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#### • What is Hodgkin lymphoma?

Lymphoma is a broad term for cancer that begins in cells of the lymph system and usually occur in lymph nodes. These lymph nodes are small organs distributed in various parts of the body like, neck, groin, axilla, inside the chest and deep inside the abdomen. Since lymph cells are found in many other organs, lymphomas can also arise in any other organ of the body. 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). Hodgkin lymphoma usually starts in B lymphocytes. The cancer cells in HL are called Reed-Sternberg cells.

HL is diagnosed based on a lymph node biopsy and is characterized by the presence of characteristic large cells called Reed-Sternberg (RS) cells. HL usually starts in the lymph nodes; however, it can spread from one lymph node to another and can also spread to other organs.

The most common signs and symptoms of HL include swelling of the lymph nodes (which is usually painless), fever, sweating at night, unexplained weight loss, itching, and 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.

#### Who is affected by Hodgkin lymphoma?

HL can occur in both children and adults, but it is most commonly diagnosed in adults. It is most common in young adults between the ages of 20 and 34 years and again in older adults between the ages of 70 and 84 years.

## What causes Hodgkin lymphoma?

In most cases, we do not really know what causes lymphoma. Some people, especially with certain viral infections and weak immune systems, can be more pre-disposed to developing 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 are the symptoms of Hodgkin lymphoma?

The most common signs and symptoms of HL include swelling of the lymph nodes (which is usually painless), fever, sweating at night, unexplained weight loss, itching, and 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.

# What tests are done for Hodgkin lymphoma?

The most crucial test is an adequate lymph node biopsy from an enlarged lymph node. Sometimes fluid is aspirated from the lymph node which may indicate a lymphoma but a biopsy (where a bit of tissue or whole lymph node is taken out) is preferred to make an accurate diagnosis of lymphomas. This is because there are multiple subtypes of lymphomas which may look similar when only little material is available with the pathologist. In order to ensure that an accurate diagnosis is made, a biopsy is required. In patients with lymphoma, other than history and physical examination, the following tests are usually done:

Tests to know how healthy the blood, kidneys and liver are (to know whether the lymphoma has affected these and also to safely administer chemotherapy)

- Complete blood counts and ESR
- Metabolic panel including kidney and liver function tests, lactate dehydrogenase to check for viral infections
  - Virology screen: HIV, HbsAg and anti-HCV

Staging (this is to know how far the lymphoma has spread)

PET/CT is the standard test for this purpose in Hodgkin' lymphomas. If not available,
 CECT scans with bone marrow tests may be needed.

- Bone marrow examination aspiration, biopsy to look for involvement with lymphoma. If a PET-CT scan has been done, then this is adequate and a BM biopsy is not required.
- o Tests for heart function like ECG and echocardiography before starting chemotherapy

#### How is the diagnosis of Hodgkin lymphoma confirmed?

This is the most important initial step in the process of diagnosis - A biopsy from the involved lymph node is examined under a microscope by a pathologist who will interpret the histological picture and give a diagnosis.

# What are subtypes of Hodgkin lymphoma?

Based on the histopathology, the pathologist can classify the Hodgkin lymphoma into different subtypes, however with the exception of Nodular Lymphocyte Predominant Hodgkin lymphoma (which is more similar to Non-Hodgkin lymphoma), the treatment will be the same.

The subtypes of HL are as follows:

- Nodular sclerosis Hodgkin lymphoma
- Mixed cellularity Hodgkin lymphoma
- Lymphocyte-rich Hodgkin lymphoma
- Lymphocyte-depleted Hodgkin lymphoma: This is a rare form of Hodgkin disease. It's seen mainly in older people and those with HIV infection. It's more aggressive than other types of HL and likely to be advanced when first found.

## What are the treatment options for Hodgkin lymphoma?

Chemotherapy (chemo) is the use of drugs to kill cancer cells. Chemo is usually injected into a vein under the skin or taken in tablet form. Chemo is the main treatment for most people with Hodgkin lymphoma. Sometimes chemo is followed by radiation therapy.

There are different treatment protocols used for the treatment of HL, and these treatment protocols may vary slightly from centre to centre, but the most common of these is a regimen called ABVD, composed of 4 chemo drugs - Adriamycin® (doxorubicin), Bleomycin, Vinblastine and Dacarbazine (DTIC)

#### 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 the 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 poor 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.

- Doxorubicin can damage the heart, so your doctor may order tests to check your heart function before and during treatment with this drug.
- Bleomycin can damage the lungs, so some doctors order tests of lung function (called pulmonary function tests) before starting patients on this drug.
- 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 for HL today do not cause infertility, however it is good to clarify this with your doctor before the treatment starts.

Before starting chemo, ask your doctor to explain possible side effects and your chances of having them.

Do all patients with Hodgkin lymphoma receive the same treatment?

Treatment for Hodgkin lymphoma may vary from person-to-person based on the patient's age, other illnesses, general fitness and stage of the disease.

After someone is diagnosed with 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 HL that affects an organ outside of the lymph system, the letter E is added to the stage (for example, stage IE or IIE).

Bulky disease is a term used to describe tumours in the chest that are at least 10 centimeters 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, and more intensive treatment is often recommended. If no B symptoms are present, the letter A is added to the stage.

## 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 stage), and whether radiation therapy is required after completion of chemotherapy (based on bulky disease).

## • 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 2-3 cycles of ABVD 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 stage of disease.

Other factors which impact outcome are the patient's age, gender, general fitness, hemoglobin, serum LDH and WBC/lymphocyte count.

• 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 if 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 4 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 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. Beyond 2 years, patients are usually reviewed once in 6 months for 5 years.

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. Ongoing clinical trials on Hodgkin lymphoma in India can be found at: http://ctri.nic.in/Clinicaltrials/login.php

