

Adult T-cell leukemia/lymphoma (ATLL) is a rare T-cell lymphoma that can be found in the *blood* (leukemia), *lymph nodes* (lymphoma), skin, or multiple other areas of the body.

Symptoms vary depending on the different ATLL subtypes (described below). The most common symptoms are:

- Skin rash.
- Swollen lymph nodes (bean-shaped structures that help the body fight infection, **Figure 1**).
- Swollen liver or spleen.
- Fever.
- Night sweats.
- Weight loss.

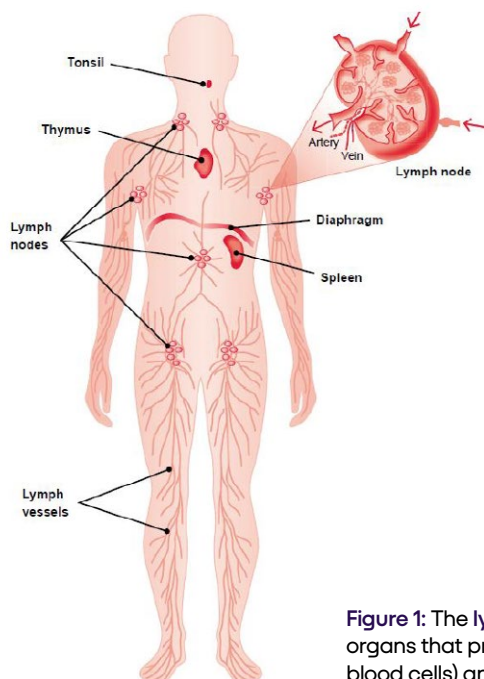


Figure 1: The **lymphatic system** (tissues and organs that produce, store and carry white blood cells) and lymph nodes.

ATLL has been linked to infection with the human T-cell lymphotropic virus type 1 (HTLV-1; a virus that infects the T-cells and may cause disease in some patients) however, only 5% of individuals with HTLV-1 will develop ATLL. Currently, physicians have no way of predicting which infected patients will develop ATLL. The HTLV-1 virus is most common in parts of Japan, the Caribbean, and some areas of South and Central America, and Africa. The HTLV-1 virus can be passed through sexual contact or contact with infected blood, but is most often passed from mother to child through the placenta, at childbirth, and during breastfeeding. In most cases, infection with HTLV-1 is not associated with any symptoms.

For more information on ATLL diagnosis and symptoms, please view *Understanding Lymphoma and CLL Guide* on the Foundation's website (visit lymphoma.org/publications).

Subtypes of ATLL

There are four subtypes of ATLL:

- Acute.
- Lymphoma.
- Chronic.
- Smoldering.

The acute and lymphoma subtypes are aggressive (fast-growing) forms of ATLL, whereas chronic and smoldering are *indolent* (slow-growing).

- **Acute:** Symptoms develop rapidly and may include *fatigue* (extreme tiredness), skin rash, and enlarged lymph nodes in the neck, underarm, or groin. The characteristics of acute ATLL are a high level of white blood cells (cells that help the body fight infections and cancer) often with *hypercalcemia* (elevated calcium levels in the blood), which can cause confusion, irregular heartbeat and severe constipation (a condition in which stool becomes hard, dry, and difficult to pass, and bowel movements don't happen very often). Acute ATLL may spread to *extranodal* tissues (tissues outside the lymph nodes).
- **Lymphoma:** This aggressive type of ATLL is found primarily in the lymph nodes, causes swollen or enlarged lymph nodes and may cause an increase in the level of white blood cell, skin rash, and hypercalcemia.
- **Chronic:** This slow-growing type of ATLL can result in elevated lymphocytes in the blood, enlarged lymph nodes, skin rash, or fatigue. It can also be found in other areas of the body such as the spleen and liver.
- **Smoldering:** This slow-growing type of ATLL is associated with very mild symptoms, such as a few skin lesions and/or rash.

Depending on the subtype, diagnosing ATLL will require a biopsy. During this procedure a needle is used to take a small sample of the affected tissue which is then observed under a microscope.

A blood test (a sample of blood is collected to measure the amount of certain molecules in the blood or count blood cells) will also be necessary to measure the number of white blood cells, calcium levels, and the presence of the HTLV-1 virus. Other tests, such as a *bone marrow* (the spongy tissue inside the bones) biopsy, a computed tomography (CT) scan of the chest, abdomen, liver, and spleen, and/or a positron emission tomography (PET, an imaging scan that uses a special dye to locate the cancer in the body) scan may be used to determine where the cancer is located.

Treatment Options

For some patients who have one of the slower-growing subtypes of ATLL with mild or no symptoms, physicians may recommend not treating the disease right away. This is called active surveillance (also known as “watchful waiting” or “observation”). In this case, patients are monitored through regular physical exams (to check for any swollen lymph nodes) or periodic imaging tests (like CT scans). If patients begin to have symptoms or signs of disease progression, treatment is initiated. For more information about active surveillance, please see the *Active Surveillance* publication on the Foundation's website (lymphoma.org/publications).

For ATLL affecting the skin, skin-directed therapies such as topical (applied to the skin surface), steroids or local radiation (applied only to the affected area in the body) may be prescribed. Because ATLL is such a rare disease, there have not been enough patients enrolled in clinical trials (a type of research study that tests how well new treatments work) to establish treatment standards (the proper treatment that is widely used by healthcare professionals and accepted by medical experts) in the United States and Europe, especially for the acute and lymphoma subtypes. As a result, common *frontline* (initial) therapies used to treat ATLL are the same as those used to treat other types of T-cell lymphomas. These include:

- **Chemotherapy** (drugs that stop the growth of or kill cancer cells).
 - CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone).
 - CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone).
 - Dose-adjusted EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone).
 - Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high dose methotrexate and cytarabine (Cytosar).
- **Chemoimmunotherapy** is a combination of chemotherapy with immunotherapy (drugs that use the body's immune system to fight cancer), such as antibody-drug conjugates (ADC).
 - An ADC is a monoclonal antibody (a protein made in the laboratory that binds to cancer cells and helps the immune system destroy them) attached to a chemotherapy drug. The monoclonal antibody in the ADC recognizes and binds to a protein on the cancer cell surface. Once the ADC is inside the cell, the chemotherapy drug separates from the ADC and kills the cancer cell by targeting cell multiplication.
 - BV-CHP is a combination of the ADC brentuximab vedotin (Adcetris) and the chemotherapy regimen cyclophosphamide, doxorubicin, and prednisone (CHP). This combination is used for the treatment of lymphomas that are positive for CD30 (molecule present on the surface of certain lymphomas).
- **Antiviral therapy** (treatment of infections caused by a virus).
 - Zidovudine (Retrovir, AZT) in combination with interferon-alpha, to treat the underlying HTLV-1 infection (in patients with slow-growing ATLL).
- **Stem cell transplantation (SCT)** may be appropriate in some patients following *remission* (disappearance of signs and symptoms). During this procedure the patient is treated with high-dose chemotherapy or radiation and then receives healthy stem cells to restore the immune system and the bone marrow's ability to make new blood cells.
 - **Autologous SCT** (uses patient's own stem cells)
 - **Allogeneic SCT** (uses stem cells from a related or unrelated donor)

Patients seeking more information about SCT should view the *Understanding Cellular Therapy* guide on the Foundation's website (lymphoma.org/publications).

Similar to the frontline treatment, standard treatment for *relapsed* (disease returns after treatment) ATLL has not been established. Many chemotherapy regimens used to treat other T-cell lymphomas following relapse are also being used to treat ATLL, including the following:

- DHAP (dexamethasone, cytarabine, and cisplatin).
- ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin).
- GDP (gemcitabine, dexamethasone, and cisplatin).
- ICE (ifosfamide, carboplatin, and etoposide).
- Pralatrexate (Folotylin).
- Belinostat (Beleodaq).

Treatments Under Investigation

Several new drugs are being studied in clinical trials for ATLL, as single-agent (one drug) therapy or as part of a combination (two or more drugs) therapy regimen, including the following:

- Bortezomib (Velcade).
- Tolinapant (ASTX660).
- Mogamulizumab (Poteligeo).
- Valemetostat (DS-3201b).

It is critical to remember that today's scientific research is always 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 the Lymphoma Research Foundation for any treatment updates that may have recently appeared.

Clinical Trials

Clinical trials are crucial in identifying effective drugs and the best treatment doses for patients with lymphoma. Because ATLL is a rare disease, clinical trial enrollment is critical for establishing more effective, less toxic treatments. The rarity of the disease also means that the latest treatments are often available only through clinical trials. Patients interested in participating in a clinical trial should view the Understanding Clinical Trials fact sheet on the Foundation's website (visit lymphoma.org/publications) and the *Clinical Trials Search Request Form* at lymphoma.org, talk to their physician, or contact the Foundation's Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing helpline@lymphoma.org.

Follow-up

Patients with lymphoma should have regular visits their physician. During those visits, medical tests (such as blood tests and CT/PET scans) may be required at various times during remission to evaluate the need for additional treatment.

Some treatments can cause side effects that are long-term (occur **during** treatment and continue for months or years) or late side effects (appear only months, years or decades **after** treatment has ended). These side effects can vary depending on the following factors:

- Duration of treatment (how long was the treatment given).
- Frequency of treatment (how often was the treatment administered).
- Type of treatment given.
- Age and gender of the patient.
- Patient overall health at the time of treatment.

A physician will check for these side effects during follow-up care. Visits may become less frequent the longer the patient stays in remission.

Patients and their care partners are encouraged to keep copies of all medical records. This includes test results, as well as information on the types, amounts, and duration of all treatments received. Medical records are important for keeping track of any side effects resulting from treatment or potential disease recurrences. The Foundation's award-winning *Focus on Lymphoma* mobile app (lymphoma.org/mobileapp) or our *Lymphoma Care Plan* (lymphoma.org/publications) can help patients manage this documentation.

Lymphoma Care Plan

Keeping your information in one location can help you feel more organized and in control. This also makes it easier to find information pertaining to your care and saves valuable time. The Foundation's Lymphoma Care Plan document organizes information on your health care team, treatment regimen, and follow-up care. You can also keep track of health screenings and any symptoms you experience to discuss with your health care provider during future appointments. The Lymphoma Care Plan document can be accessed by visiting lymphoma.org/publications.

Patient Education Programs

The Foundation also offers a variety of educational activities, including live meetings and webinars for individuals looking to learn directly from lymphoma experts. These programs provide the lymphoma community with important information about the diagnosis and treatment of lymphoma, as well as information about clinical trials, research advances and how to manage/cope with the disease. These programs are designed to meet the needs of a lymphoma patient from the point of diagnosis through long-term survivorship. To view our schedule of upcoming programs, please visit lymphoma.org/programs.

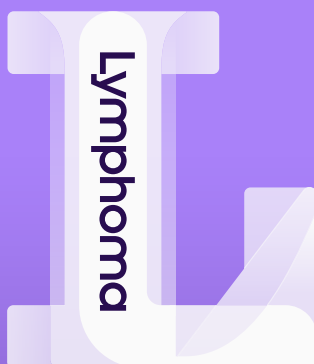
Helpline

The Foundation's Helpline staff are available to answer your general questions about lymphoma and treatment information, as well as provide individual support and referrals to you and your loved ones. Callers may request the services of a language interpreter. The Foundation also offers a one-to-one peer support program called the Lymphoma Support Network and clinical trials information through our Clinical Trials Information Service. For more information about any of these resources, visit our website at lymphoma.org, or contact the Helpline at (800) 500-9976 or helpline@lymphoma.org.

Para información en Español, por favor visite lymphoma.org/es. (For Information in Spanish please visit lymphoma.org/es).

Focus on Lymphoma Mobile App

Focus on Lymphoma is the first app to provide patients and their care partners with tailored content based on lymphoma subtype, and actionable tools to better manage diagnosis and treatment. Comprehensive lymphoma management, conveniently in one secure and easy-to-navigate app, no matter where you are on the care continuum. Get the right information, first, with resources from the entire Lymphoma Research Foundation content library, use unique tracking and reminder tools, and connect with a community of specialists and patients. To learn more about this resource, visit our website at lymphoma.org/mobileapp, or contact the Foundation's Helpline at (800) 500-9976 or helpline@lymphoma.org.



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