

Lymphoma

Summary

Lymphoma is a cancer that affects a part of the immune system called the lymphatic system. Like any cancer, the earlier lymphoma is diagnosed, the easier it is to treat. In general, HIV treatment (Antiretroviral therapy; ART) significantly reduces the chance of people with HIV developing lymphoma. ART also strengthens the immune system and this can make the cancer easier to treat.

About the lymphatic system

The lymphatic system is an extensive network of vessels that branches out into all parts of the body. The lymphatic system helps fight off infections and diseases. These vessels carry lymph, a clear fluid that contains cells of the immune system. Throughout the lymphatic system, small clusters of tissue, or lymph nodes, trap and filter germs. Larger groups of lymph nodes are found in the neck, armpits and groin. (These are the “swollen glands” you or your doctor may notice when you are ill.)

In addition to lymph nodes, other types of lymphatic tissue that are throughout your body include the tonsils, spleen, bone marrow and thymus, as well as patches of lymphatic tissue around your intestines. Because the immune system is so extensive, lymphoma can develop in, and spread to, almost any part of the body, including the spinal cord and brain.

What is lymphoma?

Lymphoma is an umbrella term used to describe different cancers that affect the lymphatic system. There are two main types of lymphoma:

- Hodgkin’s lymphoma
- non-Hodgkin’s lymphoma

Lymphoma can be further divided into several subtypes based on the appearance of tumours when viewed under a microscope. These subtypes can include the following:

- diffuse large B-cell lymphoma (DLBCL)
- plasmablastic lymphoma
- primary effusion lymphoma

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- primary CNS lymphoma (this affects the brain and/or spinal cord)
- Burkitt lymphoma

Who is at risk for lymphoma?

Large studies in the present era have found that HIV-positive people are at increased risk for these cancers. Researchers in North America, working with health-related information collected from nearly 90,000 HIV-positive and 200,000 HIV-negative people have estimated that by the age of 75 years about 5% of HIV-positive people will likely develop non-Hodgkin's lymphoma and about 1% will likely develop Hodgkin's lymphoma. The risk for these cancers is many times greater among HIV-positive people compared to people who are HIV negative.

It is very important to take ART exactly as prescribed, and achieve and maintain an undetectable viral load, as this helps to strengthen the immune system. Although ART can make the amount of HIV in the blood undetectable and lengthen a person's survival, ART does not always penetrate well into the lymphatic system. As a result, HIV can still infect cells of the immune system within lymph nodes and lymphatic tissues. These cells produce HIV-related proteins that can stimulate abnormal development and growth of cells of the immune system. Over time, one or more of these cells can become over-stimulated, become pre-cancerous and in very rare cases, turn into tumours. The cells that can turn into lymphoma tumours are mostly B-cells though, uncommonly, T-cells can also sometimes form lymphoma.

A relatively large study from Germany has investigated CD4+ and CD8+ cell counts a year prior to the diagnosis of lymphoma among HIV-positive people. Doctors found that in people with an undetectable viral load who were taking ART exactly as directed, CD4+ cell counts decreased by an average of 168 cells, 12 months before lymphoma was diagnosed. CD8+ cell counts decreased by about 352 cells 12 months before lymphoma was diagnosed. These decreasing cell counts may be a warning signal that lymphoma (or another cancer) is developing. The figures we have listed were average changes in cell counts. In some

patients the decreases in cell counts were relatively small. Cell counts may also decrease for other reasons and by itself a cell count decrease does not mean that you have lymphoma or another form of cancer.

Common members of the herpes virus family such as EBV (Epstein-Barr virus) have been linked to an increased risk for lymphoma.

Symptoms

The most common symptom of lymphoma is swelling of the lymph nodes in the neck, armpits or groin. This swelling is usually painless. If you notice persistently swollen lymph glands, tell your doctor.

Other symptoms that often accompany swollen lymph nodes include:

- fever
- night sweats
- unintentional weight loss
- unexpected fatigue

Both swollen lymph nodes and the other symptoms mentioned above are common to many illnesses that can affect HIV-positive people. In other words, the presence of swollen lymph nodes with or without these symptoms does not always mean that you have cancer. However, it does mean that you need to see your doctor to have your health assessed.

If lymphoma develops in other parts of the body, it can cause symptoms related to those parts of the body. For example:

- Lymphoma in the gastrointestinal tract may cause abdominal pain or lead to an enlarged liver.
- Lymphoma in the mouth may cause pain and swelling in the mouth.
- Lymphoma in the brain can cause a headache, seizures or difficulty concentrating.

Diagnosis

Lymphoma is diagnosed using a procedure called a biopsy. To do a biopsy, a doctor removes a small piece of tissue from the area of concern. The biopsied tissue is later examined under a microscope to determine if lymphoma is present, what types of cells are involved, and how quickly the cancer cells are growing.

If a biopsy shows lymphoma, your doctor will likely recommend additional tests—such as an X-ray, or more sophisticated imaging techniques such as CT, MRI or PET scans.

These scans generally provide more information than an X-ray and help your doctor find out the size of the tumour(s), whether the cancer has spread and how far it may have spread. This process, called staging, will help determine the most suitable treatment.

In some cases, an operation, called a laparotomy, may be done to allow your doctor to view internal organs and do more biopsies. A bone marrow biopsy and spinal tap may also be required to judge the extent of the lymphoma.

Treatment

ART can make non-Hodgkin's lymphoma easier to treat. Since the 1990s, studies have found that HIV-positive people who take ART and who are later diagnosed with non-Hodgkin's lymphoma have been living longer than people who do not take ART. Your cancer doctor will develop a lymphoma treatment plan for you. The cancer treatment your doctor recommends will depend on the type of lymphoma you have, how far it has spread, how quickly it is growing, and your overall health—especially the health of your immune system. Your doctor will likely recommend one of the following approaches:

A wait-and-see approach

If the lymphoma is small and growing slowly and has been diagnosed at a very early stage, your doctor may suggest a wait-and-see approach. This may seem surprising but bear in mind that treatment may not be initially necessary in some

very early stages of cancer. Your doctor will continue to monitor your cancer closely and only advise therapy if and when the lymphoma starts to grow.

If your cancer is spreading more quickly, your doctor may recommend anti-cancer drugs (chemotherapy) or radiation therapy. When a tumour is developing and growing rapidly it is usually more susceptible to chemotherapy and radiation.

Chemotherapy

Non-Hodgkin's lymphoma is usually treated with drugs (called chemotherapy or chemo) that kill cancer cells. The drugs may be taken as pills or injected into a vein (intravenous), into a muscle (intramuscular) or into the fluid that surrounds the spinal cord and brain. Side effects from chemotherapy are temporary and can include nausea, vomiting, fatigue, diarrhea, sores in the mouth, and hair loss. Your doctor may prescribe additional drugs to reduce the side effects. Your cancer nurse and pharmacist can help you find ways to cope with some of these temporary side effects.

ART has the potential to interact with chemotherapy, raising or lowering levels of chemotherapy drugs in your body. This can weaken its anti-cancer effect or cause you to experience enhanced side effects. Usually, a pharmacist at your cancer treatment centre will review your ART (and all the medicines and any supplements that you are taking) to be sure that it does not interact with chemotherapy. Doctors who treat HIV-positive people who have cancer increasingly tend to ensure that their ART contains an integrase inhibitor. As a group, integrase inhibitors tend to have very few interactions with anti-cancer medicines.

Radiation therapy

Radiation therapy may be used instead of, or in addition to, chemotherapy. This treatment uses radiation to help shrink tumours and destroy cancer cells.

Radiation therapy uses a machine outside the body to direct high-energy X-rays at a specific area of the body. The number of radiation treatments required varies from person to person, depending

on the person's overall health and immune status, the location of the lymphoma, and how well the treatments are tolerated.

In a minority of cases, after it has been treated and resolved, lymphoma may recur. Clinical trials have found that stem cell transplants can help HIV-positive people recover from lymphoma recurrence.

Unfortunately, both chemotherapy and radiation treatment temporarily weaken the immune system, and in some cases can put a person at risk of developing serious, sometimes life-threatening, infections called opportunistic infections. Your doctor may give you antibiotics and/or other drugs to reduce your risk of developing these infections.

Outlook

Treatment can usually cause tumours to shrink and even disappear. As a result, the signs and symptoms of the cancer can also disappear. Once high-resolution scans (CT, MRI or PET) cannot find any more tumours and your symptoms have resolved, ask your doctor if your cancer is in remission. People who have survived for five years in remission are generally considered to be cured. As ART has dramatically improved the overall health and survival of HIV-positive people, survival rates after lymphoma has gone into remission are very good.

Note that, in a minority of cases, the lymphoma can return. If this happens, your doctor(s) can develop a new treatment plan and discuss options. Progress is being made in the field of cancer treatment and options for managing recurrence may be different from your initial treatment of cancer. There are new combinations of anti-cancer therapies in clinical trials.

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