LYMPHOMA
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Getting the Facts

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T-Cell Lymphoma

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).

T-cell lymphomas can develop in lymphoid tissues such as the lymph nodes and spleen, or outside of lymphoid tissues (i.e., gastrointestinal tract, liver, nasal cavity, skin, and others). A similar lymphocyte called a natural killer (NK) cell shares many features with T cells. When NK cells become cancerous, the cancer is called NK or NK/T-cell lymphoma and is generally grouped with other T-cell lymphomas. T-cell lymphomas account for about seven percent of all NHLs in the United States according to the Surveillance, Epidemiology, and End Results program. Each particular subtype of T-cell lymphoma is very uncommon. They can be *aggressive* (fast-growing) or *indolent* (slow-growing).

Lymphomas are often, but not always, named from a description of the normal cell that leads to cancer. Lymphomas that arise from mature T cells are sometimes categorized together under the general term peripheral T-cell lymphoma (PTCL), which distinguishes them from the lymphoma that arise from immature T cells or lymphoblastic lymphoma. Under this broad meaning, almost all types of T-cell lymphoma fall under the category of PTCL. More specific subtypes of T-cell lymphoma are listed here.

Common Types of T-Cell Lymphoma

Peripheral T-Cell Lymphoma, Not Otherwise Specified (PTCL-NOS) refers to a group of diseases that do not fit into any of the other PTCL subtypes. PTCL-NOS accounts for about 20 percent of T-cell lymphomas and is the most common PTCL subtype. Although most patients with PTCL-NOS are diagnosed with their disease confined to the lymph nodes, sites outside the lymph nodes, such as the liver, bone marrow, gastrointestinal tract, and skin, may also be involved. Patients with this subtype of PTCL will frequently have constitutional symptoms (i.e., fevers, serious night sweats, and unexplained weight loss). For more information, view the *Peripheral T-Cell Lymphoma* fact sheet on the Lymphoma Research Foundation's (LRF's) website at www.lymphoma.org.

Anaplastic Large Cell Lymphoma (ALCL) describes several types of T-cell lymphomas and accounts for approximately one percent of all NHLs and 11 percent of all T-cell lymphomas. Initial symptoms of ALCL can include fever, backache, painless swelling of lymph nodes, loss of appetite, itching, skin rash, and tiredness.

ALCL can be either *systemic* (occurring throughout the body) or *cutaneous* (limited to the skin). Systemic ALCL is typically in an advanced stage at diagnosis and can progress rapidly. The systemic subtype is further classified as ALK-positive or ALK-negative, depending on whether or not it contains an abnormal anaplastic lymphoma kinase (ALK) fusion protein that results from a genetic event. Systemic ALCL, especially ALK-positive disease, can respond well to treatment and is potentially curable. ALK-negative patients may require more aggressive treatments, and *relapse* (disease returns after treatment) occurs more frequently than in ALK-positive disease. The non-systemic type is called primary cutaneous anaplastic large cell lymphoma, appears only on the skin, and has a good prognosis. For more information, view the *Anaplastic Large Cell Lymphoma* fact sheet on LRF's website at www.lymphoma.org.

Angioimmunoblastic T-Cell Lymphoma (AITL) is a rare, aggressive type accounting for about seven percent of all patients with T-cell lymphomas in the United States. Most patients are middle-aged to elderly and are diagnosed with advanced stage disease. There is some evidence that AITL develops from an ongoing immune response potentially due to a latent viral infection (like Epstein-Barr virus). Initial symptoms often include fever, night sweats, skin rash, itching, and some autoimmune disorders such as autoimmune hemolytic anemia (AIHA; where the immune system attacks red blood cells) and immune thrombocytopenia (ITP; where the immune system attacks platelets). For more information, view the *Angioimmunoblastic T-Cell Lymphoma* fact sheet on LRF's website at www.lymphoma.org.

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Cutaneous T-Cell Lymphoma (CTCL) accounts for two to three percent of all NHL cases and usually affects adults. The term cutaneous T-cell lymphoma describes a group of typically indolent lymphomas that appear on, and are most often confined to, the skin.

Mycosis fungoides, which appears as skin patches, plaques, or tumors, is the most common type of CTCL. Patches are usually flat, possibly scaly, and look like a rash; plaques are thicker, raised, usually itchy lesions that are often mistaken for eczema, psoriasis, or dermatitis; and tumors are raised bumps, which may or may not ulcerate. More than one type of lesion may be present at any time.

Sézary syndrome is a less common form of CTCL that affects both the skin and blood. Most cases occur in adults over the age of 60 years. The most common symptoms are swollen lymph nodes and a red, very itchy rash that covers large portions of the body. Abnormal T cells, called Sézary cells, can be seen under a microscope and are present in both the skin and blood.

Other, rare forms of CTCL include primary cutaneous anaplastic large cell lymphoma and lymphomatoid papulosis. For more information, view the *Cutaneous T-Cell Lymphoma* fact sheet on LRF's website at www.lymphoma.org.

Uncommon Types of T-Cell Lymphoma

Adult T-Cell Leukemia/Lymphoma (ATLL) is a rare and often aggressive form of T-cell lymphoma that can be found in the blood (leukemia), lymph nodes (lymphoma), skin, or multiple areas of the body. ATLL has been linked to infection by the human T-cell lymphotropic virus type 1 (HTLV-1). This virus is commonly found in people from the Caribbean, parts of Japan, and some areas of South and Central America and Africa, as well as sporadic cases from around the world. People usually acquire the virus at birth or during breastfeeding. Less than five percent of those who carry the virus will develop lymphoma. This lymphoma requires urgent treatment in most patients and stem cell transplantation is frequently needed for cure. For more information, view the *Adult T-Cell Leukemia/Lymphoma* fact sheet on LRF's website at www.lymphoma.org.

Enteropathy-Type T-Cell Lymphoma is an extremely rare and aggressive subtype of T-cell lymphoma that appears in the intestines. One form of this disease is frequently preceded by chronic diarrhea and gluten sensitivity and is associated with celiac disease. Another form of this disease is not generally associated with celiac disease. Other symptoms include abdominal pain and weight loss. It requires aggressive treatment that frequently is followed by stem cell transplantation.

Hepatosplenic Gamma-Delta T-Cell Lymphoma is an extremely rare and aggressive disease that starts in and involves the liver and/or spleen. It can spread into the blood and bone marrow. It most often occurs in teenagers and young adults and is more common in males. This lymphoma is associated with immunosuppressive treatments. Patients, especially children, who have been treated with azathioprine and infliximab (Remicade) for Crohn's disease may be more susceptible to this type of lymphoma.

Lymphoblastic Lymphoma can arise from either immature B cells or T cells, but more commonly comes from T cells, comprising more than 80 percent of all lymphoblastic lymphomas. This type of lymphoma is most often diagnosed in adolescents and young adults and is a bit more common in men than women. Tumors frequently arise in the middle of the chest, or mediastinum, though lymphoma cells may appear in the lymph nodes as well as in the bone marrow or spleen. Central nervous system involvement is more common than in other T-cell lymphomas. This lymphoma, like other subtypes, can result in impaired immunity and opportunistic infections, and interfere with the body's ability to make blood cells resulting in fatigue and bleeding. This lymphoma is aggressive and can progress rapidly, if not properly treated. With intensive chemotherapy, the complete remission rate can be very high and many patients can be cured.

Nasal NK/T-Cell Lymphomas develop from natural killer (NK) cells, which are closely related to and often have features that overlap with T cells. Although this aggressive lymphoma is relatively rare in the United States, it is more common in Asia and parts of Latin America. This subtype has been associated with the Epstein-Barr virus. It typically originates in the lining of the nose or upper airway at the back of the throat but may appear in the gastrointestinal tract, skin, and other organs (in which case it is referred to as *nasal type*).

Treatment-Related T-Cell Lymphomas sometimes referred to as post-transplant lymphoproliferative disorder (PTLD), appear in patients who are intentionally immunosuppressed after solid organ or bone marrow transplantation. While this subtype is more commonly a proliferation of B cells, it can occasionally arise from T cells. The immune system suppression that is required to prevent rejection of the transplanted organ puts patients at risk for this type of lymphoma.

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Treatment Options

Because there are so many different types of T-cell lymphoma, treatment varies widely. Standard lymphoma therapies may include chemotherapy, immunotherapy (like antibody drug conjugates) radiation, stem cell transplantation, and surgery. Patients diagnosed with rare forms of lymphoma should consult their medical team to find new promising therapies or to enroll into clinical trials.

Treatments aimed at the skin, such as topical corticosteroids, topical retinoids, topical chemotherapy, ultraviolet light therapy, or *electron beam therapy* (a type of radiation that does not penetrate to internal organs), are effective for many of the slow-growing T-cell lymphomas that appear in the skin (CTCL).

In addition, a procedure called extracorporeal photopheresis (ECPP) is approved to treat people with CTCL. For this procedure, blood is removed from the patient and treated with ultraviolet light, and with drugs that become active when exposed to ultraviolet light. Once the blood has been treated, it is then returned back into the patient's body.

When systemic chemotherapy treatments are appropriate, initial treatment is typically a combination chemotherapy regimen, such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), CHOEP (CHOP plus etoposide) or EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone), or other multidrug regimens. Treatments might vary widely depending on the subtype of lymphoma that you have.

In some cases, it may be determined that transplantation is the most appropriate approach to treatment. For more information on transplants, view the *Understanding The Stem Cell Transplantation Process* booklet on LRF's website at www.lymphoma.org.

Patients with relapsed disease are usually treated with combination chemotherapy such as ICE (ifosfamide, carboplatin, and etoposide) if stem cell transplantation is contemplated as the next step in therapy. However, some regimens or transplant might not be suited for everyone because of their high toxicity levels. Less toxic single-agent therapies are also available and might induce a long lasting remission in such patients. These therapies include belinostat (Beleodaq), brentuximab vedotin (Adcetris), pralatrexate (Folotyn), and romidepsin (Istodax). These drugs are approved by the U.S. Food and Drug Administration (FDA) for patients who have relapsed or those who have not responded to their first line of chemotherapy.

Treatments Under Investigation

Treatment options for the different types of T-cell lymphomas are expanding as new treatments are discovered and current treatments are improved. Treatments currently being investigated singly or in combination include:

- Alisertib (MLN8237)
- Bendamustine (Treanda)
- Bortezomib (Velcade)
- Brentuximab vedotin (Adcetris) (approved for relapsed or refractory ALCL only)
- Crizotinib (Xalkori)
- GDP (gemcitabine, dexamethasone, and cisplatin)
- Lenalidomide (Revlimid)
- Nivolumab (Opdivo)
- Panobinostat (Farydak)
- Pembrolizumab (Keytruda)

In addition, a number of promising clinical trials are exploring combinations of these new agents which in some cases may be more active than the single agent alone. It is critical to remember that today's scientific research is continuously evolving. Treatment options may change as new treatments are discovered and current treatments are improved. Therefore, it is important that patients check with their physician or with LRF for any treatment updates that may have recently emerged.

Clinical Trials

Clinical trials are crucial for identifying effective drugs and determining optimal doses for patients with lymphoma. In many of the rare subtypes of T-cell lymphoma, no standard of care is established. Clinical trial enrollment is critical for establishing more effective, less toxic treatments. In rare diseases, novel treatments are also often only available through clinical trials. Patients interested in participating in a clinical trial should talk to their physician or contact the LRF Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing helpline@lymphoma.org. For more information on clinical trials, view the *Understanding Clinical Trials* fact sheet on LRF's website at www.lymphoma.org.

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Follow-up

Patients in remission should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests and computed tomography [CT] scans) may be required at various times during remission to evaluate the need for additional treatment.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any effects resulting from treatment or potential disease recurrences. LRF's award-winning mobile application (app) *Focus On Lymphoma* can help patients track this information in one location.

Support

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. LRF's Lymphoma Support Network, connects patients and caregivers with volunteers who have experience with T-cell lymphomas, similar treatments, or challenges, for mutual emotional support and encouragement. You may find this useful whether you or a loved one is newly diagnosed, in treatment, or in remission.

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of T-cell lymphomas, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people with T-cell lymphomas, as well as disease-specific websites, videos, and e-Updates for current lymphoma information and treatment options. For more information about any of these resources, visit our website at www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.