LYMPHOMA
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Understanding Lymphoma: Hodgkin Lymphoma: Relapsed/Refractory

Hodgkin lymphoma (HL), also known as Hodgkin disease, represents about 10% of all lymphomas in the United States. It is estimated that 8,830 new cases of HL will be diagnosed in the United States in 2023. HL can occur in both children and adults, but it is most common in young adults between the ages of 20 and 29 years.

HL is often characterized by the presence of very large cells called Reed-Sternberg (RS, Figure 1) cells. This type of lymphoma usually starts in the lymph nodes (small bean-shaped structures that help the body fight disease; Figure 2) and can spread to other lymph nodes and, rarely, to other organs.

Common signs and symptoms of HL include:

- Swelling of the lymph nodes (usually painless)
- Fever
- Night sweats
- Unexplained weight loss
- Itching
- 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.

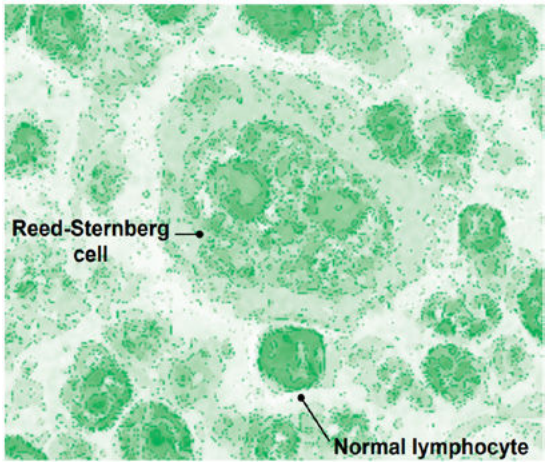

Figure 1. Example of a normal lymphocyte (a type of white blood cell that fights infection and cancer) and a Reed-Sternberg cell found in HL.

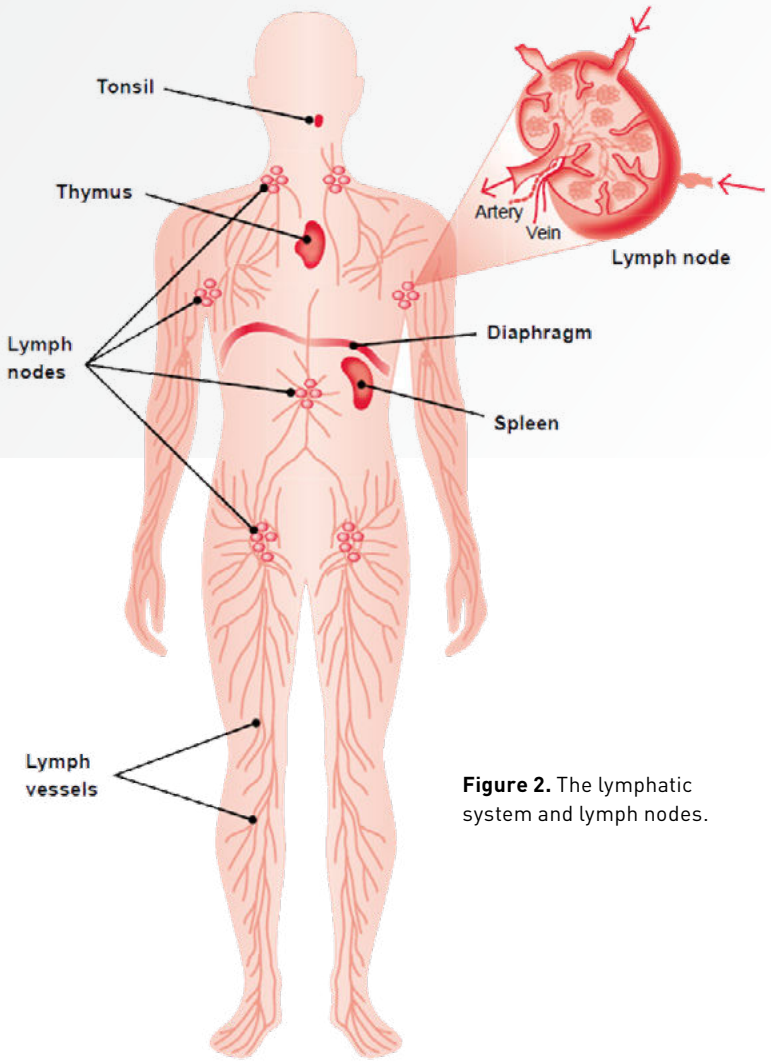

Figure 2. The lymphatic system and lymph nodes.

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COMMON TYPES OF HL

The two main types of HL are classical HL (cHL, which accounts for over 90% of all cases) and nodular lymphocyte-predominant HL (NLPHL, around 5% of all cases).

The four subtypes of cHL are:

- Nodular sclerosis
- Mixed cellularity
- Lymphocyte-depleted
- Lymphocyte-rich

Treatment options for patients with NLPHL differ from those available to patients with cHL.

RELAPSED OR REFRACTORY DISEASE

For patients who relapse (disease returns after treatment) or become refractory (disease does not respond to treatment), secondary therapies are often successful in providing remission (disappearance of signs and symptoms) and may even cure the disease. For cHL, most relapses usually occur within the first three years following diagnosis, although some relapses occur much later. Patients who relapse often have the same symptoms they had when first diagnosed with HL.

TREATMENT OPTIONS

A number of treatment options are available for patients with relapsed or refractory cHL. The exact treatment a doctor may recommend depends on several factors, including the timing of the relapse (the time it takes for the disease to return after finished treament), age and overall health of the patient, disease stage (the growth and spread of the cancer), and previous therapies received.

The standard treatment (the proper treatment that is widely used by healthcare professionals and accepted by medical experts) for patients with relapsed/refractory cHL, without other major health conditions, consists of systemic therapy (treatment with drugs that travel in the bloodstream throughout the body) and can include:

- Immunotherapy (drugs that stimulate the immune system to fight cancer; see Table 1). These can be used alone, in combination with each other, or in combination with chemotherapy (also known as chemoimmunotherapy)
- Chemotherapy regimens (see Table 2)

Table 1. Immunotherapy Drugs Approved To Treat Relapsed or Refractory cHL

Treatment	Approved Indications
Brentuximab vedotin (Adcetris) Antibody-drug conjugate that targets the CD30 protein	• Adult patients with a) previously untreated stage III or IV cHL (in combination with AVD), b) at high risk of relapse or progression after auto-HSCT, c) after failure of auto-HSCT, d) or after failure of ≥ 2 chemotherapy regimens (in patients who are not auto-HSCT candidates) • Pediatric patients (≥ 2 years old) with previously untreated high-risk cHL (in combination with EPOCH)
Nivolumab (Opdivo) Immune checkpoint inhibitor that blocks the PD-1 receptor	• Adult patients with cHL that has relapsed or progressed after auto-HSCT and brentuximab vedotin (Adcetris) or ≥ 3 lines of systemic therapy (including auto-HSCT)
Pembrolizumab (Keytruda) Immune checkpoint inhibitor that blocks the PD-1 receptor	• Adult patients with relapsed or refractory cHL • Pediatric patients with refractory cHL, or cHL that has relapsed after ≥ 2 lines of therapy

AVD, doxorubicin, vinblastine and dacarbazine; cHL, classical Hodgkin lymphoma; EPOCH, etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin; auto-HSCT, autologous hematopoietic stem cell transplant; PD-1, programmed death receptor-1

Table 2. Chemotherapy Regimens Used To Treat Relapsed or Refractory cHL

Regimen	Description
BvB	Brentuximab vedotin (Adcetris) and bendamustine (Treanda)
DHAP	Dexamethasone, cisplatine, and high-dose cytarabine
GVD	Gemcitabine, vinorelbine, and doxorubicin
ICE	Ifosfamide, carboplatin, and etoposide
IGEV	Ifosfamide, gemcitabine, and vinorelbine

cHL, classical Hodgkin lymphoma

Systemic therapies are sometimes followed by autologous stem cell transplantation (auto-HSCT, in which a patient's own stem cells are infused after high-dose chemotherapy). Patients may also receive radiation therapy as consolidation (treatment given after cancer has disappeared following initial therapy to kill any cancer cells that may be left in the body). Involved-site radiation therapy (ISRT) may also be used. For more information on transplantation, view the *Understanding Cellular Therapy* guide on the Lymphoma Research Foundation's (LRF's) website (**lymphoma.org/publications**).

Therapeutic options for relapsed or refractory NLPHL include systemic therapy with the anti-CD20 antibody rituximab (Rituxan), either alone or in combination with chemotherapy. Radiation therapy may also be used.

TREATMENTS UNDER INVESTIGATION

In addition to conventional (traditional) chemotherapies, there are several new agents (treatments) currently being tested in clinical trials for patients with relapsed or refractory cHL:

- AB-205 (E-CEL cells)
- Anti-CD30-chimeric antigen receptor (CAR) T-cells
- AZD7789
- Camidanlumab tesirine (ADCT-301, Cami)
- Camrelizumab (SHR-1210)
- Everolimus (Afinitor)
- Ibrutinib (Imbruvica)
- Itacitinib (INCB039110)
- Ipilimumab (Yervoy)
- Lenalidomide (Revlimid)
- Magrolimab (5F9)
- Penpulimab
- Ruxolitinib (Jakafi)
- Tislelizumab (BGB-A317)

It is critical to remember that scientific research is always changing. 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 appeared.

CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and optimal treatment doses for patients with lymphoma. Because the optimal HL treatment may vary for each patient, clinical trials are very important and will identify the best treatment options in this disease. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on LRF's website (**lymphoma.org/publications**), 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 their physician. During these visits, medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required to evaluate the need for additional treatment.

Patients and their caregivers are encouraged to keep copies of all medical records. This includes test results as well as information on the type, amount, and duration of all treatments received. Medical records are 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 information.

LYMPHOMA CARE PLAN AND PATIENT EDUCATION PROGRAMS

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. LRF's *Lymphoma Care Plan* fact sheet 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* fact sheet can be accessed by visiting **lymphoma.org/publications**. LRF also offers a variety of educational activities, including live meetings and webinars, for individuals looking to learn directly from lymphoma experts. To view our schedule of upcoming programs, please visit **lymphoma.org/programs**.

LRF Helpline

The LRF 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. LRF 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 LRF 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**).

LRF FOCUS ON LYMPHOMA MOBILE APP

Focus on Lymphoma is the first app to provide patients and their caregivers with tailored content based on lymphoma subtype and actionable tools to better manage diagnosis and treatment. Experience 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 LRF content library, use unique tracking and reminder tools, and connect with a community of specialists and patients. To learn more this resource, visit our website at **lymphoma.org/mobileapp**, or contact the LRF Helpline at **800-500-9976** or **helpline@lymphoma.org**.

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