Lymphoma - Non-Hodgkin - Subtypes [1]

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ON THIS PAGE: You will find descriptions of the most common types and subtypes of NHL, as well as information about how each may be treated. To see other pages, use the menu on the side of your screen.

There are different types and many subtypes of NHL, and it is very important to know which type and subtype has been diagnosed. Below are the most common types and subtypes, including information about how each may be treated. For more information about the treatment information described here, please read the Treatment Options [3] section.

First, the doctor will determine what type of cell the lymphoma started in and classify the disease within three major groups:

B-cell lymphoma. About 90% of people with lymphoma have B-cell lymphoma.

T-cell lymphoma. About 10% of people with lymphoma have T-cell lymphoma.

NK-cell lymphoma. Less than 1% of people with lymphoma have NK-cell lymphoma.

NHL is also described by how quickly the cancer is growing: indolent or aggressive. Indolent and aggressive NHL are equally common in adults. In children, aggressive NHL is more common.

Indolent NHL. These types of lymphoma grow very slowly. As a result, people with indolent NHL may not need to start treatment when it is first diagnosed. They are followed closely, and treatment is only started when they develop symptoms or the disease begins to change. This is called watchful waiting [3]. When indolent lymphoma is located only in one area, it is called

localized disease (stages I and II, see the Stages [4] section). For people with localized disease, radiation therapy may eliminate the NHL. However, most patients with indolent NHL have later-stage disease, stage III or IV, at the time of diagnosis. There are many effective treatments for these stages of indolent NHL, but it may come back months or years after treatment has finished, requiring additional treatment.

Aggressive NHL. These types of lymphoma may develop rapidly, and treatment is usually started immediately. These types of lymphoma usually need more intensive chemotherapy. Radiation treatment may be recommended in addition to chemotherapy, especially in patients with limited stage disease (stage I or II). Many forms of aggressive lymphoma may be cured with effective treatment.

Some subtypes of lymphoma cannot easily be classified as indolent or aggressive. For example, mantle cell lymphoma (see below) has features of both indolent and aggressive NHL.

Subtyping

In addition to determining if the NHL is indolent or aggressive and whether it is B-cell, T-cell, or NK-cell lymphoma, it is very important to determine the subtype of NHL. This is because each subtype can behave differently and may require different treatments. There are about 35 subtypes of NHL. The most common subtypes are described below, along with some basic information about different treatments. Learn more in the Treatment Options [3] section.

Distinguishing between the different subtypes of NHL can be difficult and requires pathologists or hematopathologists who are experts in the diagnosis of lymphoma. Such specialists will use sophisticated techniques and work closely with experienced oncologists. The diagnosis is based on how the lymphoma looks under the microscope and confirmed by additional information from other tests, including tests of genetic material within the lymphoma cells. For more information on this process, see the Diagnosis [5] section.

Subtypes of B-cell lymphoma

The most common subtypes of B-cell lymphoma are described below.

Diffuse large B-cell lymphoma (DLBCL). This is the most common form of lymphoma; about 30% of people in the United States with NHL have this type. It is an aggressive form of NHL that involves organs other than the lymph nodes about 40% of the time. About two out of three people with DLBCL are cured with chemotherapy given in combination with rituximab (Rituxan); see the Treatment Options [3] section for more information. Radiation therapy is also used for some patients, especially if the lymphoma is localized in a small area. Treatments to prevent the lymphoma from spreading to the brain, called central nervous system (CNS) prophylaxis, may be given, but most patients do not need this type of treatment. Recent research has shown that there are different types of DLBCL, known as germinal center and non-germinal center. Research studies, called clinical trials [6], continue to look at whether different types of

treatment should be used for these different types of DLBCL.

Follicular lymphoma. This is the second most common form of lymphoma in the United States and Europe. About 20% of people with NHL have this type. It usually begins in the lymph nodes, is most often indolent, and grows very slowly. There is no known cure; however, recent studies show that more than 85% of patients live for at least five years after being diagnosed with follicular lymphoma, and 50% are estimated to live longer than 12 years. Patients with follicular lymphoma may receive a combination of chemotherapy; monoclonal antibodies, a type of targeted therapy; and/or radiation therapy. Or they may be followed closely with watchful waiting. See the Treatment Options [3] section for more information.

Recent clinical trials have suggested that the survival for patients with follicular lymphoma has improved over the last few decades. Drugs such as bendamustine (Treanda) and lenalidomide (Revlimid), usually in combination with rituximab, have been shown to be effective for this subtype and can be used as part of first-line treatment, which is the initial treatment given after diagnosis. There are many new drugs being tested for use as part of first-line treatment for follicular lymphoma

Over time, follicular lymphoma may turn into DLBCL (see above), which will then require more aggressive treatment. This is called transformation. Stem cell transplantation, tumor vaccines, and monoclonal antibody treatments may also be available in clinical trials.

Localized radiation therapy is often a common treatment choice for early-stage disease (stages I and II) [7], but it may be combined with other treatments as well.

Mantle cell lymphoma. About 7% of people with NHL have mantle cell lymphoma. It most often appears in people older than 60 and is much more common in men than women. It usually involves the bone marrow, lymph nodes, spleen, and gastrointestinal system, which includes the esophagus, stomach, and intestines. Mantle cell lymphoma is identified by a protein called the cyclin D1 protein or a genetic change in the lymphoma cells involving chromosomes 11 and 14.

The initial approach to treating mantle cell lymphoma is to use a combination of chemotherapy drugs with a monoclonal antibody. Because many people with mantle cell lymphoma will have the disease return after finishing chemotherapy, some patients may be offered high-dose chemotherapy followed by autologous stem cell transplantation at the end of their initial chemotherapy treatment. Patients who do not have a stem cell transplant may be offered maintenance therapy [8] with monoclonal antibodies. Radiation therapy may also be used to control local symptoms.

If chemotherapy does not work, there are differing opinions on the best way to treat mantle cell lymphoma. Drugs such as bortezomib (Velcade), bendamustine, lenalidomide, and ibrutinib (Imbruvica) have been shown to be effective for this subtype and are being studied in clinical trials as part of first-line treatment. Other new drugs are also being studied for mantle cell lymphoma. Some patients may have a slower growing form of the disease that may be managed like follicular lymphoma (see above).

Small lymphocytic lymphoma. This type of lymphoma is very closely related to a disease called B-cell chronic lymphocytic leukemia (CLL) [9], and about 5% of people with NHL have this subtype. It is considered an indolent lymphoma. Patients with small lymphocytic lymphoma may receive a combination of chemotherapy, monoclonal antibodies, and/or radiation therapy; or they may be followed closely with watchful waiting. Stem cell transplantation, tumor vaccines, and monoclonal antibody treatments may also be available in clinical trials. Ibrutinib is now approved for patients who have had their disease return after initial treatment. In some patients, ibrutinib can be used as part of initial treatment, although this is still being studied.

Mediastinal large B-cell lymphoma. This is an aggressive form of DLBCL (see above). It appears as a large mass in the chest area, which may cause breathing problems or superior vena cava syndrome (SVCS) [10], a collection of symptoms caused by the partial blockage or compression of the superior vena cava, the major vein that carries blood from the head, neck, upper chest, and arms to the heart. Mediastinal large B-cell lymphoma is most common in women between 30 and 40 years old, and about 2.5% of people with NHL have this subtype. It is treated most often with anthracycline-based chemotherapy, and most patients also receive rituximab and radiation therapy to the chest. Newer chemotherapy treatments may eliminate the need for radiation therapy.

Splenic marginal zone B-cell lymphoma. This type of lymphoma begins in the spleen and can also involve the blood. It is usually slow growing, and the treatment approach is often watchful waiting. If treatment is needed, this type of lymphoma is often treated similarly to follicular lymphoma. Sometimes, surgical removal of the spleen is recommended.

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT). This type of lymphoma most commonly occurs in the stomach, but it may also occur in the lung, skin, thyroid, salivary gland, or eye. Patients with this type of lymphoma sometimes have a history of autoimmune disease, such as lupus, rheumatoid arthritis, or Sjögren's syndrome. When MALT occurs in the stomach, it is often successfully treated with antibiotics to treat an infection with *Helicobacter pylori* bacteria, which is thought to cause the lymphoma. Other times, radiation therapy, surgery, chemotherapy, monoclonal antibodies, or a combination of these is the most common treatment plan. For disease in only one part of the body, radiation therapy can often cure MALT.

Nodal marginal zone B-cell lymphoma. This type of indolent lymphoma involves the lymph nodes. It is rare; about 1% of people with lymphoma have this subtype. In general, this subtype of lymphoma is treated similarly to follicular lymphoma (see above).

Lymphoplasmacytic lymphoma. This is an indolent form of lymphoma, and 1% of people with NHL have this subtype. This form of lymphoma most often involves the bone marrow, lymph nodes, and spleen. In many patients, this lymphoma produces proteins, called "M proteins," that are found at high levels in the blood. When this occurs, the condition is called Waldenstrom's macroglobulinemia (WM) [11]. Patients with WM sometimes have thickened blood, which may cause symptoms such as headache, blurry vision, dizziness, and shortness of breath. Treatment

is similar to chronic lymphocytic lymphoma/leukemia or follicular lymphoma and may include watchful waiting, chemotherapy, monoclonal antibodies, or combinations of chemotherapy and monoclonal antibodies. Chemotherapy followed by stem cell transplantation is being studied in clinical trials and may be useful if the lymphoma returns after initial treatment.

Primary effusion lymphoma. This very aggressive form of lymphoma most often occurs in people who have the human immunodeficiency virus (HIV, the virus that causes autoimmune deficiency syndrome or AIDS), people whose immune system does not work well for other reasons, or people who are elderly. It begins in the lung, heart, or abdominal cavities. Often, there are no tumors. It is treated the same as other diffuse large cell lymphomas (see above).

Burkitt lymphoma/Burkitt cell leukemia. This is a very rare and aggressive form of lymphoma. There are three forms of Burkitt lymphoma: endemic, sporadic, and immunodeficiency-related lymphoma. The endemic subtype occurs most commonly in Africa, appears most often in the jawbones of children, and is usually associated with infection with EBV. It can also be associated with HIV. In the United States, Burkitt lymphoma appears most commonly with a mass in the abdomen. Because this type of lymphoma spreads quickly, it needs immediate treatment that includes intensive chemotherapy, usually with some treatment for the central nervous system to prevent it from spreading to the brain. This type of NHL is often curable with immediate treatment.

Subtypes of T-cell and NK-cell lymphoma

The most common subtypes of T-cell and NK lymphoma are described below.

Anaplastic large cell lymphoma, primary cutaneous type. This subtype of lymphoma only involves the skin. It is often indolent, although aggressive subtypes of the disease are possible. When the cancer is localized, radiation therapy is often effective. If it has spread, chemotherapy is the usual treatment. New drugs have recently been developed for the treatment of cutaneous lymphomas, some of which can be given as a pill that is swallowed.

Anaplastic large cell lymphoma, systemic type. This form makes up about 2% of all lymphomas and about 10% of all childhood lymphomas. An increased amount of the ALK-1 protein may be found in the cancer cells of this subtype for some people. Those who have this subtype of lymphoma with the ALK-1 protein in the cells often have a better prognosis than those who have this subtype without the ALK-1 protein in the cell. It is an aggressive form of lymphoma, but treatment often works well, including new treatments such as the monoclonal antibody brentuximab vendotin (Adcetris). See the Treatment Options [3] section for more information. Stem cell transplantation may sometimes be an option, especially for the subtype without the ALK-1 protein.

Peripheral T-cell lymphoma, NOS. This is an aggressive form of lymphoma that is most often found when it is advanced. It is most common in people older than 60 and makes up about 6% of all lymphomas in the United States and Europe. The cells of this lymphoma are variable in

size, and they have certain types of proteins, called CD4 or CD8, on their surface. It is treated with chemotherapy like DLBCL (see above) or other drugs. Many new drugs are also being studied in clinical trials. Stem cell transplantation may sometimes be an option.

Angioimmunoblastic T-cell lymphoma. This is an aggressive form of lymphoma with specific symptoms: swollen lymph nodes, fever, weight loss, rash, and high levels of antibodies called gamma globulin in the blood. Since patients with angioimmunoblastic lymphoma have lowered immune systems, infections are also common. This type of lymphoma is identified by what it looks like under a microscope and by certain proteins found in the tumor cells. It is treated like other aggressive lymphomas.

Adult T-cell lymphoma/leukemia (human T-cell lymphotropic virus type I positive). This type of lymphoma is caused by a virus called the human T-cell lymphotropic virus type I. It is an aggressive disease that most often involves the bone and skin. Often, lymphoma cells are found in the blood, which is why this condition is sometimes also called leukemia. Chemotherapy does not usually work well for this form of lymphoma, although zidovudine (Retrovir) and interferon have helped some patients. About two-thirds of patients experience a temporary or permanent absence of cancer symptoms, called remission.

Extranodal NK/T-cell lymphoma, nasal type. This is an aggressive type of lymphoma that is very rare in the United States and Europe overall but more common in Asian and Hispanic communities. It can occur in children or adults, most often involving the nasal area and sinuses. It can also involve the windpipe, gastrointestinal tract, skin, or a man’s testicles. Standard chemotherapy does not always work well for this type of NHL, and combining radiation therapy with chemotherapy is an important addition to treatment. Compared to other T-cell lymphomas, this subtype responds better to asparaginase (Elspar), which is now a standard part of initial treatment and is also used when this subtype of lymphoma comes back after treatment. Stem cell transplantation for this type of lymphoma is being studied in clinical trials.

Enteropathy-associated T-cell lymphoma. This type of lymphoma is rare in the United States but is more common in Europe. It is an aggressive form of T-cell lymphoma that involves the intestines of patients who have celiac disease or a history of gluten intolerance. High-dose chemotherapy may be used to treat enteropathy type T-cell lymphoma.

Gamma/delta hepatosplenic T-cell lymphoma. This is an aggressive form of peripheral T-cell lymphoma that involves the liver and spleen. It occurs most often in adolescent and young men. It is treated as a high-risk diffuse large cell lymphoma (see above).

Subcutaneous panniculitis-like T-cell lymphoma. This is a form of peripheral T-cell lymphoma that is similar to gamma/delta hepatosplenic T-cell lymphoma (see above). It involves the tissue under the skin and is often first diagnosed as panniculitis, inflammation of fatty tissues. It is treated as a high-risk aggressive lymphoma.

Mycosis fungoides. This is a rare T-cell lymphoma that primarily involves the skin. It often has a very long and indolent course, but may become more aggressive and spread to lymph nodes

or internal organs. Radiation therapy, chemotherapy, or immunotherapy can help treat this form of NHL. New drugs have been developed for the treatment of cutaneous lymphomas, some of which can be taken orally as a pill.

More information on the specific treatment options described above can be found in the Treatment Options [12] section.

The next section helps explain the different stages for this type of cancer. Use the menu on the side of your screen to select Stages, or you can select another section, to continue reading this guide.

Links
[1] http://www.cancer.net/cancer-types/lymphoma-non-hodgkin/subtypes
[2] http://www.cancer.net/about-us
[3] http://www.cancer.net/node/19215
[4] http://www.cancer.net/cancer-types/lymphoma-non-hodgkin/stages
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