# Lymphoma

Maxime Coles MD

Lymphoma is a broad term for a cancer involving the lymphatic system. Lymph tissue is found mainly in the lymph nodes, spleen, liver, bone marrow. There are two main types: Hodgkin Lymphoma and Non-Hodgkin Lymphoma. This disease is often curable but the prognosis depends on the specific type. The term “Lymphoma” described the two forms of cancer which often can be cured.

Non-Hodgkin Lymphoma is a group of blood cancers that include all type of lymphomas except for the Hodgin’s lymphoma itself. Patients present with symptoms like fever, night sweats, enlarged lymph nodes, weight loss and extreme fatigue. They have also chest pain, bone pain, itchiness. Some forms are slow-growing and others are fast-growing. Enlarged lymph nodes may be felt as a lump under the skin and may become commonly itchy, red or purple. If localized in the brain, they may cause weakness, seizures, personality changes or problems in thinking. There is also an association between Lymphoma and Endometriosis that has been described as an entity.

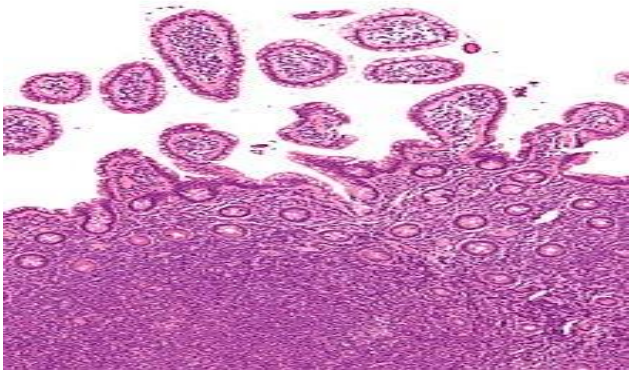
A classification is needed for the Lymphoma because this is a so large group of different diseases for which Henry Rappaport tried in 1956 and then in 1966 to propose a classification, but it is really in 1982 that standard classification was proposed, introducing the term “non-Hodgkin lymphoma” (NHL) and three grades were defined. NHL consists in many conditions grouped depending on their behavior and subtypes were listed.

Lymphoma comprises a variety of cancer, fairly common, developing from a white blood cell called “Lymphocyte”. At least, 4. 5 million people were diagnosed with non-Hodgkin lymphoma in 2015 and data has shown that around 235,000 between the age of 65 and 75 were affected by the disease at a certain time of their life. A five-year survival rates was found to be close to 70%. Manifestation of poor immune function like found in any other auto immune disease or in multiple viral infections like hepatitis C, Epstein-Barr, Retrovirus, HIV-AIDS virus or even with Helicobacter pylori infections (Gram negative bacterium) and even obesity, exposition to Herbicides have been named as risks factors.
Unfortunately, more than 60 specific types of Non-Hodgkin’s Lymphoma have been described although the diagnosis is asset through the examination of the bone marrow specimen or through the biopsy of a lymph node. Further Medical Imaging will help in the staging of the disease. Although, lymph tissue is found in the lymph nodes, spleen, liver, bone marrow, and other sites, an abdominal CT scan can show tumor masses (malignant lymphomas) in the area behind the peritoneal cavity (retroperitoneal space). Let us try to differentiate the Lymphomas:

A lymphoma can be of a slow or a fast-growing in nature or can be localized in a typical area. There is an armamentarium of methods of treatment including Chemotherapy, Radiation, Immunotherapy, Targeted therapy, Stem-cell transplantation, Surgery. Plasmapheresis (Plasma exchange or Apheresis) can also be used especially when the blood become thick. Radiation and Chemotherapy are also used but may increase the risks of developing secondary cancers, or any heart disease or even nerve inflammation over the years following the diagnosis. Although, lymph tissue is found in the lymph nodes, spleen, liver, bone marrow, and other sites, an abdominal CT scan may also show tumor masses (malignant lymphomas) in other areas like, behind the peritoneal cavity (retroperitoneal space). Let us try to differentiate the Lymphomas:

In a Non-Hodgkin Lymphoma, an enlarged lymph node generally is found in a 65-year-old presenting with night sweats, weight loss, itching and extreme fatigue. One may present with hepatomegaly, splenomegaly, back pain etc. A poor immune function, with Helicobacter pylori infection, hepatitis C, Obesity, Epstein-Barr virus infection can be added to the picture. A bone marrow or a lymph node biopsy will allow one to asset the diagnosis with more accuracy. Treatment will consist then, in Chemotherapy, Radiation therapy, Immunotherapy, targeted

Therapy, Stem cell transplantation or Surgery. Around 70% survival rate is expected with such treatment

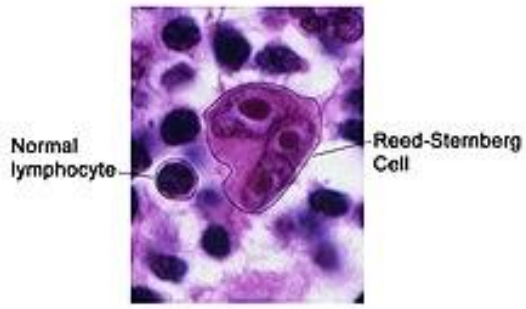


Non Hodgkin Lymphoma

In 2015, 4.3 million were affected with the Non-Hodkin Lymphoma with 231,000 deaths. To diagnose the non-Hodgkin blood count cell lymphoma type, a complete blood count cell (CBC), blood chemistry studies, Hepatitis B and Hepatitis C, HIV test, CT-Scan, Bone Marrow aspiration and Biopsy can help. It is also possible to obtain a diagnosis by studying of the cancerous cells through Immunohistochemistry, Cytogenetic analysis, Immunophenotyping.

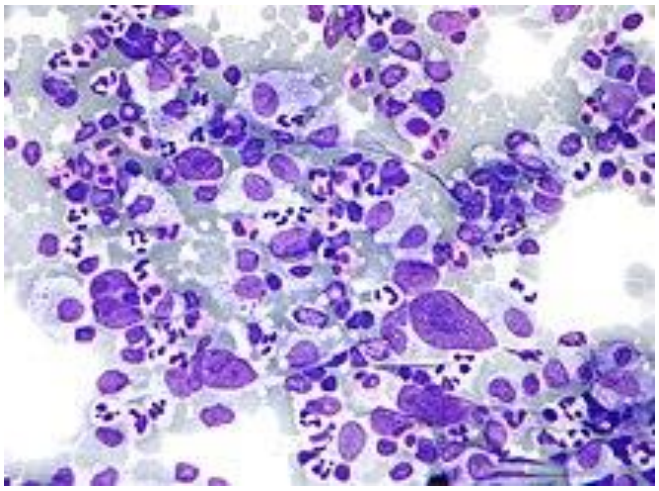
Different forms of non-Hodgkin lymphoma have been associated to the Epstein Barr virus (Burkitt's lymphoma), Follicular Dendritic cell sarcoma, Extra-nodal NK-T-cell Lymphoma and Diffuse large B-cell Lymphoma, Human T-cell Leukemia virus, associated to the adult T-cell Lymphoma.

In a Hodgkin Lymphoma **(Hodgkin lymphoma) or** (**HL**) itself, we are dealing with a lymphoma cancer's originating from a specific white blood cell (Lymphocytes) with specific multinucleated "Reed-Sternberg cells (RS cells), present in the lymph nodes. Thomas Hodgkin was the one who first described the disease in 1832. People suffering from the disease will have fever, night sweats and weight loss. Often, a painless and enlarged lymph node is discovered in the neck, under the arm (axilla) or in the groin. These patients may feel tired and experience itchiness.




Reed-Steinberg cell

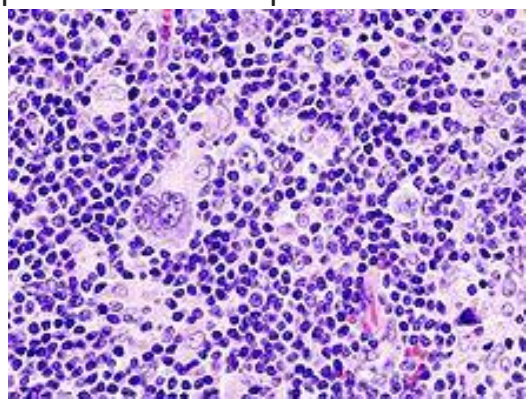
The two major types of Hodgkin lymphoma are the classic representation of a disease which can be associated to the Epstein-Barr virus (EBV) in half of the time or associated with HIV-AIDS. When the diagnosis is confirmed with the identification of the virus in the “Reed-Sternberg cells”, after a biopsy, we are dealing with a lympho-proliferative disease.



Hodgkin Lymphoma

Hodgkin disease is most common in two different age groups: Young adults (15-35) and older adults (50+). The disease is more common in males than females and seen more often in Caucasians than African-Americans. The exact cause of Hodgkin lymphoma is not well known, but many hypotheses based on viral origins have survived the test of time.
Viruses causing Mononucleosis (Epstein Bar virus: EPV) have been implicated as a cause of Hodgkin lymphoma and studies have shown that the genome of this virus is seen in almost 80% of these tumors. There is also a familial “same-sex-sibling “as well as an identical twin theory associated to the Hodgkin lymphoma.

More, there is an environmental factor residing in fewer sibling, early birth order, single family home, etc. probably due to a lack of exposure to other bacterial or viral infections at early age. In a Hodgkin lymphoma, often the typical Reed Stenberg cell will be present in the biopsied tissues.



Lymph node biopsy

The treatment of Non-Hodgkin Lymphoma include: Chemotherapy and Radiation, Therapy with added Stem cell transplants and Immunotherapy. A four-drugs-regimen with Cyclophosphamide, Doxorubicin, Vincristine and Prednisone plus Rituximab, form the “R-CHOP regimen”. In 2023, R-CHOP was supplemented with an anti-drug conjugate (Polatuzumab Vedotin) suggested by the National Comprehensive Cancer Network.

Participants receiving stem-cell transplantation may develop a graft-versus-host disease and by autoimmunity, mesenchymal stromal cells (MSC’s) may reduce the all-cause mortality when they are used for a therapeutic reason. Some believe that MSC may increase a complete response of acute and chronic “Graft versus Host disease” (GvHD). Evidences suggest that, “MSC’s” result in little difference in the disease mortality or in the relapse of the malignant diseases but surely, may have a role in reducing the incidence of “GvHD”.

Platelet transfusions can become necessary once you receive treatment with chemotherapy or undergoing stem cell transplantation because of a higher risk in bleeding or at least one significant bleeding event due to the reduction in the number of platelet transfusions.

Aerobic Physical exercises may bring little difference in the mortality rate and the quality of life and even in the physical functioning of a sick individual but it may definitely reduce the rate of depression and mental fatigue. Mainly, the prognosis will rely on the staging and the subtype of the disease, the patient’s age… etc, but

mainly, a 5-year survival in a Non Hodgkin Lymphoma is in the 70% and increases with age.
210,000 deaths were attributed to non-Hodgkin Lymphoma in 2010, from 143,000 in 1990. Up to the age of 45 years, NHL is more common among males than females. I remember a paper in the 90's in which I was involved in, at Yale New Haven and the way we were surprised to discover the disease in 2 young individuals in their mid-30's (one was a surgical resident). The paper was discussing symptoms of the two male patients with thoracic vertebra pain. A bony lesion was localized in the thoracic spine. I will try to find the references and note at the end of this article.
In Australia, 6,600 people are yearly diagnosed with the disease. In Canada, NHL is the 5$^{th}$ most common cancer in males (1 in 44 and the sixth in females (1 in 51). In the United Kingdom, 13,900 people were diagnosed with the disease during a period 2014-2016, yearly; it was the 11$^{th}$ most common cancer accounting for 4,900 deaths per year. In United States 2.2% of men and women will be diagnosed with Non Hodgkin Lymphoma at a certain point during their lifetime. In the years 2012-2016, almost 20 cases per 100,000 adults / per year will suffer from the disease with 5.6 deaths per 100,000 but around 695,000 people are living with the disease. The American Cancer Society considered Non-Hodgkin Lymphoma, as one of the most common cancer in the United States accounting for 4% of all cancers.

Complications in stem-cell transplants are seen with graft-versus host disease. When compared to a placebo in treating immune mediated inflammation post transplantation and in autoimmunity, mesenchymal stromal cells (MCSs) may reduce the all-cause mortality. Platelet transfusions may be necessary for those receiving chemotherapy or undergoing stem cell transplantation because of a higher risk of bleeding.

When comparing therapeutic versus non-prophylactic platelet transfusions, one can observe little difference in the mortality secondary to bleeding and may result in a slight reduction in the number of days of bleeding. Therapeutic transfusions of platelets result in a large increase in the number of people with significant effusion resulting in a reduction in the number of platelets to be transfused.

We do not know if aerobic physical exercise can be a supplemental to the standard treatment of any hematological malignancy among adults in reducing anxiety or other serious adverse reactions or in reducing fatigue. It may depend

on the subtype, the staging or the age but grossly, a five-year survival for non-Hodgkin Lymphoma is near 75%.

In Australia, 6600 cases of non-Hodgkin lymphoma are diagnosed yearly while around the world, 210,000 deaths were diagnosed as of 2010 with the disease more common in males than female before the age of 45. In Canada, the disease represents the 5thmore common cancer in males and the sixth in women with an incidence of one in 44 men and one in 51 women. In United Kingdom 13,900 cases are diagnosed with NHL yearly. This is also the sixth most common cancer which brings around 4,900 deaths on a yearly basis. In The United States, 100,000 cases are discovered each year with 5.6 deaths per 100,000 deaths per year although around 700,000 people are living with the disease Non-Hodgkin Lymphoma. 2.2 % of men and women suffer from the disease, accounting for 4% of all cancers.

One has to appreciate that talking about Hodgkin Lymphoma, pushes the author of an article to think about a possible classification of different groups of the same disease. Henry Rappaport was the first one to propose one in the mid 50's (1956) which became widely accepted but modified twenty years later in 1982, in non-Hodgkin lymphoma (NHL) with three different grades of Lymphomas.

It was discovered that the lymphomas may represent many entities with little in common and with different aggressivity. The lesser aggressive non-Hodgkin lymphomas are more compatible with a long survival while the more aggressive can become rapidly fatal without any treatment. Canadian Cancer Society, National Cancer institute… etc.

The choice of treatment often depends on how advanced the cancer become and whether it has favorable features or whether the disease is diagnose earlier. 88% of people diagnosed with the disease survive more than "five" (5) years or longer. People under the age of 20 may have rate of survival reaching the 90's. Radiation and Chemotherapy drugs carry in the risks of secondary cancers, heart and lung disease.

In conclusion, lymphomas are cancers involving the lymphatic system, a vast network of tissues, vessels and organs responsible for the filtration of the toxins and the waste in the body, transporting the lymph throughout the entire body. These lymphomas originate in some while blood cell known as B Lymphocytes and T lymphocytes. These cells may become diseased with cancerous component and multiply rapidly to rapidly impair the function of the immune system, rendering the body more susceptible to infection. A lymphoma may follow as a tumor,

affecting any component of the lymphatic system, including any lymphoid tissue found in the bone marrow, the lymph nodes, the spleen, the liver and the thymus. Malignant lesions can be found in the chest or the abdomen on either side of the diaphragm, in the neck, the axillae, the groins, in bony lesions interesting long bones, vertebral bodies etc. The earlier these lesions are detected, the higher chances of survival will be expected with a prompt treatment. Hodgkin lymphoma can be distinguished from non-Hodgkin lymphoma by the presence of the "Reed-Sternberg cells, larger in size than the typical healthy lymphocyte or the Hodgkin cells. If the Reed-Stenberg cells are not detected, we are dealing with a Non-Hodgkin Lymphoma.

If we believe that around the world, more than half-million people suffer from Hodgkin lymphoma, less than 5% have already died but only .2 % of people are affected at some point of their life but more people will be at risk between the age of 20 and 40. I wrote this page knowing well that one of my young Medical Resident at Meharry Medical School of Medicine, and another one at Bridgeport-Yale Health have left this world, too early, after being a victim of this disease. I wrote also this page for my little cousin undergoing active treatment and for all my friends and patients who have returned to their Creator too early. May scientists develop a cure for Hodgkin lymphoma!

Maxime Coles MD

Boca Raton FL (November 2024)

References:


1- World Cancer Report 2014. World Health Organization 2014 pp: 2.4-2.6.
2- "Different types of non-Hodgkin lymphoma". Cancer Research UK. Archived from original on 14 August 2014.
3- Audebert A (April 2005). "Women with endometriosis: are they different from others? " Gynecologie, Obtetrique & Fertilite: 33 (4): 239-246.
4- Stein ME, Lewis DC, Gershuny AR, Quigley MM, Zaidan J, Danieli NS, Whelan J, Subramanian R (April 2003)"Trauma as an etiologic Factor of primary bone lymphoma: a report of 4 cases". Journal of B U ON. 8 (2) pp163-166.
5- Cerhan JR, Slager SL: "Familial predisposition and genetic risk factors for lymphomas". Blood 125 (20) pp. 2265-73 (November 2015).
6- "Non-Hodgkin lymphoma statistics". Cancer Research UK (may 2015)

7- “Cancer Stat Facts: Non-Hodgkin Lymphoma “National Health Institute Surveillance Epidemiology and End Results (SEER) Program (August 2019.