphocytes grow abnormally. The body has two types of lymphocytes: B lymphocytes, or B-cells, and T lymphocytes, or T-cells. B-cells play an important role in making antibodies to fight bacterial infections and T-cells play a role in fighting viruses and organ rejection in transplant patients. Although both cell types can develop into lymphomas, B-cell lymphomas are more common, comprising nearly 85 percent of all non-Hodgkin lymphomas. Like normal lymphocytes, those that turn malignant can grow in any part of the body, including the lymph nodes, spleen, bone marrow, blood or other organs.

### Non-Hodgkin Lymphoma Overview

Of the more than 67 types of lymphoma, over 61 are classified as non-Hodgkin lymphoma (NHL). Nearly all non-Hodgkin lymphoma cases occur in adults, with the average age of diagnosis in the 60s. While scientists do not know the exact causes of non-Hodgkin lymphoma, they do know that it is not caused by injury or by coming into contact with someone with the disease. Most people diagnosed with NHL have no known risk factors, although increasingly many scientists believe infections may play an important role in causing select types of non-Hodgkin lymphoma to develop.

### T-Cell Lymphoma Overview

T-cell lymphoma is a rare disease in which T lymphocyte cells become cancerous. These lymphomas account for between 10 percent and 15 percent of all cases of non-Hodgkin

lymphoma in the United States (approximately 5,000 to 6,000 cases) a year. However, some forms of T-cell lymphoma are more common in Asia, Africa and the Caribbean. There are many different types of T-cell lymphoma, most of which are extremely rare, occurring in only a few patients per year throughout the world. Like the B-cell lymphomas, T-cell lymphomas are classified into two broad categories: aggressive (fast-growing) or indolent (slow-growing).

Most T-cell lymphomas are diagnosed by taking a small sample, called a biopsy, of the tumor and looking at the cells under a microscope. However, since the cells of many forms of lymphoma look similar, making an accurate diagnosis can be difficult and oftentimes other diagnostic tools such as genetic tests of the tumor, blood tests, CT (computerized axial tomography, MRI (magnetic resonance imaging) and PET (positron emission tomography) scans and a bone marrow biopsy may be done to determine the type and extent (or stage) of the disease. One of the most common forms of T-cell lymphoma is cutaneous, or skin lymphoma, because it starts in the lymphocytes in the skin. Cutaneous lymphoma actually describes many different disorders with various signs and symptoms, outcomes and treatment considerations.

### Peripheral T-Cell Lymphoma Overview

Peripheral T-cell lymphoma (PTCL) comprises a group of rare and aggressive non-Hodgkin lymphomas that develop from T-cells in different stages of maturity. The World Health Organization (WHO) has divided the various types of PTCL into two main categories: 1) precursor T/NK neoplasms, which include precursor T-lymphoblastic leukemia/lymphoma and blastic NK lymphoma; and 2) peripheral T/NK neoplasms, which are subcategorized as predominantly leukemic, predominantly nodal, predominantly extranodal and subcutaneous panniculitis T-cell.

Peripheral T-cell lymphoma generally affects people over age 60 and is diagnosed in slightly more men than women.

## Types of Peripheral T-Cell Lymphoma

**Precursor T Lymphoblastic Leukemia/Lymphoma**—This type of PTCL may present as leukemia or lymphoma or both. The cancer is most commonly diagnosed in adolescent and young adult males. With intensive chemotherapy, the disease can be cured in the majority of patients, with complete remission rates as high as 96 percent. The medication nelarabine (Arranon) has been approved to treat patients who have developed relapsed precursor T lymphoblastic leukemia/lymphoma.

**Blastic NK-Cell Lymphoma**—Blastic NK-cell lymphoma is a very rare T-cell lymphoma, affecting a small number of people (usually adults) internationally each year. This lymphoma is very fast growing, difficult to treat and can arise anywhere in the body. Since this disease is so rare, patients should consult with their medical team to find promising therapies or clinical trials.

**T-Cell Leukemias**—T-cell leukemias are derived from T-cells and can act like T-cell lymphoma. These cancers include T-cell promyelocytic leukemia, T-cell granular lymphocytic leukemia, aggressive NK-cell leukemia and adult T-cell lymphoma/leukemia. Arranon (nelarabine) has been approved to treat patients with relapsed T-cell leukemia. Several chemotherapy combinations are currently being tested against T-cell leukemias.

**Angioimmunoblastic T-Cell Lymphoma**—Angioimmunoblastic lymphoma (AILD) is a fast-growing T-cell lymphoma that accounts for between one percent and two percent of all cases of non-Hodgkin lymphoma in the United States. This type of lymphoma is often treated first with steroids, although it often progresses and requires chemotherapy and other medications. In advanced cases, bone marrow transplantation may be used. For more information, see LRF's Fact Sheet on this disease.

**Anaplastic Large-Cell Lymphoma**—This is a rare type of aggressive T-cell lymphoma comprising only about 3 percent of all lymphomas in adults and between 10 percent and 30 percent of all lymphomas in children. Anaplastic large-cell lymphoma (ALCL) can appear either in the skin or in other organs throughout the body (systemic anaplastic-large cell lymphoma). When ALCL is confined to the skin, it follows a less aggressive course and is associated with a rare condition

called lymphomatoid papulois (LyP), which, though not classified as a lymphoma, is often a precursor to the development of cutaneous anaplastic large-cell lymphoma.

Patients with systemic ALCL are divided into two groups, depending on the expression of a protein called anaplastic lymphoma kinase (ALK). The prognosis for ALCL is different based on whether a patient is ALK positive (expresses the protein) or ALK negative (does not express the protein). ALK positive disease responds well to chemotherapy, putting most patients in long-term remission or cure. Many patients with ALK negative ALCL will relapse and will potentially require more aggressive chemotherapy. For more information, see LRF's Fact Sheet on this disease.

**Peripheral T-Cell Lymphoma (Unspecified)**—Peripheral T-cell lymphoma (unspecified) (PTCLUS) comprises a group of diseases that do not fit into any of the other subtypes of peripheral T-cell lymphoma. This group of PTCLs is considered aggressive and requires standard combination chemotherapy upon diagnosis. It is the most common of all the T-cell lymphomas. Although most patients with PTCL NOS present with nodal involvement, extranodal sites, such as the liver, bone marrow, gastrointestinal and skin, may also be involved.

**Mycosis Fungoides**—Mycosis fungoides is the most common type of cutaneous T-cell lymphoma. It is generally a slow-growing cancer that usually starts in the skin and may appear as a scaly, red rash in areas of the body that are not usually exposed to the sun. The rash may appear as a red eczema-like rash; as thickened, red patches; or tumors on the skin. Limited disease may be treated with topical chemotherapy like nitrogen mustard or ultraviolet light therapy. Extensive disease is usually treated with electron beam radiation or standard chemotherapy given intravenously.

**Sézary Syndrome**—Sézary syndrome is an advanced, variant form of mycosis fungoides, and affects both the skin and the peripheral blood. It can cause widespread itchy, reddening and peeling skin as well as skin tumors and may be painful. Like mycosis fungoides, limited disease Sézary syndrome may be treated with topical chemotherapy like nitrogen mustard or ultraviolet light therapy. Extensive disease is usually treated with electron beam radiation or standard chemotherapy given intravenously.

**Nasal T-Cell Lymphoma**—Although this fast-growing lymphoma is very rare in the United States, it is relatively common in Asia and parts of Latin America, leading

researchers to suspect that some ethnic groups may be more prone to this cancer, which affects both children and adults. This type of lymphoma is associated with the Epstein-Barr virus and may involve the nasal area, the trachea, the gastrointestinal tract or skin. As with other rare cancers, patients should consult with their medical team for treatment options and the availability of clinical trials.

**Enteropathy-Type T-Cell Lymphoma**—This type of lymphoma is an extremely rare subtype of T-cell lymphoma that appears in the intestines and is strongly associated with celiac disease. As with other rare cancers, patients should discuss treatment options with their medical team.

**Hepatosplenic Gamma-Delta T-Cell Lymphoma**—Hepatosplenic gamma-delta T-cell lymphoma is an extremely rare and aggressive disease that starts in the liver or spleen. As with other rare cancers, patients should discuss treatment options with their medical team.

### Peripheral T-Cell Lymphoma Treatments

For most subtypes of peripheral T-cell lymphoma, the treatment regimen is typically CHOP-based chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone) or EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide and prednisone) in the frontline setting. Because most PTCL patients will relapse, some oncologists recommend giving high-dose chemotherapy followed by an autologous stem cell transplant to patients who have had a good response in their initial chemotherapy program. While promising, there is no firm clinical data to support that undergoing a transplant in this setting is better than not undergoing a transplant.

Relapsed PTCL patients are usually treated with ICE (ifosfamide, carboplatin and etoposide), followed by an autologous stem cell transplant. One drug, gemcitabine (Gemzar), appears effective against some forms of PTCL in the relapsed setting and is often given in combination with other chemotherapies, including vinorelbine (Navelbine) and doxorubicin (Doxil) in a regimen called GND. Other chemotherapy regimens include DHAP (dexamethasone, cytarabine and cisplatin) and ESHAP (etoposide, methylprednisolone, cytarabine and cisplatin).

### Treatments Under Investigation

Because peripheral T-cell lymphomas are so rare, finding enough patients to enroll in clinical trials is difficult.

However, several new drugs are being studied in clinical trials and are showing promising results in the treatment of some types of PTCL, including:

- Pralatrexate
- SAHA (suberoylanilide, hydroxamic acid; Vorinostat, Zolinza), which has already been approved in the treatment of cutaneous T-cell lymphoma
- Decapeptide
- Bortezomib (Velcade)
- PXD101 (Belinostat) and FK228 (Depsipeptide), both histone deacetylase inhibitors
- Obatoclox (GX15-070), ABT-262 and AT-101, all bcl-2 inhibitors

### Complementary and Alternative Therapies

Complementary and alternative medicines are nonstandard therapies that may help patients cope with their cancer and its treatment, but that should not be used in place of standard treatment. No alternative therapy has ever been proven effective against lymphoma. However, complementary therapies such as meditation, yoga, acupuncture, exercise, diet and relaxation techniques have been shown to be effective in combating some treatment side effects. Before embarking on any complementary therapies, patients should discuss the matter with their healthcare team. Certain unproven treatments, including some herbal supplements, can interfere with standard lymphoma treatments or may cause serious side effects.

### How to Prepare for Follow-Up Appointments

It is important for patients both during and after treatment to be proactive in their healthcare, including keeping a master file of medical records, asking questions, reporting new symptoms, exercising and eating a balanced diet. Some patients find it helpful to keep a diary of their symptoms, which can help the physician promptly address concerns. In addition, patients who smoke should strongly consider stopping. Follow-up visits, usually scheduled every few months, typically include physical examinations, blood tests and occasionally CT scans. Since lymphoma symptoms may resemble those of less serious illnesses, like colds or viral infections, maintaining regular medical care is imperative. Besides looking for signs of a recurrence of cancer, follow-up care can help identify and resolve unusual side effects of treatment.

# Contact Us

For more information about *Getting the Facts* or information about the



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The Lymphoma Research Foundation offers a comprehensive slate of patient education and support programs including

- *Lymphoma Helpline & Clinical Trials Information Service*
- *Lymphoma Support Network*
- Publications and newsletters
- Informational teleconferences and webcasts
- In-person conferences
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## Finding Support

A lymphoma diagnosis may provoke a range of feelings and raise many concerns. In addition, cancer treatment can cause physical and emotional discomfort. Connecting with other people who have lymphoma, or have been cured of it, can provide enormous relief. Support groups and online message boards are often useful. One-to-one peer support programs, such as the Lymphoma Research Foundation's *Lymphoma Support Network*, matches lymphoma survivors (or caregivers) with volunteers who have gone through similar experiences.

## Staying Informed

The Lymphoma Research Foundation offers a wide range of resources that address treatment issues, the latest research advances and how to cope with all aspects of lymphoma. For more information about any of these resources, visit lymphoma.org; e-mail helpline@lymphoma.org or call (800) 500-9976.

## Participating in Clinical Trials

Peripheral T-cell lymphomas comprise such a rare group of diseases it is often difficult to find enough patients to enroll in clinical trials. Clinical trials are crucial in identifying effective drugs and determining optimal doses for lymphoma patients. If you are interested in participating in a clinical trial, talk to your doctor about an appropriate trial for you. To learn more about clinical trials, visit lymphoma.org.

## Glossary of Terms

**Aggressive lymphomas** Lymphomas that are fast growing. These types of lymphoma generally need to be treated immediately, but there is a good chance for a long-term cure. These lymphomas are also called intermediate-grade or high-grade lymphomas.

**Biopsy** Removal of a small piece of tissue (for example, a lymph node) for evaluation under a microscope.

**Chemotherapy** Treatment with "chemo" drugs to stop the growth of rapidly dividing cancer cells, including lymphoma cells.

**Chemotherapy regimen** Combinations of anti-cancer drugs given at a certain dose in a specific sequence according to a strict schedule.

**Complete remission** The term used when all signs of disease have disappeared after treatment.

**Lymph nodes** Small bean-shaped glands located in the small vessels of the lymphatic system. Thousands are located throughout the body and are most easily felt in the neck, armpits and groin.

**Lymphatic system** The vessels, tissues and organs that store and carry lymphocytes that fight infection and other diseases.

**Lymphocyte** A type of white blood cell.

**Virus** A particle of nucleic acid that has the potential to inject its genetic material (DNA or RNA) into normal cells. Once inside the normal cells, the virus's genetic material can take control of the normal cells, making them malignant.