How to Use this Factsheet

This risk factor summary was developed to serve as a general fact sheet. It is an overview and should not be considered exhaustive. For more information on other possible risk factors and health effects being researched, please see the References section.

A risk factor is anything that increases a person's chance of developing cancer. Some risk factors can be controlled while others cannot. Risk factors can include *hereditary conditions*, *medical conditions or treatments*, *infections*, *lifestyle factors*, or *environmental exposures*. Although risk factors can influence the development of cancer, most do not directly cause cancer. An individual's risk for developing cancer may change over time due to many factors, and it is likely that multiple risk factors influence the development of most cancers. Knowing the risk factors that apply to specific concerns and discussing them with your health care provider can help to make more informed lifestyle and health care decisions.

For those cancer types with environmentally-related risk factors, an important factor in evaluating cancer risk is the route of exposure. This is particularly relevant when considering exposures to chemicals in the environment. For example, a particular chemical may have the potential to cause cancer if it is inhaled, but that same chemical may not increase the risk of cancer through skin contact. In addition, the dose and duration of time one might be exposed to an environmental agent is important in considering whether an adverse health effect could occur.

Gene-environment interactions are another important area of cancer research. An individual's risk of developing cancer may depend on a complex interaction between their genetic makeup and exposure to an environmental agent (for example, a virus or a chemical contaminant). This may explain why some individuals have a fairly low risk of developing cancer as a result of an environmental factor or exposure, while others may be more vulnerable.

Key Statistics

The American Cancer Society estimates 71,850 individuals will be diagnosed with NHL in the U.S. in 2015: 39,850 men and 32,000 women.[1, 2] In Massachusetts, NHL accounts for about 4% of all cancer diagnoses, which follows the national trend of 4%. NHL is predicted to account for 1,620 new diagnoses statewide in 2014.[2] Although some types of NHL are among the more common childhood cancers, more than 95% of diagnoses occur in adults.[1] Incidence generally increases with age, and most diagnoses occur in people in their 60s or older.[1, 5] NHL is more common in men than women, though there are certain types of NHL that are more common in women. In the United States, NHL affects whites more often than either African Americans or Asian Americans.[1] Nationally, incidence rates for NHL have nearly doubled since the 1970s.[9] Some of the increase may be attributed to AIDS-related NHL, but reasons for the rise are largely unknown.[11]

Types of Non-Hodgkin Lymphoma

The term "cancer" is used to describe a variety of diseases associated with abnormal cell and tissue growth. Cancers are classified by the location in the body where the disease originated (the primary site) and the tissue or cell type of the cancer (histology).

Lymphomas are cancers that start in the cells of the lymph system, which is part of the body's immune system.[1] The majority of lymphomas involve the lymph nodes and spleen but the disease may affect other areas within the body. NHL is a classification of all lymphomas except Hodgkin's disease. Thus, NHL is a group of cancers (around 35) that is characterized by the increase in malignant cells of the immune system (B or T lymphocytes).[5] B-cell lymphomas are more common than T-cell lymphomas, accounting for about 85% of all NHL diagnoses in the United States. Subtypes of B-cell lymphomas include diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, small lymphocytic lymphoma (SLL), mantle cell lymphoma, marginal zone B-cell lymphoma, and many others. Subtypes of T-cell lymphomas include precursor T-lymphoblastic lymphoma and peripheral T-cell lymphomas. Additional rarer types of NHL also exist.[1]

Although NHL is associated with a number of risk factors, the specific cause(s) of NHL in most individuals is unknown. This is complicated by the fact that NHL is actually a diverse group of cancers. Each subtype of NHL may have different risk factors associated with its development.

Established Risk Factors

Medical Conditions

NHL is more common among people who have weakened immune systems. For example, individuals taking immunosuppressant drugs following organ transplants have an increased risk of developing NHL. Similarly, autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus (SLE, or lupus) have been associated with an increased risk of NHL. Some chemotherapy drugs used to treat other cancers can increase the risk of developing NHL many years later. It is not clear if this is related to the disease itself or if it may be a result of a suppressed immune system due to treatment.[1]

Infections

Several viruses have been shown to play a role in the development of NHL. Individuals infected with human immunodeficiency virus (HIV), which can also weaken the immune system, are at increased risk of some types of NHL. Infection with human T-cell leukemia/lymphoma virus (HTLV-1) increases the risk of developing certain types of T-cell NHL. This virus is most common in parts of Japan and in the Caribbean region, but is now found throughout the world. In the United States, it is estimated to cause less than 1% of lymphomas. Infection with the Epstein-Barr virus (EBV) is an important risk factor for NHL, particularly in areas of Africa. In developed countries such as the United States, EBV is more often associated with NHL in patients infected with HIV.[1, 5, 11]

Less Well-Established Risk Factors

Infections

Recent studies have found that a type of bacteria, *Helicobacter pylori*, known to cause stomach ulcers, has been linked to some lymphomas of the stomach. The importance of this discovery is that treatment with antibiotics may help prevent some NHL of the stomach. Several studies have found that infection with hepatitis C virus (HCV) may be a risk factor for developing certain types of lymphoma. However, more research is needed to better understand this possible association.[1, 5]

Lifestyle Factors

Several studies have suggested that being overweight or obese may increase the risk of NHL. Some studies have suggested that a diet high in vegetables may lower the risk, although more research is needed to confirm this.[1, 11]

Environmental Exposures

Studies of survivors of atomic bombs and nuclear reactor accidents have shown that exposure to ionizing radiation does increase the risk of developing several types of cancer, including NHL. In addition, patients treated with radiation therapy for other cancers have a slightly increased risk of developing NHL later in life. This risk appears to be greater for patients who are treated with both radiation therapy and chemotherapy.[1]

Some studies have suggested that chemicals such as benzene and certain herbicides and insecticides may be linked with an increased risk of NHL. Research to clarify these possible links is still underway.[1]

Other Risk Factors That Have Been Investigated

Lifestyle Factors

Smoking has been studied in relation to NHL in multiple investigations. A positive association between smoking and certain types of NHL has been found in some studies. Several studies have examined whether people who use hair color products have an increased risk of NHL; however, some studies have shown an association and others have not. The body of current evidence suggests no increased NHL risk, certainly none to the large majority of users.[11]

Non-Hodgkin Lymphoma in Children

NHL accounts for about 6% of all childhood cancers.[2, 3] There are three major types of NHL in children: small non-cleaved NHL (Burkitt and non-Burkitt type, which account for 40% of NHL in children), lymphoblastic lymphoma (LBL) (25 - 30%), and large cell NHL

(LCL) (25%).[3, 6] Childhood NHL occurs more often in boys than girls, and it is more common in white children than African American children.[2, 3, 12]

An increased incidence of NHL[3] has been found in children with inherited immunodeficiency syndromes including:

- Wiskott-Aldrich syndrome
- Severe combined immunodeficiency syndrome (SCID)
- Ataxia-telangiectasia
- Common variable immunodeficiency
- X-linked lymphoproliferative syndrome
- Bloom syndrome

Although these inherited immune deficiency diseases can be passed on to children, patients with NHL who do not have these inherited diseases do not pass an increased risk of NHL on to their children.[1] It is also important to remember that most children with NHL have no known risk factors. There is nothing these children or their parents could have done to prevent this cancer.

For More Information / References

Much of the information contained in this summary has been taken directly from the following sources. This material is provided for informational purposes only and should not be considered as medical advice. Persons with questions regarding a specific medical problem or condition should consult their physician.

American Cancer Society (ACS). http://www.cancer.org

1. ACS. 2015. Detailed Guide: Non-Hodgkin Lymphoma.
2. ACS. 2015. Cancer Facts & Figures 2015.
3. ACS. 2015. Detailed Guide: Childhood Non-Hodgkin Lymphoma.
4. ACS. 2014. Fact Sheet: Hair Dyes.

American Society of Clinical Oncology (ASCO). http://www.cancer.net

5. ASCO. 2014. Guide to Non-Hodgkin Lymphoma.
6. ASCO. 2014. Guide to Childhood Non-Hodgkin Lymphoma.

Massachusetts Cancer Registry (MCR), Massachusetts Department of Public Health.

7. MCR. 2014. Cancer Incidence and Mortality in Massachusetts 2007-2011: Statewide Report. Available at: http://www.mass.gov/eohhs/docs/dph/cancer/state/registry-statewide-report-07-11.pdf
8. MCR. 2014. Childhood Cancer in Massachusetts 2000-2009. Available at: http://www.mass.gov/eohhs/docs/dph/cancer/registry-child-cancer-00-09.pdf

National Cancer Institute (NCI). http://www.cancer.gov

9. Surveillance, Epidemiology, and End Results Program (SEER). 2014. Interactive Tools: Fast Stats. Statistics by Cancer Site. Incidence of Lymphoma, 1975-2011. Generated at: http://seer.cancer.gov/faststats/index.php
10. NCI. 2008. What You Need To Know About Non-Hodgkin Lymphoma.

Schottenfeld and Fraumeni.

11. Hartge P, Wang SS, Bracci PM, Devesa SS, Holly EA. 2006. Non-Hodgkin Lymphoma. In: Cancer Epidemiology and Prevention. 3rd Ed, edited by Schottenfeld D, Fraumeni JF. New York: Oxford University Press: P. 898-918.

12. Ross JA and Spector LG. 2006. Cancers in Children, Non-Hodgkin Lymphoma. In: Cancer Epidemiology and Prevention. 3rd Ed, edited by Schottenfeld D, Fraumeni JF. New York: Oxford University Press: P. 1251-1268.