LYMPHOMA RESEARCH • FOUNDATION

Understanding Hodgkin Lymphoma

Hodgkin lymphoma (HL), also known as Hodgkin disease, represents about 10 percent of all lymphomas in the United States. Approximately 8,100 new cases of HL are diagnosed in the United States each year.

HL can occur in both children and adults, but it is most commonly diagnosed in adults. Incidence peaks in young adults between the ages of 20 and 34 years and again in older adults between the ages of 70 and 84 years.

HL is often characterized by the presence of very large cells called Reed-Sternberg (RS) cells and usually starts in the lymph nodes; however, it can spread to other lymph nodes and to other organs.

Common signs and symptoms of HL include swelling of the lymph nodes (which is often, but not always, painless), fever, night sweats, unexplained weight loss, itching, and lack of energy. While most people who have these complaints do not have HL, anyone with persistent symptoms should see a physician to make sure that lymphoma is not present.

COMMON TYPES OF HL

HL is divided into two main classifications: classical HL (cHL), which accounts for 93 percent of cases, and nodular lymphocyte-predominant HL. The type of HL a patient has may affect their treatment choices.

CLASSICAL HL

Nodular Sclerosis cHL is the most common subtype of HL, accounting for 60 to 80 percent of all cHL cases. In *nodular* (knot-like) sclerosis cHL, the involved lymph nodes contain RS cells mixed with normal white blood cells. The lymph nodes often contain a lot of scar tissue, which is where the name nodular *sclerosis* (scarring) originates. The disease is more common in women than in men, and it usually affects adolescents and adults under the age of 50 years. The majority of patients are cured with current treatments.

Mixed Cellularity cHL accounts for about 15 to 30 percent of all HL cases. The disease is more common in men than in women, and it primarily affects older adults. With this type of cHL, the lymph nodes contain many RS cells in addition to several other cell types. More advanced disease is usually present by the time this subtype is diagnosed.

Lymphocyte-Rich cHL accounts for less than five percent of HL cases. The disease may be *diffuse* (spread out) or nodular in form and is characterized by the presence of numerous normal-appearing lymphocytes and classic RS cells. This subtype of HL is usually diagnosed at an early stage in older adults and has a low *relapse* (disease returns after treatment) rate.

Lymphocyte-Depleted cHL is rarely diagnosed (about 1 percent of all cHL cases). Abundant RS cells and few normal lymphocytes are present in the lymph nodes of patients with this subtype, which is aggressive and usually not diagnosed until it is widespread throughout the body.

LYMPHOCYTE-PREDOMINANT HL

Nodular Lymphocyte-Predominant HL accounts for 7 percent of all HL cases. It affects men more often than women and is usually diagnosed before the age of 35 years. Typical RS cells are usually not found in this subtype, but large, abnormal B cells (sometimes referred to as popcorn cells) can be seen, as well as small B cells, which may be distributed in a nodular pattern within the tissues. This subtype is usually diagnosed at an early stage and is not very aggressive. This form of HL resembles *indolent* (slow-growing) B-cell non-Hodgkin lymphoma (NHL) and is characterized by late recurrences (return of NHL after brief disappearance).

TREATMENT OPTIONS

The majority of patients with newly diagnosed HL can be cured. Most patients treated for HL receive some form of chemotherapy, sometimes followed by radiation therapy, as their first treatment. Standard *frontline* (initial) chemotherapy for HL is ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) with or without radiation therapy or other agents, depending on the patient's type and stage of HL as well as their overall health status. In 2018, brentuximab vedotin (Adcetris) in combination with chemotherapy, was approved by the U.S. Food and Drug Administration (FDA) for frontline treatment of patients with Stage III or IV cHL. Other chemotherapy regimens may also be recommended, but not always as initial therapy. ABVD tends to be recommended for Stage I or II disease, but it may also be used to treat more advanced HL. The ABVE-PC (adriamycin, bleomycin, vinblastine, etoposide, prednisone and cyclophosphamide) regimen is generally standard for higher-risk pediatric patients. Other chemotherapy regimens (like BEACOPP, which includes bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone), may be suggested for patients with more advanced-stage disease.

A vast number of single-agent and combination treatments are also available for patients with relapsed (disease returns after treatment) or refractory (disease does not respond to treatment) HL, including stem cell transplantation, brentuximab vedotin (Adcetris), nivolumab (Opdivo), pembrolizumab (Keytruda), and chemotherapy regimens.

For more information on relapsed and refractory HL, view the *Hodgkin Lymphoma: Relapsed/Refractory* fact sheet on the Lymphoma Research Foundation's (LRF's) website (click **here**).

TREATMENTS UNDER INVESTIGATION

Although the cure rate in HL is already high (75 percent in newly diagnosed patients), research continues in order to develop more effective therapies with fewer short- and long-term toxicities. New drugs under study include immune checkpoint inhibitors like camrelizumab, sintilimab and tislelizumab.

Investigators are also looking for ways to treat the minority of patients who are refractory to treatment and those who relapse. Studies for relapsed/refractory HL are looking at new combinations of targeted therapies or immunotherapies including ibrutinib (Imbruvica), lenalidomide (Revlimid), and a different class of drugs called histone deacetylase (HDAC) inhibitors (like panobinostat). Clinical trials are also ongoing for the use of ADCT-301 (camidanlumab tesirine) and anti-CD30-CAR (chimeric antigen receptor) T-cell therapy in relapsed/refractory HL.

CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on LRF's website (click **here**), 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.

FOLLOW-UP

Patients with lymphoma 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]/positron emission tomography [PET] scans) may be required at various times during remission to evaluate the need for additional treatment.

Since HL is a highly curable malignancy mostly affecting young people with long life expectancy, there is a growing number of HL survivors who may have special medical needs such as screening for secondary cancers or monitoring for long-term toxicities of therapy. Additional resources for adolescents and young adults living with cancer are available on LRF's website (click **here**).

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 side effects resulting from treatment or potential disease recurrences. LRF's award-winning *Focus On Lymphoma* mobile app (lymphoma.org/mobileapp) and *Lymphoma Care Plan* (lymphoma.org/publications) can help patients manage this documentation.

LRF'S HELPLINE AND LYMPHOMA SUPPORT NETWORK

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. The LRF Helpline staff members are available to answer your general questions about a lymphoma diagnosis 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. A part of the Helpline is LRF's one-to-one peer support program, Lymphoma Support Network. This program connects patients and caregivers with volunteers who have experience with HL, similar treatments, or challenges for mutual emotional support and encouragement. Patients and loved ones may find this useful whether the patient is newly diagnosed, in treatment, or in remission.

MOBILE APP

Focus On Lymphoma is the first mobile application (app) that provides patients and caregivers comprehensive content based on their lymphoma subtype, including HL, and tools to help manage their lymphoma, such as keep track of medications and blood work, track symptoms, and document treatment side effects. The *Focus On Lymphoma* mobile app is available for download for iOS and Android devices in the Apple App Store and Google Play. For additional information on the mobile app, visit FocusOnLymphoma.org. To learn more about any of these resources, visit our website at lymphoma.org, or contact the LRF Helpline at 800-500-9976 or helpline@lymphoma.org.

Resources

LRF offers a wide range of free resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and HL. LRF also provides many educational activities, including our in-person meetings, podcasts, and webinars for people with lymphoma. For more information about any of these resources, visit our websites at lymphoma.org/HL or lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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