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Non-Hodgkin's lymphoma

The various types of non-Hodgkin's lymphoma are divided into high-grade (fast-growing) and low-grade (slow-growing).

What is non-Hodgkin's lymphoma?

Non-Hodgkin's lymphoma (NHL) is a type of cancer which develops in the lymphatic system. See also the leaflet on The Immune System for more information about the lymphatic system.

Cancers of all three are usually termed haematological cancers (or cancers of the blood) and are managed by blood and cancer specialists - haematologists and oncologists. Many people with non-Hodgkin's lymphoma are cured. Around 4 out of 5 cases of lymphoma are non-Hodgkin's lymphoma. The other type of lymphoma is called Hodgkin's lymphoma.

What causes a non-Hodgkin's lymphoma?

The cause is not known. If your immune system does not work well (for example, if you have AIDS) your risk of developing a non-Hodgkin's lymphoma is increased. However, this only accounts for a small number of cases.

Other risk factors which have been identified include:

- Hepatitis C.
- Epstein-Barr virus the glandular fever virus.
- Exposure to factors in the environment such as pesticides, dusts, solvents.

Is non-Hodgkin's lymphoma hereditary?

It is not an inherited condition and does not run in families.

How does non-Hodgkin's lymphoma develop?

The cancer seems to start from one abnormal cell. In the case of non-Hodgkin's lymphoma, the cancer develops from a type of lymphocyte cell which becomes abnormal. The exact reason why the cell becomes cancerous is unclear. It is thought that something damages or alters certain genes in the cell. This makes the cell abnormal. If the abnormal cell survives, it may multiply and produce many abnormal cells. See the separate leaflet called Cancer for more general information about cancer.

The cancerous lymphocytes tend to collect in lymph glands (lymph nodes). The lymph nodes become bigger and form cancerous tumours. Some abnormal cells may travel to other parts of the lymphatic system such as the spleen. So you may develop lots of large cancerous lymph nodes and an enlarged spleen.

Cancerous lymphocytes can also form lymphoma tumours in places in the body outside of the lymphatic system. This is because lymphocytes can also travel in the bloodstream. Differing types of non-Hodgkin's lymphoma can cause tumours to develop in the lining of the stomach or, rarely, in the brain.

How common is non-Hodgkin's lymphoma?

Anyone can be affected. Most cases occur in people over the age of 50. 13,600 people in the UK developed a non-Hodgkin's lymphoma in 2015. It is the sixth most common type of cancer in the UK. Men are more commonly affected than women.

Non-Hodgkin's lymphoma symptoms

Swollen lymph glands (lymph nodes)

The most common early symptom of a non-Hodgkin's lymphoma is to develop one or more swollen lymph nodes in one area of the body - most commonly the side of the neck, an armpit or the groin. The swollen lymph nodes tend to be painless and gradually become bigger. They can sometimes be painful though.

If the affected lymph nodes are in the chest or tummy (abdomen), you may not be aware of them in the early stages of the disease.

The most common cause of swollen lymph nodes is infection. For example, it is very common to develop swollen nodes in the neck during tonsillitis. Lymphoma is an uncommon cause of swollen lymph nodes. However, a lymphoma may be suspected if lymph nodes remain swollen, or if there is no infection to cause the swelling.

Other symptoms

Other general symptoms may develop - for example:

- Sweats (especially at night).
- Episodes of high temperature (fevers).
- Weight loss.
- Tiredness.
- Being off food.
- Anaemia.
- Itch all over the body.

Various other symptoms may develop if the lymphoma occurs outside of the lymphatic system. For example, stomach pain if the lymphoma develops in the stomach.

As a non-Hodgkin's lymphoma develops you may feel generally unwell. If the lymphoma tumours become large and press on nearby parts of the body, various other symptoms can develop. For example, you may develop a cough or breathing problems if the tumour is in the chest.

How do you diagnose non-Hodgkin's lymphoma?

To confirm the diagnosis of non-Hodgkin's lymphoma

If your doctor suspects that you may have a lymphoma you will be referred to a specialist. A specialist will normally arrange a biopsy of one of the swollen lymph glands (lymph nodes).

A lymph node biopsy is a procedure in which a small sample of tissue is removed from a part of the body. Sometimes an entire lymph node is removed. The sample is then viewed under a microscope to look for abnormal cells. The sample is also tested in other ways.

Dr Krishna Vakharia, 16th October 2023

The National Institute for Health and Care Excellence (NICE) has recommended that an adult person should receive a diagnosis or ruling out of cancer within 28 days of being referred urgently by their GP for suspected cancer.

Grade of the lymphoma

The microscope allows abnormal cells to be seen. When being diagnosed with non-Hodgkin's lymphoma, looking at certain features of the cells and doing various other tests on the cells means the exact type of lymphoma can be diagnosed.

Assessing the extent and spread (staging)

If the biopsy confirms that you have a non-Hodgkin's lymphoma then further tests are usually advised. For example, you may have a computerised tomography (CT) scan or a magnetic resonance imaging (MRI) scan, blood tests, a bone marrow biopsy or other tests. This assessment is called staging.

Non-Hodgkin's lymphoma types

Examples of types of non-Hodgkin's lymphoma include:

- Diffuse large B-cell lymphoma.
- Lymphoblastic lymphoma.
- Follicular lymphoma.
- Anaplastic large-cell lymphoma.
- Lymphoplasmacytic lymphoma.
- Mantle cell lymphoma.

However, there are other types. Although there are many types of non-Hodgkin's lymphoma, they are generally divided (graded) into two categories - high-grade and low-grade.

- **High-grade (fast-growing)**. The cancerous cells tend to grow and multiply quite quickly and are more aggressive.
- Low-grade (slow-growing). The cancerous cells tend to grow and multiply quite slowly and are not so aggressive.

Non-Hodgkin's lymphoma stages

The aim of staging is to find out how much the lymphoma has grown locally and whether it has spread to other lymph nodes or to other parts of the body. The staging system that is commonly used for non-Hodgkin's lymphomas is:

- Stage 1 the lymphoma is confined to one group of lymph nodes only.
- Stage 2 the lymphoma affects two or more groups of lymph nodes. However, they are all on the same side of the diaphragm. (The diaphragm is the large muscle that separates the chest from the tummy (abdomen) and helps us to breathe. So, for stage 2, all the affected nodes will either be above or below the diaphragm.)
- **Stage 3** the lymphoma affects nodes on both sides of the diaphragm.
- Stage 4 the lymphoma affects parts of the body outside of the lymphatic system.

Each stage is also divided into A or B. A means that you do not have symptoms of night sweats, episodes of high temperature (fevers) or weight loss. B means that you do have one or more of these symptoms. So, for example, if you have stage 2B, it means that you have two or more groups of lymph nodes affected. However, both are either above or below the diaphragm and you also have one or more of night sweats, fevers or weight loss.

By finding out the type, grade and stage of the lymphoma it helps doctors to advise on the best treatment options. It also gives a reasonable indication of outlook (prognosis). See the separate leaflet called Stages of Cancer for more details.

Non-Hodgkin's lymphoma treatment

The treatment advised for each case depends on various factors such as the exact type and stage of the lymphoma. In particular, whether it is high-grade or low-grade, your age, your general health, the size of the affected lymph glands (lymph nodes) and which parts of the body are affected.

Treatment may aim to cure the lymphoma. Some non-Hodgkin's lymphomas can be cured. In particular, most high-grade non-Hodgkin's lymphomas can be cured with treatment. Doctors tend to use the word remission rather than the word cured. Remission means there is no evidence of lymphoma following treatment. If you are in remission, you may be cured. However, in some cases, a lymphoma returns months or years later. This is why doctors are sometimes reluctant to use the word cured.

Treatment may aim to control the lymphoma. If a cure is not realistic, it is often possible to limit the growth or spread of the lymphoma with treatment. This usually means that it progresses less rapidly. This may keep you free of symptoms for some time. Many low-grade non-Hodgkin's lymphomas cannot be cured but can be controlled, often for quite some time.

Treatment may aim to ease symptoms. If a cure is not possible, treatments may be used to reduce the size of lymphoma tumours. This may ease symptoms such as pain. If a non-Hodgkin's lymphoma is advanced then you may require treatments such as painkillers or other treatments to help keep you free of pain or other symptoms.

Treatments which may be considered include the following:

Chemotherapy

Chemotherapy is a treatment which uses anti-cancer medications to kill cancer cells, or to stop them from multiplying. High-grade non-Hodgkin's lymphomas are usually treated with chemotherapy medicines given straight into the vein (intravenous chemotherapy).

A combination of medicines is usually used. The most common combination used is with the medicines: cyclophosphamide, doxorubicin, vincristine and prednisolone. (This combination is often called CHOP.)

Another medicine called rituximab is also often used for treatment.

For low-grade non-Hodgkin's lymphomas, when active treatment is advised then intravenous chemotherapy or chemotherapy tablets are the most commonly used treatments.

Dr Krishna Vakharia, 23rd March 2023

NICE has recommended a combination of medications for untreated diffuse large B-cell lymphoma that has been shown to be effective under certain criteria. Polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin and prednisolone (R-CHP) can help increase the time before someone's cancer gets worse under certain conditions.

Monoclonal antibodies

This treatment is sometimes used in addition to chemotherapy. (For example, a product called rituximab is the commonly used monoclonal antibody.) Monoclonal antibodies are small proteins and are different to normal chemotherapy. They work by attaching to the abnormal lymphocytes, which helps to destroy them without harming other cells.

Radiotherapy

Radiotherapy is a treatment which uses high-energy beams of radiation which are focused on cancerous tissue. This kills cancer cells, or stops cancer cells from multiplying. It tends to be mainly used if you just have one or two affected lymph nodes. See the separate leaflet called Radiotherapy for more details.

Stem cell transplant

A stem cell transplant (sometimes called a bone marrow transplant) is sometimes done. Stem cells are the immature cells that develop into mature blood cells (including lymphocytes) in the bone marrow.

First high-dose chemotherapy (and sometimes radiotherapy) is given to kill all the abnormal lymphocytes. However, this also kills the stem cells that make normal blood cells. So, after the chemotherapy, you are given a transplant of stem cells which then make normal blood cells. The transplant will usually come from someone else, who has healthy cells. See the separate leaflet called Stem Cell Transplant.

Surgery

Surgery is not used very often. Occasionally, an operation may be done to remove an organ (such as the spleen) or part of an organ that is badly damaged by a lymphoma. Sometimes a large mass of tumour may be removed to de-bulk the tumour prior to chemotherapy.

Watch and wait

No treatment may be advised initially for low-grade non-Hodgkin's lymphomas. This approach is called watch and wait. This approach is mainly used if you feel generally well and have no symptoms from the lymphoma (apart from painless swollen lymph nodes).

Low-grade non-Hodgkin's lymphomas can grow very slowly and may not need any treatment for quite some time - often over a year. Chemotherapy or other treatments may be delayed until the disease causes symptoms.

Your specialist will want to review you regularly to check on the size of the lymph nodes and how fast they are growing and to check you over. They will advise on when treatment should be started.

Vaccinations

If you have non-Hodgkin's lymphoma it's important to keep your vaccinations up to date, particularly those that protect you from flu and pneumonia.

Some people may also be offered meningococcal group C conjugate vaccine and Haemophilus influenzae.

Non-Hodgkin's lymphoma prognosis

The outlook (prognosis) depends on various factors which include the exact type, grade and stage of the lymphoma. Very generally for people with non-Hodgkin's lymphoma in England:

- About 80 out of every 100 people survive their cancer for one year or more after they are diagnosed.
- About 65 out of every 100 people survive their cancer for five years or more after diagnosis.
- About 55 out of every 100 people survive their cancer for 10 years or more after they are diagnosed.

High-grade non-Hodgkin's lymphoma

Many people with a high-grade non-Hodgkin's lymphoma will be cured. Therefore, the usual aim of treatment for high-grade non-Hodgkin's lymphoma is to cure it. A cure is most likely in cases which are at an early stage. However, there is still a good chance of a cure even with those in more advanced stages. Although a high-grade non-Hodgkin's lymphoma is fast-growing and aggressive, the cells tend to be more easily killed with chemotherapy than low-grade non-Hodgkin's lymphomas.

Slow-growing low-grade non-Hodgkin's lymphoma

With slow-growing low-grade non-Hodgkin's lymphomas, chemotherapy is less likely to be curative than with high-grade non-Hodgkin's lymphomas. However, treatment may control the disease and keep you free of symptoms for months or years. Also, because they are slow-growing, often low-grade non-Hodgkin's lymphomas appear slow to cause any pain (indolent) and not really to progress very much for quite some time.

The treatment of cancers such as non-Hodgkin's lymphoma is a developing area of medicine. New treatments continue to be developed and the information on outlook above is very general. The specialist who knows your case can give more accurate information about your particular outlook, and how well your type and stage of non-Hodgkin's lymphoma are likely to respond to treatment.

Further reading

- Bone Marrow Transplantation and Peripheral Blood Stem Cell Transplantation;
 National Cancer Institute (US)
- Haematological cancers: improving outcomes; NICE Guidance (May 2016)
- Non-Hodgkin's lymphoma: diagnosis and management; NICE Guideline (July 2016)

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- Non-Hodgkin lymphoma; Cancer Research UK.
- Polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma; NICE Technology appraisal guidance, March 2023

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