

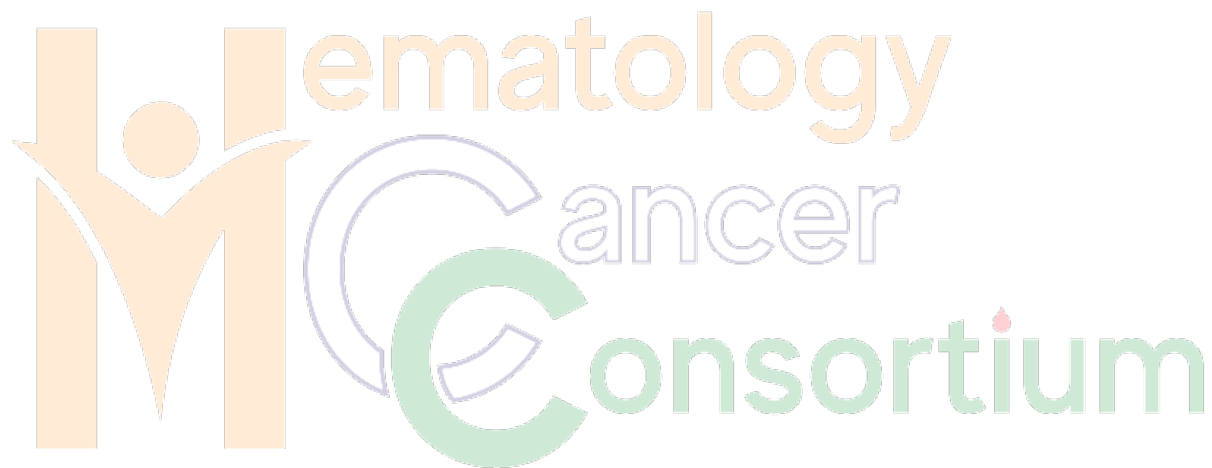
NON-HODGKIN LYMPHOMA

Dr. Anu Korula

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- **What is non-Hodgkin lymphoma?**

Lymphoma is a broad term for cancer that begins in cells of the lymph system. The lymph system is part of the immune system, which helps fight infections and some other diseases. The lymph system is made up of cells called **lymphocytes**, a type of white blood cell. There are 2 main types of lymphocytes, B cells and T cells, which are part of the immune system.

The two main types of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). NHL is a broad term that covers many different types of lymphomas and depending on the type of NHL; chemotherapy will vary from patient to patient.

Non-Hodgkin lymphomas can be divided broadly into either indolent or aggressive, and this depends on the rate of growth of the lymphoma. Indolent lymphomas are more common in older people, and may often be diagnosed incidentally, or by chance, when the patient is asymptomatic but is tested for some other reason – for e.g. a medical check-up. Indolent lymphomas often do not require immediate treatment as they may remain static or very slow growing over the years. Aggressive lymphomas, on the other hand, are life-threatening and need immediate treatment with chemotherapy.

We will first address some issues related to aggressive lymphomas, and then move on to indolent lymphomas.

Aggressive Non-Hodgkin lymphoma

- **What are the most common types of aggressive non-Hodgkin lymphoma?**

Aggressive lymphomas can arise from either B lymphocytes (B-NHL) or T lymphocytes (T-NHL). Diffuse large B cell lymphoma is the most common type of aggressive B-NHL. Other types include Burkitt lymphoma, primary CNS lymphoma and other high-grade B cell lymphomas. Aggressive lymphomas arising from T cells are numerous, and they include anaplastic large cell

lymphoma, Peripheral T cell lymphoma, NK/T cell lymphoma, angio-immunoblastic T cell lymphoma, subcutaneous panniculitis-like T cell lymphoma – to name a few.

- **Who is affected by aggressive non-Hodgkin lymphoma?**

Aggressive B-NHL can occur in both younger and older adults. Rarely, children can be affected by aggressive lymphomas.

- **What are the symptoms of aggressive non-Hodgkin lymphoma?**

Aggressive NHLs usually start in the lymph nodes; however, in many cases, it may involve lymphoid tissue in the tonsils or gut, or even non-lymphoid tissue, for example, the skin, breast, kidneys, other soft tissues, bones and even the brain.

Depending on the site involved most common signs and symptoms of aggressive NHL may vary, but usually include rapid enlargement of lymph nodes, fever, unexplained weight loss and lack of energy.

- **What causes aggressive non-Hodgkin lymphoma?**

In most cases, we do not know what causes aggressive NHL. Some people, especially with certain viral infections (Epstein-Barr virus, HTLV-1, HIV), auto-immune disease and weak immune systems, can be more pre-disposed to developing non-Hodgkin lymphoma. One cannot catch lymphoma from someone else, and one cannot give it to anyone else. It does not pass on from parent to child.

- **What are the tests for aggressive non-Hodgkin lymphoma?**

The most crucial test is an adequate lymph node biopsy from an enlarged lymph node or involved organ. In patients with lymphoma, other than history and physical examination, the tests done are:

- Complete blood counts and ESR
- A metabolic panel including kidney and liver function tests, lactate dehydrogenase
- Virology screen: HIV, HbsAg and anti-HCV

- PET/CT to look for the extent of involvement with lymphoma. MRI may be done in lymphoma involving the CNS or bones.
- Bone marrow examination – aspiration and a biopsy to look for involvement with lymphoma.
- Test for heart function like ECG and echocardiography before starting chemotherapy
- **How is the diagnosis of aggressive non-Hodgkin lymphoma confirmed?**

This is the most important initial step in the process of diagnosis - a biopsy from the involved lymph node/involved organ is examined under a microscope by a pathologist who will interpret the histological picture and give a diagnosis after further tests such as immunohistochemistry and FISH (if required).

- **What happens after the diagnosis of aggressive non-Hodgkin lymphoma is confirmed?**

After someone is diagnosed with non-Hodgkin lymphoma (HL), it is important to understand how far the disease has spread. This process is called **staging**, which is based on:

- The physical examination
- Imaging tests, which typically include a chest x-ray, CT scan of the chest/abdomen/pelvis, and PET scan
- If you have certain symptoms (B symptoms – see below)
- Bone marrow aspiration and biopsy (sometimes, but not always done)

The staging system used for Hodgkin lymphoma is the **Lugano classification**, and has 4 stages (I, II, III, and IV). If NHL that affects an organ outside of the lymph system (eg kidneys, breast, bone, soft tissues), the letter E is added to the stage (for example, stage IE or IIE).

Bulky disease is a term used to describe tumours that are at least 7.5centimeters across and is indicated by adding the letter X to the stage. Bulky disease may require more intensive treatment and radiation therapy after completion of chemotherapy.

Each stage will also be assigned a letter (A or B). B is added (stage IIIB, for example) if a person has any of these **B symptoms** - Loss of more than 10% of body weight over the previous 6 months (without dieting), unexplained fever of at least 100.4°F (38°C) or drenching night sweats. If a person has any B symptoms, it usually means the lymphoma is more advanced. If no B symptoms are present, the letter A is added to the stage.

- **What are the treatment options for non-Hodgkin lymphoma?**

Chemotherapy (chemo) is the use of drugs (medicines) to kill cancer cells. The medicines are usually injected into a vein under the skin or taken in tablet form. Chemotherapy is the main treatment for most people with aggressive non-Hodgkin lymphoma. Sometimes, chemotherapy is followed by radiation therapy as per the need.

Treatment for non-Hodgkin lymphoma will vary from person-to-person based on the specific type of lymphoma, the patient's age, other co-existing illnesses, general fitness and stage of the disease.

Since there are many subtypes of aggressive NHL, it is beyond the scope of this information booklet to deal with the individual types of treatment and prognosis in each subtype, however, it is important that you speak to your doctor about the type of chemotherapy being used, specific side effects and what are the expected costs and outcomes.

- **What are the side-effects of chemotherapy?**

Chemotherapy drugs can cause side effects. These depend on the type and dose of drugs given and how long treatment lasts. The most common short-term side effects are hair loss, mouth sores, loss of appetite, nausea and vomiting. There is also an increased chance of infection because of low blood counts, or because of weak immunity which is related to the disease itself. These side effects are usually short-lived and go away over time after treatment ends. If serious side effects occur, chemotherapy may have to be delayed or the doses reduced.

Late or long-term side effects: Some chemo drugs can have long-lasting side effects. Some chemo drugs can increase the risk of getting a second type of cancer later in life (such as leukemia), especially in patients who also get radiation therapy.

Most of the regimens used today do not cause infertility, however, it is good to clarify this with your doctor before the treatment starts.

What happens after diagnosis and staging?

After the diagnosis, initial baseline tests and staging is complete, the treating team will decide on how many cycles of chemotherapy are required (based on type of lymphoma, age, stage, co-morbidities), and whether radiation therapy is required after completion of chemotherapy (based on bulky disease).

What are the tests to check the response to treatment? What is the chance of a cure?

Usually, a CT scan or PET scan will be done after between 3 cycles of chemotherapy to assess the response to disease. After the scan report, your doctor will decide how many cycles of chemotherapy are required and whether a change in chemotherapy is required.

The chance of cure depends on many factors, the most important of which is the type of lymphoma and the stage of the disease. Other factors which impact outcome are the patient's age, general fitness, serum LDH and extra-nodal disease.

What if there is no response to initial treatment or if the disease comes back after treatment?

If there is no response to initial treatment, your doctor will discuss this with you, and depending on the patient's age and general fitness, a decision will be taken to choose an appropriate treatment. A more intensive chemotherapy schedule can be used, and if the response is good, consolidation with an autologous stem cell transplant will be performed. In autologous transplantation, stem cells are taken from the patient and stored in a frozen state. After giving

high-dose chemotherapy, these cells are returned to the patient so that they can form healthy bone marrow cells again.

Autologous stem cell transplantation permits a high dose of chemotherapy to be given without permanent effects to the bone marrow.

What is the total duration of the treatment? How frequent are the hospital visits after completing treatment and how long is follow up required?

The total duration of treatment varies from 6 to 8 months, depending on the number of cycles of chemotherapy required and the need for radiation therapy.

After completion of therapy, regular follow-up visits every 3 months are required for 2 years. At these follow-up visits, aside from a few basic blood tests, usually, no further scans are done. It is normal to be anxious about the recurrence of the disease. However, studies have shown that there is no benefit from doing regular scans to detect recurrence, compared to a proper physical examination and doing a scan only if the patient is symptomatic.

Indolent Non-Hodgkin lymphoma

- **What are the most common types of indolent non-Hodgkin lymphoma?**

Indolent lymphomas can arise from either B lymphocytes (B-NHL) or T lymphocytes (T-NHL). Chronic lymphocytic leukemia and Follicular lymphoma are the 2 most common types of indolent B-NHL. Other types include MALT lymphoma, marginal zone lymphoma, Hairy cell leukemia. Indolent lymphomas arising from T cells include mycosis fungoides, T-prolymphocytic leukemia, T-large granular lymphocytic leukemia – to name a few.

- **Who is affected by indolent Non-Hodgkin lymphoma?**

Indolent NHL usually occurs in older adults and is more common in the elderly population.

- **What are the symptoms of indolent non-Hodgkin lymphoma?**

In many patients, indolent lymphomas give rise to no symptoms, especially in the early stages of the disease. Indolent NHLs may start with a slow, progressive increase in the size of the lymph

nodes; however, in many cases, it may involve lymphoid tissue in the tonsils or gut, or even non-lymphoid tissue, for example, the skin.

Symptoms of indolent NHL in advanced stages may vary, but usually include prolonged fever, unexplained weight loss and lack of energy.

- **What causes indolent non-Hodgkin lymphoma?**

In most cases, we do not know what causes low-grade NHL. It is more common in older people, and some people, especially with certain viral infections (Epstein-Barr virus, HTLV-1, HIV), certain bacteria (H.pylori, Chlamydiae), auto-immune disease and weak immune systems, can be more pre-disposed to developing non-Hodgkin lymphoma. You cannot catch lymphoma from someone else, and you cannot give it to anyone else. It cannot be passed on from parent to child.

- **What tests are done for indolent non-Hodgkin lymphoma?**

Indolent lymphomas are usually detected incidentally – that is when the patient has no symptoms but has been tested for some other reason. Sometimes a blood test will pick up the presence of abnormal cells in the peripheral blood (usually in chronic lymphocytic leukemia CLL). If slowly growing lymph nodes/swellings at other sites are noted, a biopsy is done to give a diagnosis.

After diagnosing an indolent lymphoma, other than history and physical examination, the following tests are usually done:

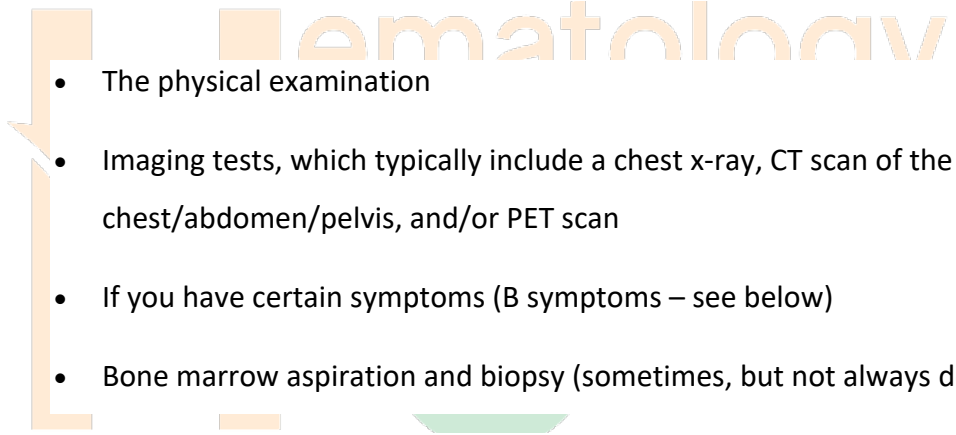
- Complete blood counts and ESR
- A metabolic panel including kidney and liver function tests, lactate dehydrogenase
- Virology screen: HIV, HbsAg and anti-HCV
- PET/CT to look for the extent of involvement with lymphoma. It is important to note that a PET scan may not pick up all types of indolent lymphoma, and these may be better seen on a CT scan.
- Bone marrow examination – aspiration, biopsy to look for involvement with lymphoma.
- Test for heart function like ECG and echocardiography if chemotherapy is required.

- **How is the diagnosis of indolent non-Hodgkin lymphoma confirmed?**

This is the most important initial step in the process of diagnosis - a biopsy from the involved lymph node/involved organ is examined under a microscope by a pathologist who will interpret the histological picture and give a diagnosis after further tests such as immunohistochemistry and FISH (if required).

- **What happens after the diagnosis of indolent non-Hodgkin lymphoma is confirmed?**

After someone is diagnosed with non-Hodgkin lymphoma (HL), it is important to understand how far the disease has spread. This process is called **staging**, which is based on:

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- The physical examination
 - Imaging tests, which typically include a chest x-ray, CT scan of the chest/abdomen/pelvis, and/or PET scan
 - If you have certain symptoms (B symptoms – see below)
 - Bone marrow aspiration and biopsy (sometimes, but not always done)

The staging system used for Hodgkin lymphoma is the **Lugano classification**, and has 4 stages (I, II, III, and IV). If NHL that affects an organ outside of the lymph system (eg kidneys, breast, bone, soft tissues), the letter E is added to the stage (for example, stage IE or IIE).

Each stage will also be assigned a letter (A or B). B is added (stage IIIB, for example) if a person has any of these **B symptoms** - Loss of more than 10% of body weight over the previous 6 months (without dieting), unexplained fever of at least 100.4°F (38°C) or drenching night sweats. If a person has any B symptoms, it usually means the lymphoma is more advanced than a person who does not have B symptoms. If no B symptoms are present, the letter A is added to the stage.

- **Do all patients with an indolent lymphoma require treatment?**

The approach to the treatment of indolent lymphomas differs from aggressive lymphomas, because low-grade lymphomas are often incidentally detected, and can progress slowly over many years without causing any discomfort or risk to the patient. On the other hand, the use of chemotherapy is associated with several risks, therefore in indolent lymphomas it is recommended to wait until symptoms begin before initiating any therapy.

- **If I have an indolent lymphoma, which is a type of cancer, shouldn't I be treated as soon as possible?**

It is important to understand the reason for delaying treatment in indolent lymphomas. In most cases, indolent lymphomas cannot be cured, and the aim of treating the patient is to keep him/her free of symptoms for as long as possible. If the indolent lymphoma by itself is not causing any symptoms, and the use of chemotherapy will not completely cure the disease, there is no real benefit of treating the lymphoma, and the chemotherapy will expose the patient to unnecessary risks. Instead of immediate treatment, your doctor will monitor you regularly (every 3 months) to ensure that the lymphoma is not progressing rapidly.

- **What are the treatment options for indolent non-Hodgkin lymphoma?**

- Chemotherapy (chemo) is the use of drugs (medicines) to kill cancer cells. The medicines are usually injected into a vein under the skin or taken in tablet form. Chemotherapy is the main treatment for most people with indolent and advanced stage, symptomatic indolent non-Hodgkin lymphoma. In some cases, radiation therapy alone is effective.

Treatment for non-Hodgkin lymphoma will vary from person-to-person based on the specific type of lymphoma, the patient's age, other co-existing illnesses, general fitness and stage of the disease.

Since there are many subtypes of indolent NHL, it is beyond the scope of this information booklet to deal with the individual types of treatment and prognosis in each subtype, however, it is important that you speak to your doctor about the type of chemotherapy being used, specific side effects and what are the expected costs and outcomes.

- **What are the side-effects of chemotherapy?**

Chemo drugs can cause side effects. These depend on the type and dose of drugs given and how long treatment lasts. The most common short-term side effects are hair loss, mouth sores, loss of appetite, nausea and vomiting. There is also an increased chance of infection because of low blood counts, or because of weak immunity which is related to the disease itself. These side effects are usually short-lived and go away over time after treatment ends. If serious side effects occur, chemo may have to be delayed or the doses reduced.

Late or long-term side effects: Some chemo drugs can have long-lasting side effects. Some chemo drugs can increase the risk of getting a second type of cancer later in life (such as leukemia), especially in patients who also get radiation therapy.

Most of the regimens used today do not cause infertility, however, it is good to clarify this with your doctor before the treatment starts.

- **What happens after diagnosis and staging?**

After the diagnosis, initial baseline tests and staging is complete, the treating team will decide on whether or not you require immediate treatment with chemotherapy, or whether it will be better to monitor you over the next few months. If you require chemotherapy, they will decide how many cycles of chemotherapy are required (based on type of lymphoma, age, stage, co-morbidities).

- **What tests are done to check response to treatment? What is the chance of cure?**

Usually, a CT scan or PET scan will be done after between 3 cycles of chemotherapy to assess the response to disease. After the scan report, your doctor will decide how many cycles of chemotherapy are required, and whether a change in chemotherapy is required.

Indolent lymphomas are usually not curable, and after successful treatment the lymphoma will remain quiescent for several years before gradually increasing again.

- **What if there is no response to initial treatment or if the disease comes back after treatment?**

If there is no response to initial treatment, your doctor will discuss this with you, and depending on the patient's age and general fitness a decision will be taken to choose appropriate treatment. A more intensive chemotherapy schedule can be used, and if the response is good, consolidation with an autologous stem cell transplant will be performed. In an autologous transplantation, stem cells are taken from the patient and stored in a frozen state. After giving high dose chemotherapy, these cells are given back to the patient so that they can form normal bone marrow cells again.

This permits a high dose of chemotherapy to be given without permanent effects to the bone marrow.

What is the total duration of the treatment? How frequent are the hospital visits after completing treatment and how long is follow up required?

The total duration of treatment varies from 6 to 8 months, depending on the number of cycles of chemotherapy required. In some cases, a lower intensity maintenance treatment is given for up to 2 years.

After completion of therapy, regular follow-up visits every 3 months are required for a period of 2 years. At these follow-up visits, aside from a few basic blood tests, usually no further scans are done. It is normal to be anxious about recurrence of the disease, but studies have shown that there is no benefit from doing regular scans to detect recurrence, compared to a good physical examination and doing a scan only if the patient is symptomatic.

What is a clinical trial? Are there any clinical trials on this disease in India?

Every new treatment or practice is studied methodically in series of studies called “clinical trials” before it becomes a part of standard treatment. Clinical trials are carefully designed and continuously monitored by expert clinicians and researchers to ensure patient safety and scientific accuracy. Patient participation in past clinical trials has resulted in the “standard” treatments and practices which we have today.

