



WHAT IS CHRONIC LYMPHOCYtic LEUKEMIA?

Chronic lymphocytic leukemia (CLL) is a slow-growing blood cancer involving the abnormal overgrowth of a type of white blood cell called B-lymphocytes. In CLL, not only are too many abnormal B-lymphocytes produced, but the cancerous cells also live longer than healthy B-lymphocytes do. With time, these cancerous B-lymphocyte cells accumulate in the blood, bone marrow, lymph nodes, and spleen. CLL is also classified as a type of non-Hodgkin's Lymphoma. Although CLL is the most common adult leukemia in North America, it is considered a rare cancer with only 21,000 cases diagnosed annually.

WHAT CAUSES CHRONIC LYMPHOCYtic LEUKEMIA?

The exact cause of CLL is still unknown. As with many types of cancer, advancing age plays a significant role. Researchers are continually working to understand the exact mechanisms that cause the disease. While many suspect the cause might be related to genetic mutations occurring in the DNA, specific genes that cause CLL have not yet been identified. The disease typically occurs spontaneously. CLL is generally not considered hereditary in the sense that it cannot be directly passed down to children. However, some new research suggests that in rare cases there may be a connection to a family history of blood cancers.

WHAT ARE SOME OF THE RISK FACTORS FOR DEVELOPING CHRONIC LYMPHOCYtic LEUKEMIA?

- **Age:** CLL is usually diagnosed in people that are over 60 years old, but it can also occur in much younger adults. CLL is extremely rare in children. About 90% of people diagnosed are older than 50 years old, with the average age of diagnosis being 71 years old.
- **Gender:** Men are almost twice as likely to develop CLL compared to women.
- **Race/Ethnicity:** Individuals who are White are more frequently affected by CLL than other racial or ethnic groups, followed by Blacks, Hispanics, and Native Americans. It is rare in Asians. There is a higher disease association with Europeans of Ashkenazi Jewish descent.
- **Environmental, Occupational, and Chemical Exposure:** People exposed to certain chemicals and toxins seem to be at greater risk for developing CLL. For example, those living on or near a farm have increased risk, but it is not clear if factors such as pesticides are contributing to this risk. There is some suspicion that high levels

of radon exposure in homes may also increase the risk of developing CLL.

- **Veterans:** The U.S. Department of Veterans Affairs lists CLL as a disease associated with exposure to Agent Orange, a chemical used during the Vietnam War. An increased risk has also been associated with exposure to burn pits in the war with Iraq.

HOW IS CHRONIC LYMPHOCYtic LEUKEMIA DIAGNOSED?

Usually, after a routine complete blood count (CBC) shows an elevated absolute lymphocyte count (ALC), a special test called flow cytometry is done (using either a sample of blood or bone marrow) to confirm that the cause of the high ALC is due to CLL. Flow cytometry looks for specific markers (such as CD5) on the surface of the cancerous cells. The diagnosis of CLL requires a finding of more than $5 \times 10^9/L$ genetically identical (clonal) CLL cells through flow cytometry.

WHAT ARE THE SYMPTOMS OF CHRONIC LYMPHOCYtic LEUKEMIA?

It is very common to have no symptoms when the diagnosis of CLL is made. However, symptoms may include:

- Swollen, painless lymph nodes in the neck, armpit, or groin (that can grow to be unsightly and uncomfortable)
- An enlarged spleen, which can cause abdominal pain or a feeling of fullness, and can result in discomfort and a lack of appetite
- Severe fatigue that makes it difficult to work or perform usual daily activities
- Abnormal bruising or bleeding
- Recurrent or frequent infections
- Unexplained weight loss (more than 10% of an individual's total body weight in the previous six months)



- Fevers higher than 100.4°F for at least two weeks without evidence of infection
- Drenching night sweats (soaking the bed sheets) that occur for more than one month without evidence of infection
- An exaggerated response to insect bites (such as mosquitos)
- Rarely, a low red blood cell count or low platelet count that is otherwise unexplained can be a presenting symptom

WHY ARE THOSE WITH CHRONIC LYMPHOCYTIC LEUKEMIA CONSIDERED IMMUNOCOMPROMISED?

CLL is a cancer of the B-lymphocytes, which are an important part of the immune system that fight off infection. In CLL, the cancerous B-lymphocytes have a suppressive effect on other important cells that are also part of the immune system (including the normal B-lymphocytes, T-lymphocytes, and natural killer cells). Because these other parts of the immune system do not work as well, the immune system is weakened, and individuals are at much higher risk of developing severe infections. Although vaccines do provide some protection, those with CLL often have a weakened protective response to vaccines. This results in an even greater risk for poor outcomes associated with respiratory infections (including pneumonia, COVID-19, RSV, and influenza).

IS CHRONIC LYMPHOCYTIC LEUKEMIA TREATABLE?

Most people diagnosed with CLL will not need treatment upon diagnosis, and some will never need treatment. Instead, a period of active observation (also called watch and wait) is the standard of care.

During this time when treatment is not yet needed, there will be close monitoring by a healthcare provider. Research indicates that starting treatment for CLL right away when there are no symptoms present does not result in improved outcomes. Chemoimmunotherapy should almost never be used to treat CLL anymore due to the development of newer and better targeted oral therapies that do a better job of treating the disease. If the disease progresses and meets the criteria to begin treatment, there are many different drug options to choose from.

CAN CHRONIC LYMPHOCYTIC LEUKEMIA BE CURED?

With rare exceptions, CLL is generally considered a chronic incurable cancer. But it can be managed very well with treatment and close monitoring. CLL can go into remission, but it often comes back repeatedly over time. Outcomes are variable from person to person, but it is important to understand that most people diagnosed will die *with* their CLL, not *from* their CLL. Due to the development of new and improved therapies and better strategies to manage the disease, life expectancy is now almost the same as those who do not have CLL.

CLL SOCIETY MISSION

CLL Society is an inclusive, patient-centric, physician-curated nonprofit organization that addresses the unmet needs of the chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL) community through patient education, advocacy, support, and research.