About Chronic Lymphocytic Leukemia

Overview and Types

If you've been diagnosed with chronic lymphocytic leukemia or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- What Is Chronic Lymphocytic Leukemia?

Research and Statistics

See the latest estimates for new cases of chronic lymphocytic leukemia and deaths in the US and what research is currently being done.

- Key Statistics for Chronic Lymphocytic Leukemia
- What's New in Chronic Lymphocytic Leukemia Research and Treatment?

What Is Chronic Lymphocytic Leukemia?

Cancer starts when cells start to grow out of control. Cells in nearly any part of the body can become cancer and can spread to other parts of the body. To learn more about how cancers start and spread, see What Is Cancer?[1]

Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults. It's a type

of cancer that starts in cells that become certain white blood cells (called **lymphocytes**) in the bone marrow. The cancer (leukemia) cells start in the bone marrow but then go into the blood.

In CLL, the leukemia cells often build up slowly. Many people don't have any symptoms for at least a few years. But over time, the cells grow and spread to other parts of the body, including the lymph nodes, liver, and spleen.

What is leukemia?

Leukemia is cancer that starts in the blood-forming cells of the bone marrow. When one of these cells changes and becomes a leukemia cell, it no longer matures the way it should and grows out of control. Often, it divides to make new cells faster than normal. Leukemia cells also don't die when they should. This allows them to build up in the bone marrow, crowding out normal cells. At some point, leukemia cells leave the bone marrow and spill into the bloodstream. This increases the number of white blood cells in the blood. Once in the blood, leukemia cells can spread to other organs, where they can prevent other cells in the body from functioning normally.

Leukemia is different from other types of cancer that start in organs like the lungs, colon, or breast and then spread to the bone marrow. Cancers that start elsewhere and then spread to the bone marrow are not leukemia.

Knowing the exact type of leukemia[2] helps doctors better predict each patient's outlook and select the best treatment.

What is a chronic leukemia?

In chronic leukemia, the cells can mature partly (and more are like normal white blood cells). but not completely. These cells may look fairly normal, but they're not. They generally don't fight infection as well as normal white blood cells do. The leukemia cells survive longer than normal cells, and build up, crowding out normal cells in the bone marrow. It can take a long time before chronic leukemias cause problems, and most people can live with them for many years. But chronic leukemias tend to be harder to cure than acute leukemias.

What is a lymphocytic leukemia?

Leukemia is **myeloid** or **lymphocytic** depending on which bone marrow cells the cancer starts in.

Lymphocytic leukemias (also known as lymphoid or lymphoblastic leukemia) start in the cells that become lymphocytes. Lymphomas are also cancers that start in those cells. The main difference between lymphocytic leukemias and lymphomas is that in leukemia, the cancer cells are mainly in the bone marrow and blood, while in lymphoma they tend to be in lymph nodes and other tissues.

Different types of CLL

Doctors agree that there seem to be 2 different kinds of CLL:

- One kind of CLL grows very slowly. So it may take a long time before the patient needs treatment.
- The other kind of CLL grows faster and is a more serious disease.

The leukemia cells from these 2 types look alike, but lab tests can tell the difference between them. The tests look for proteins called ZAP-70 and CD38. If the CLL cells have low amounts of these proteins, the leukemia tends to grow more slowly and have better long-term outcomes.

Rare forms of lymphocytic leukemia

The common form of CLL starts in B lymphocytes. But there are some rare types of leukemia that share some features with CLL.

Prolymphocytic leukemia (PLL): In this type of leukemia the cancer cells are a lot like normal cells called prolymphocytes. These are immature forms of B lymphocytes (B-PLL) or T lymphocytes (T-PLL). Both B-PLL and T-PLL tend to grow and spread faster than the usual type of CLL. Most people with it will respond to some form of treatment, but over time they tend to relapse (the cancer comes back). PLL may develop in someone who already has CLL (in which case it tends to be more aggressive), but it can also occur in people who have never had CLL.

Large granular lymphocyte (LGL) leukemia: This is another rare form of chronic leukemia. The cancer cells are large and have features of either T lymphocytes or another type of lymphocyte called natural killer (NK) cells. Most LGL leukemias are slow-growing, but a small number are more aggressive (they grow and spread quickly). Drugs that suppress the immune system may help, but the aggressive types are very hard to treat.

Hairy cell leukemia (HCL): This is rare cancer of the lymphocytes that tends to

progress slowly. The cancer cells are a type of B lymphocyte but they're different from those seen in CLL. There are also important differences in symptoms and treatment. This type of leukemia gets its name from the way the cells look under the microscope -- they have fine projections on their surface that make them look "hairy." Treatment for HCL[3]can work very well.

Hyperlinks

1. www.cancer.org/treatment/understanding-your-diagnosis/what-is-cancer.html
2. www.cancer.org/cancer/leukemia.html
3. www.cancer.org/cancer/chronic-lymphocytic-leukemia/treating/hairy-cell-leukemia.html

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Normal Bone Marrow, Blood, and Lymphoid Tissue

Different types of leukemia start in different types of blood cells. It helps to understand some basics about blood cells.

Bone marrow

Blood cells are made in the bone marrow.

Bone marrow is the soft inner part of some bones, like the skull, shoulder blades, ribs, pelvis, and backbones. Bone marrow is made up of:

- A small number of blood stem cells
- More mature blood-forming cells
- Fat cells
- Supporting tissues that help cells grow

Inside the bone marrow, blood stem cells divide and mature to make new blood cells. During this process, the cells become either lymphocytes (a kind of white blood cell) or other blood-forming cells. These other blood-forming cells mature into red blood cells, white blood cells (other than lymphocytes), or platelets.

Types of blood cells

Red blood cells carry oxygen from the lungs to all other tissues in the body, and take carbon dioxide back to the lungs to be removed. Having too few red blood cells (anemia) can make you feel tired, weak, and short of breath because your body tissues aren't getting enough oxygen.

Platelets are actually cell pieces made by a type of bone marrow cell called the megakaryocyte. Platelets are important in plugging up holes in blood vessels caused by cuts or bruises. Having too few platelets (thrombocytopenia) may cause you to bleed or bruise easily.

White blood cells help the body fight infections. Having too few white blood cells (*neutropenia*) lowers your immune system and can make you more likely to get an infection.

Types of white blood cells

Lymphocytes are mature, infection-fighting cells that develop from lymphoblasts, a type of blood stem cell in the bone marrow. Lymphocytes are the main cells that make up lymphoid tissue, a major part of the immune system. Lymphoid tissue is found in lymph nodes, the thymus gland, the spleen, the tonsils, and adenoids. It's also scattered throughout the digestive and respiratory systems and the bone marrow. The 2 main types of lymphocytes are:

- **B lymphocytes (B cells)** protect the body from invading germs by developing (maturing) into plasma cells, which make proteins called antibodies. The antibodies attach to the germs (bacteria, viruses, and fungi), which helps other white blood cells called granulocytes recognize and destroy them. B lymphocytes are the cells that most often develop into chronic lymphocytic leukemia (CLL) cells.
- **T lymphocytes (T cells)** can recognize cells infected by viruses and directly destroy these cells. They also help regulate the immune system.

Granulocytes are mature, infection-fighting cells that develop from myeloblasts, a type of blood forming cell in the bone marrow. Granulocytes have granules in them that look like spots under the microscope. These granules contain enzymes and other substances that can destroy germs, such as bacteria. The 3 types of granulocytes -- neutrophils, basophils, and eosinophils -- are distinguished under the microscope by the size and color of their granules.

Monocytes develop from blood-forming monoblasts in the bone marrow and are related to granulocytes. After circulating in the bloodstream for about a day, monocytes enter body tissues to become macrophages, which can destroy some germs by surrounding and digesting them. Macrophages also help lymphocytes recognize germs and start making antibodies to fight them.

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Key Statistics for Chronic Lymphocytic Leukemia

The American Cancer Society's estimates for leukemia in the United States for 2023 are:

- About 59,610 new cases of leukemia and about 23,710 deaths from leukemia (all kinds)
- About 18,740 new cases of chronic lymphocytic leukemia (CLL)
- About 4,490 deaths from CLL

CLL accounts for about one-quarter of the new cases of leukemia. The average person's lifetime risk of getting CLL is about 1 in 175 (0.57%). The risk is slightly higher in men than in women.

CLL mainly affects older adults. The average age of people when they are diagnosed is around 70 years. It's rarely seen in people under age 40, and is extremely rare in children.

Visit the American Cancer Society's Cancer Statistics Center[1] for more key statistics.

Hyperlinks

1. cancerstatisticscenter.cancer.org/

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What's New in Chronic Lymphocytic Leukemia Research and Treatment?

Research on chronic lymphocytic leukemia (CLL) is taking place in many university hospitals, medical centers, and other institutions around the world. Each year, scientists find out more about what causes the disease, how to prevent it, and how to better treat it.

Most experts agree that treatment in a clinical trial[1] should be considered for any type or stage of CLL. This way people can get the best treatment available now and may also get the new treatments that are thought to be even better. The new and promising treatments discussed here are only available in clinical trials.

Genetics of chronic lymphocytic leukemia

Scientists are learning a lot about the biology of CLL cells, such as details about the gene changes in the cells. This information is being used to help know whether treatment needs to be started, what type of treatment to use, which treatments are likely to work, and what long-term outlook can be expected. It's also changing the way CLL is treated[2]. New treatments that focus on these gene changes are proving to have a great impact on the treatment options available and how well treatment is tolerated, as well as

how well it works.

Learning about these gene changes is also helping researchers understand why these cells grow too quickly, live too long, and fail to develop into normal blood cells.

As doctors learn more about the many gene changes that can take place in CLL cells, they're looking at the need to break CLL into groups of sub-types. This could lead to better understanding of the many treatment outcomes seen in people with CLL today. It could also help researchers learn more about how CLL develops.

New drugs for chronic lymphocytic leukemia

Dozens of new drugs are being tested for use against CLL. Most of these drugs are targeted[3]at specific parts of cancer cells (like gene changes in CLL cells).

Doctors are looking at the best ways to use these drugs, as well as how they can be used in combinations or along with chemo to get even better results. They're also looking at how these drugs might be used in elderly patients who may have health problems that keep them from getting standard chemo.

Vaccine therapy

The use of vaccines[4] as cancer treatment is a research interest in many different kinds of cancer. These vaccines do not prevent cancer. Instead, they try to get the immune system to mount an attack against cancer cells in the body. Early studies are using vaccines made from the patient's CLL cells and a protein that stimulates the immune system to boost immune system's ability to kill the CLL cells. These studies are in very early phases, and it will take time before we know whether vaccine therapy works.

CAR T-cell therapy

CAR (chimeric antigen receptor) T-cell therapy[5] is another way of getting your immune system to find and kill CLL cells. The patient's T cells, a type of white blood cell, are removed, reprogrammed, and grown (multiplied) in the lab. They're then given back to the patient so they can destroy CLL cells in the patient's body. These treatments have shown promise in some types of cancer, including ALL , but a lot more research is needed as a treatment for CLL.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html
2. www.cancer.org/cancer/chronic-lymphocytic-leukemia/treating.html
3. www.cancer.org/cancer/chronic-lymphocytic-leukemia/treating/targeted-therapy.html
4. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/cancer-vaccines.html
5. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/car-t-cell1.html

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Written by

The American Cancer Society medical and editorial content team (www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

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