

## What Leukemia Is

Leukemia is a malignant disease of the blood-forming cells. It involves white blood cells that do not mature and that reproduce too rapidly. Eventually, they replace the normal bone marrow, leaving insufficient room for the “good” cells. Such cells include red blood cells, non-malignant white cells, and platelets, all of which are vital for the body to function properly. The leukemic white cells take over the bone marrow and make it impossible for normal cells to grow and mature to function as they should. Leukemic cells look different from healthy cells under the microscope and are unable to do their normal jobs.

The information in this fact sheet comes from Henderson, Lister, and Greaves' *Leukemia*, sixth edition; from the National Cancer Institute's *Report on Leukemia*; and from the tenth edition of Wintrobe's *Clinical Hematology*.

### Understanding blood

Blood is composed of two parts: the plasma, a straw-colored, clear fluid, and the blood cells, also known as corpuscles, carried by the plasma. There are three different kinds of corpuscles in blood: the red cells (erythrocytes), the white cells (leukocytes), and the platelets (thrombocytes). White cells have nuclei, but red cells don't.

Blood cells are formed in the bone marrow (the spongy tissue inside the bones) from precursor cells called stem cells. These stem cells produce several types of blood cells: red blood cells, some varieties of white blood cells (WBC), and platelets. Each stem cell can reproduce (clone) itself and give birth to a number of immature cells (blasts) and committed precursor cells.

Normal bone marrow is composed of many different clones all reproducing themselves and forming new cells that will, in turn, develop into red blood cells, white blood cells, and platelets. The normal marrow also balances the production of these different cell types so they appear in the blood in their proper proportions. Some blood cells develop in the spleen and lymph nodes as well. Blood circulates in the marrow and throughout the body.

### Red blood cells

Erythrocytes, or red blood cells (RBC), make up the largest proportion of blood cells in the body. Constituting approximately 45 percent of blood volume, they contain hemoglobin, an iron-rich protein. The RBC's function is to bind oxygen from the air in the lungs, carry it to cells throughout the body, and exchange it for carbon dioxide, which is then eliminated from the lungs through exhalation.

### White blood cells

Leukocytes (lymphocytes), or white blood cells (WBCs), are fewer in number than red blood cells. White blood cells are part of the body's immune system. White cells constantly scan the body for disease-causing cells, such as bacteria, fungi, or viruses. Different types of white cells have different roles, for instance in fighting particular types of invaders. When there is an invasion of disease-causing cells, extra white cells are produced to battle the infection. Once the white blood cells have done their jobs, the white cell levels return to normal.

Types of white cells include monocytes, lymphocytes, and granulocytes. Each has a specific function.

- Monocytes, the largest white blood cells, literally engulf and destroy invading bacteria and fungi. They clean up the debris left after other white cells have successfully overcome other invaders, and they clean up dying cells as well. When they enter tissues or organs, they are larger in size and are called macrophages: these cells continue to destroy invading cells.
- Lymphocytes, the smallest of the white cells, are essential to the immune system. They fight viral infections and assist in the destruction of parasites, fungi, and bacteria. Each cell has markers on its surface that tell whether it is a natural killer cell (NK), a T cell (thymus-derived cell), or a B cell (bone-marrow-derived cell) and, if a B cell, what antibodies it expresses.
- Antibodies are proteins produced in response to the presence of foreign substances, known as antigens. B cells manufacture antibodies, or immunoglobulins, that attach to foreign substances and

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make it easier for them to be destroyed. T cells, the second group, are the body's main defense against viruses, producing substances that help regulate the immune response. T cells also help the B cells produce antibodies, and they control the activities of various other white blood cells. New lymphocytes grow continually in the bone marrow and the lymph nodes, and many clusters of lymphocytes grow in the spleen.

- Granulocytes, the first defense against many types of infection, take up bacteria and destroy them with potent chemicals. Granulocytes are divided into several categories:
  - Neutrophils are the infection-fighter cells. They carry granules of bacteria-killing enzymes. Bacterial infections are likely to develop when the neutrophil count is very low.
  - Basophils are the rarest and least understood of the white cells. They play an important role in allergic reactions, such as asthma, hives, and drug reactions.
  - Eosinophils defend the body against parasites and also play an important role in allergic reactions, particularly in conditions known as delayed hypersensitivity reactions.

### Platelets

Platelets, or thrombocytes, are the smallest elements in the bloodstream. Platelets are essential to control bleeding. They are the cells that allow your blood to clot, and they stop the bleeding if you are cut. When platelets are low, minute red or purple dots may appear in the skin or mucous membranes. These dots, called petechiae, are caused by the escape of small drops of blood. They are a warning that platelet numbers may be abnormally and seriously low.

### Blasts

A blast is an immature cell derived from a stem cell. In bone marrow, lymphoid organs, or blood, it may be a monocyte (monoblast), lymphocyte (lymphoblast),

myelocyte (myeloblast), erythrocyte (erythroblast), or the platelet parent megakaryocyte (megakaryoblast). Blasts generally constitute less than 5 percent of the cells seen in the bone marrow and should never be seen in the peripheral blood. Normal blast cells divide over and over again, and it is their growth that fills the marrow with the diverse types of immature and developing blood cells that are seen in a normal bone marrow specimen. Normal blasts develop into functioning cells. Leukemia blasts remain in a semi-mature state, multiply excessively, and may be present in large numbers in the bloodstream. These leukemic blasts do not provide defenses against infection.

### Immunoglobulins

Plasma cells (committed B cells) make five different types of immunoglobulins (Ig) or antibodies (Ab). They are IgA, IgD, IgE, IgG, and IgM. More is known about some of these than others.

Little to nothing is known about IgD. IgE seems to be increased in allergic reactions. IgA is found in body secretions (tears, blood, intestinal fluid, saliva, and such). Apparently it is used as protection against antigens coming into the body from the gastrointestinal tract and other mucous membranes. IgM is the first antibody made in response to an antigen attack and is the first antibody to be made by the fetus. While it can be made fast, it is quite primitive and doesn't work all that well.

IgG is the best known of the immunoglobulin classes. It is highly reactive, increasing the activity and specificity of the granulocytes and monocytes and able to move into interstitial fluids and other places with ease. It neutralizes bacterial toxins and initiates complement activity, which in turn further increases the action of granulocytes and monocytes. Complement can also break down certain antigens all by itself.

When you are deficient in IgG, everything about your immune system works a little slower and less effectively. When you have enough IgG, simple everyday things (say, the bacteria that enter the blood stream during normal tooth brushing) are eliminated within minutes, and you don't notice it. But when there is less or less-

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effective IgG, then there is more stress on the system, and it takes longer for the same elimination to occur. Something that you might have shrugged off becomes noticeable, and something that might have been noticeable becomes important.

IV IgG is a collection of plasma taken from donors. It should contain a high amount of effective IgG and, as a consequence of having that, your overall efficiency in handling antigens is increased.

### How leukemia begins

Leukemia is a disease of the white blood cells. Each kind of leukemia involves a particular white blood cell and reflects the level of maturation of the cell. The blood cell involved mutates to become a cancer cell. This process of mutation is believed to be multisteped, occurring at several different times in the cell's maturation process.

In leukemia, white cells in the bone marrow and/or lymphoid tissues begin to reproduce uncontrollably. The rapidly multiplying cells start out in the bone marrow, crowding out the useful cells. After a while they spill over into the blood stream and may be found in vital organs of the body. The most commonly affected organs are lymph nodes, the spleen, liver, and skin. Sometimes the kidneys, brain, or other parts of the nervous system are involved. Ultimately all tissue and organs are susceptible to leukemic infiltration.

### How leukemia is diagnosed

Leukemia diagnoses may come like a bolt out of the blue. Sometimes painful or annoying symptoms appear, so a trip to the doctor becomes a necessity. Often, fatigue or repeated infections finally push you to visit the doctor. The initial diagnosis of leukemia usually is made through evaluation of the blood work. In some leukemias, the diagnosis is an accidental finding when a blood test is ordered for some other reason.

Early signs of the leukemias are similar, so laboratory analysis of blood samples is required to determine which particular leukemia is present. Fortunately, today sophisticated tests are available to help doctors discov-

er cell patterns that indicate specific leukemic types, but sometimes the pathologists still may be unable to type a particular patient's leukemia definitively at first.

Diagnosing leukemia can be difficult and confusing. Often, the doctor will want to do sophisticated blood tests to discover which kind of chromosome or genetic pattern is present. Other tests, like biopsies (samples of tissue from the affected organ) may be needed. A bone marrow aspiration and biopsy (BMB) may be used to verify blood test results. Whatever the reasons, diagnosis will be based on blood test results, the patient's description of symptoms, pathology reports, and the doctor's findings after physical examinations. Family history and reports of occupational and environmental exposures may also be considered. Often, additional information is obtained from x-ray examinations and body scans. Staging and risk levels will be determined at this time and serve as the basis for subsequent treatment decisions.

In some cases a patient is diagnosed with one form of leukemia, and later his doctor discovers that it is really another form entirely. Acute lymphocytic leukemia may be confused with acute myelogenous leukemia, hairy cell leukemia, or non-Hodgkin's lymphoma. The symptoms of lymphomas and leukemias often overlap in their initial presentations. Hairy cell leukemia and mantle cell lymphomas are also often misdiagnosed as chronic lymphocytic leukemia.

### Kinds of adult leukemia

There are many kinds of leukemias. Although there are different leukemia diagnoses, there are many similarities among the types. They all are characterized by excessive production of non-functioning white blood cells, present with similar symptoms, can show genetic and chromosomal abnormalities, and may share similar environmental exposure. These similarities are part of the reason that difficulties are sometimes encountered in making a diagnosis.

Differences among types of leukemia become clear when the blood work is evaluated. Genetic differences are seen in the cells. Chromosome patterns are not the same. Specific cancer cells are identified by their chem-

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ical composition or by unique arrangements of constituents on the cell surfaces and are found in certain patterns.

In order to distinguish among the types, leukemias are subdivided into acute or chronic forms. The determination as to whether a type of leukemia is chronic or acute is based upon the level of maturation of the cells involved. The sections that follow describe the various types of leukemias.

### Acute leukemias

In acute leukemia, the majority of cells are non-functioning blasts. The number of blasts increases rapidly, crowding out the working cells, and the disease gets worse quickly. Treatment is needed at once or the disease is likely to be fatal.

Two major kinds of acute leukemias have been identified, both presenting with identical symptoms. The type of white cell involved determines the diagnosis of which kind of acute leukemia is made. One is lymphocytic leukemia, affecting the lymphocytes, and the other is myelogenous leukemia, involving the granulocytes.

### Acute lymphocytic leukemia (ALL)

This is the most common form of childhood leukemia (75 to 80 percent of all childhood leukemias). Only 20 percent of all adult leukemias are classified as ALL. The number of individuals diagnosed increases significantly after age 50. ALL is characterized by extreme proliferation of lymphocyte cells in the bone marrow and in the lymphatic system. B cells or T cells may be involved.

### Acute myelogenous leukemia (AML)

This disease occurs in both adults and children, but it is far less common in young people. It is also called acute nonlymphocytic leukemia because lymphocytes are not affected. The cells involved in AML are the myeloblasts that proliferate uncontrollably and prevent other needed cells from doing their jobs. AML affects about 1.5 percent of people with leukemia.

### Chronic leukemias

In chronic leukemia, some blasts are present, but often these cells have matured further and can carry out some

of their duties for a longer period of time. These cells increase gradually, so this cell development pattern is called "chronic." Treatment of chronic leukemias may be delayed until physical symptoms and blood work indicate it is needed.

### Chronic myelogenous leukemia (CML)

CML accounts for 15 percent of the adult leukemias. It is one of the chronic leukemias that eventually moves into an acute phase, becoming AML 70 percent of the time and ALL in 30 percent. Some 90 percent of patients with CML show a unique chromosome abnormality known as the Philadelphia chromosome (Ph).

CML is also called chronic myeloid or chronic myelocytic leukemia. It is also known as chronic granulocytic leukemia (CGL). CML is a form of leukemia that affects the cells that make granulocytes and platelets. In its early stages it produces an increase in the numbers of granulocytes and platelets, but these cells still function normally and the patient may have no symptoms. This situation may continue for three or four years (known as chronic phase). Eventually the nature of the disease changes, and CML starts to behave like other leukemias.

### Chronic lymphocytic leukemia (CLL)

This has been the most common adult leukemia, comprising 25 to 30 percent of all adult leukemias. It affects 17 percent of people with leukemia. CLL has been considered a disease of elderly men, with a 2:1 ratio of men to women. Now, increasing numbers of younger people are also being diagnosed with CLL, possibly because routine blood exams are more common and may be facilitating earlier detection. In past years, treatment and research options were not undertaken because it was believed that if you had CLL you would die of something else before you needed treatment. Today there is a great deal of research being done, providing more promising treatment options.

CLL is a disease in which the affected lymphocytes divide slowly but in a poorly regulated manner. They live much longer than usual and over time are unable to perform their proper functions.

CLL is divided into subsets depending upon whether T lymphocytes or B lymphocytes are involved. T-CLL is

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also known as large granular-cell lymphocytosis. It is associated with exposure to HTLV-1 (human T cell lymphotropic retrovirus). This should not be confused with HTLV-3 (also known as HIV-1), the virus responsible for acquired immunodeficiency syndrome (AIDS). In 1977, a new leukemia classification was created called adult T-cell leukemia (ATL).

The subclassification of CLL is as follows:

- B-CLL (more than 95 percent of all CLL cases) has also been described as small lymphocytic lymphoma, and often a pathology report will say CLL/SLL when providing a diagnosis because the same cell is affected in both diseases. In one instance, it behaves like a leukemia with a high white blood count and, in the other, it behaves like a small lymphocytic lymphoma, with tumorous lumps in the lymph nodes.
- CLL/PL: a mixture of CLL cells and prolymphocytes are present in the blood sample. Ten to 55 percent of the cells are prolymphocytes (see below).
- CLL/Mixed: variations in cell sizes are seen with some cells larger than CLL lymphocytes. Some have irregular nuclei that appear to have clefts in them.

### Other chronic lymphocytic leukemias

Many variants of lymphoid neoplasms are known and recognized. They differ from true CLL in the picture they present under the microscope and in the surface markers of specific cells that are proliferating. In hairy cell and splenic lymphoma, the cells have finger-like projections, like a veil, that look hairy under the microscope. Prolymphocytic leukemia, on the other hand, is believed to arise from cells called prolymphocytes.

- Hairy cell leukemia (HCL). Hairy cell leukemia accounts for only 2 percent of adult leukemias. The cells involved in HCL are lymphocytes with filamentous (hairy) projections from the cell surface. It is a rare chronic leukemia. HCL may involve B cells or T cells, but the latter is extremely uncommon. In about one-half of HCL

patients, the marrow is scarred, so it is difficult to do a simple bone marrow aspiration, and a core biopsy may be required for diagnosis.

- Splenic lymphoma with villous lymphocytes (SLVL). This variant of CLL is associated with hairy cell leukemia, above. Both HCL and SLVL always show spleen involvement. Villous lymphocytes have small protrusions—like veils or filaments extending from the cell membrane—that are wider and more billowy than those seen in HCL. SLVL is also often confused with CLL, but the cell markers are more consistent with non-Hodgkin's lymphoma than CLL.
- Prolymphocytic leukemia (PLL). PLL presents as a proliferation of cells called prolymphocytes. To sustain a diagnosis of PLL there must be more than 55 percent prolymphocytes. The spleen is involved but not the lymph nodes. PLL may affect either B cells (B-PLL) or T cells (T-PLL). The latter accounts for 20 percent of all cases of PLL. Sometimes both lymphocytes and prolymphocytes are involved. Then the disease is described as CLL/PLL.
- Adult T cell leukemia (ATL). Established as a distinct clinical entity in 1977 in Kyoto, Japan, this leukemia appears later in life, with frequent rashes, skin involvement, and lymph node and spleen enlargement. Sometimes the peripheral white cell count is elevated with abnormal lymphoid cells, but often there is only anemia, low platelets, and bone marrow infiltration. Patients show human T cell lymphotropic virus type-1 (HTLV-1) as a causative agent. Exposure to the virus appears to occur in childhood. The disease then seems to manifest itself after a long period of dormancy. The largest number of cases has been seen in southwestern Japan. There are four subtypes: acute or prototypic ATL in which patients are often resistant to chemotherapy; lymphoma-type ATL, which presents with prominent lymph node involvement but few ATL cells; chronic ATL (which used to be classified as T cell CLL), in which the WBC is elevated and skin lesions are

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present; and smoldering ATL, in which there may be 5 percent or more abnormal lymphocytes of the T cell type in the peripheral blood for many years and may present with skin or lung lesions.

This fact sheet was adapted from *Adult Leukemia* (forthcoming), by Barbara B. Lackritz © 2000 by Patient-Centered Guides. The content on which this fact sheet is based has been reviewed by several MDs and will receive further technical review prior to publication. For more information, call **(800) 998-9938** or check [www.patientcenters.com](http://www.patientcenters.com) for publication announcement.