Childhood Leukemia

The word leukemia literally means "white blood." Leukemia is the term used to describe cancer of the blood-forming tissues known as bone marrow. This spongy material fills the long bones in the body and produces blood cells. In leukemia, the bone marrow factory creates an overabundance of diseased white cells that cannot perform their normal function of fighting infection. As the bone marrow becomes packed with diseased white cells, production of red cells (which carry oxygen and nutrients to body tissues) and platelets (which help form clots to stop bleeding) slows and stops. This results in a low red blood cell count (anemia) and a low platelet count (thrombocytopenia).

Leukemia is a disease of the blood

Blood is a vital liquid which supplies oxygen, food, hormones, and other necessary chemicals to all of the body's cells. It also removes toxins and other waste products from the cells. Blood helps the lymph system to fight infection and carries the cells necessary for repairing injuries. Blood also contains important clotting factors.

Whole blood is made up of plasma, which is a clear fluid, and many other components, each with a specific task. The three main elements involved in leukemia are red blood cells, platelets, and white blood cells.

Red blood cells (erythrocytes or RBCs) contain hemoglobin, a protein that picks up oxygen in the lungs and transports it throughout the body. RBCs give blood its red color. When leukemia cells in the bone marrow slow down the production of red cells, the child develops anemia. Anemia can cause tiredness, weakness, irritability, pale skin, and headache.

Platelets (thrombocytes) are tiny, disc-shaped cells that help form clots to stop bleeding. Leukemia can dramatically slow down the production of platelets, causing children to bleed excessively from cuts or in some cases from their nose or gums. Children with leukemia can develop large bruises or small red dots (called petechiae) on their skin.

White blood cells (leukocytes or WBCs) destroy foreign substances in the body such as viruses, bacteria, and fungi. WBCs are produced and stored in the bone marrow and are released when needed by the body. If an infection is present, the body produces extra WBCs. There are two main types of WBCs:

- Lymphocytes. There are two types that interact to prevent infection, fight viruses and fungi, and provide immunity to disease:
    - T cells attack infected cells, foreign tissue, and cancer cells.
    - B cells produce antibodies which destroy foreign substances.
- Granulocytes. There are four types that are the first defense against infection:
    - Monocytes are cells that contain enzymes that kill foreign bacteria.
    - Neutrophils are the most numerous WBCs and are important in responding to foreign bacteria.
    - Eosinophils respond to allergic reactions as well as foreign bacteria and parasites.
    - Basophils are the rarest of the white cells and play a special role in allergic reactions.

The different types of leukemia are cancers of a specific white blood cell type. For instance, acute lymphoblastic leukemia affects only lymphocytes.

What is a blast?

"Blast" is a short name for an immature white blood cell such as lymphoblast, myeloblast, or monoblast. Normally, less than 5 percent of the cells contained in healthy bone marrow at any one time are blasts. Normal blasts develop into mature, functioning white blood cells, and are not usually found in the bloodstream. Leukemic blasts remain immature, multiply continuously, provide no defense against infection, and may be present in large numbers in the bloodstream.

How does leukemia begin?

When a population of abnormal blasts appears in the bone marrow, they multiply rapidly and lose their abil-

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ity to grow up into normal white cells. They begin to crowd out the normal cells that usually develop there. After accumulating in the bone marrow, leukemic cells spill over into the blood. Leukemic cells may also cross the blood-brain barrier and invade the central nervous system (brain and spinal cord).

When the leukemic blasts begin to fill the marrow, production of healthy red cells, platelets, and white cells cannot be normally maintained. As the number of normal cells decreases, symptoms appear. Low red cell counts cause fatigue and pale skin. Low platelet counts may result in bruising and bleeding problems. If mature neutrophils and lymphoblasts are crowded out by the blasts, the child will have little or no defense against infections.

Who gets leukemia?

Acute leukemia is the most common childhood cancer. Although generally thought of as strictly a childhood disease, many more adults than children develop leukemia. Each year in the United States, approximately 25,000 adults and 2,500 children are diagnosed with acute leukemia.

Childhood leukemia is most commonly diagnosed at ages two to seven, with the highest incidence at approximately four years of age. In the United States, leukemia is more common in whites than in blacks, and boys have a slightly higher incidence than girls. Children with genetic diseases such as Down syndrome, Bloom's syndrome, or Fanconi's anemia have a higher risk of developing leukemia than the general population. However, most children with these syndromes do not develop leukemia.

Although the exact cause of childhood leukemia is a mystery, certain factors are known to increase the risk of developing the disease.

Genetic factors

It is known that persons with extra chromosomes (genetic material contained in cells) or certain chromosomal abnormalities have a greater chance of developing leukemia. It is uncertain whether this is a cause or merely an association. In cases where one identical twin has leukemia, the other twin has a 25 percent chance of developing the disease within one year, but this risk decreases with an older age at diagnosis and with time. It is not known whether this is caused by an inherited trait or a simultaneous exposure to the same carcinogen. Leukemia is not contagious; it cannot be passed from one person to another.

Environmental factors

Exposure to ionizing radiation and certain toxic chemicals may predispose individuals to leukemia and other problems involving the bone marrow. Many Japanese who were exposed to fallout from the atomic bomb during World War II and some of the people living near the Chernobyl accident in the Ukraine have developed leukemia. Chronic exposure to benzene has been associated with leukemia in adults. However, most children are not exposed to large amounts of radiation or industrial chemicals. The data so far indicates that there is no increased risk of leukemia from exposure to electromagnetic fields. Although scientists are examining associations with many environmental factors, there are no clear environmental causes of childhood leukemia.

Rates of childhood cancer have increased every year for the last three decades. In response to this and other threats to children's health, in 1997 the US formed the Federal Task Force on Protecting Children from Environmental Health Risks and Safety Risks. Information on this task force can be found on the Internet at *http://www.epa.gov/children/six.htm*.

The US Environmental Protection Agency (EPA) has a Children's Health Resources branch that maintains publications on children's health topics, information on hot lines, and links to Internet resources at (888) 372-8255 and on the Internet at *http://www.epa.gov/children*.

For information about the US government's electromagnetic field (EMF) research efforts, including public information materials developed by the EMF RAPID program, refer to the EMF RAPID home page on the Internet: *http://www.niehs.nih.gov/emfrapid/home.htm*.

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Viral factors

Viruses that cause leukemia in cows, cats, chickens, gibbons, and mice have been found. A T-cell virus has been identified which causes a rare type of leukemia-lymphoma in adults; however, no virus has been found which causes the types of leukemia commonly found in children.

Currently, it is thought that a complex interaction among genetic, environmental, immunologic, and possibly viral factors predisposes individuals to leukemia. The most important point for parents to remember is that at present there is no way to predict or prevent leukemia. Nothing that parents did or did not do caused or could have prevented the leukemia.

How is leukemia diagnosed?

A tentative diagnosis is made after a physical examination of the child and microscopic analysis of a blood sample. Physical findings may include pale skin; bruising or unusual bleeding; enlarged liver, spleen, or lymph nodes; ear or other infections (frequently resistant to treatment); weakness; and fever. Parents or children may describe irritability, night sweats, fatigue, bone pain, and loss of appetite. Blood tests may show decreased red cells, decreased platelets, and either abnormally low or high white blood cell counts. There may be blast cells circulating in the blood.

The T-cell type of ALL sometimes involves the thymus gland in the neck. Enlargement of the thymus can pressure the nearby trachea (windpipe), causing coughing or shortness of breath. The superior vena cava (SVC), a large vein that carries blood from the head and arms back to the heart, passes next to the thymus. An enlarged thymus gland may compress the SVC and cause swelling of the head and arms.

Some children with leukemia have the disease in their central nervous system (brain and spinal cord) at diagnosis. Less than 10 percent of children or teens with leukemia have symptoms of CNS disease, including headache, poor work or school performance, weakness, seizures, vomiting, blurred vision, and difficulty in maintaining balance.

Children with AML are sometimes diagnosed after developing a chloroma—a tumor arising from myeloid tissue and containing a pale green pigment. These are most often found under the skin of the skull.

To confirm a diagnosis of leukemia, bone marrow is sampled and tested. The bone marrow is examined microscopically by a pediatric oncologist and/or a pathologist, a physician who specializes in body tissue analysis. More than 25 percent blasts in the marrow confirms the diagnosis of leukemia. A portion of the bone marrow (and chloroma biopsy if done) is sent to a specialized laboratory that analyzes many other features of the leukemic cells to help determine which type of leukemia is present.

How is leukemia best treated?

At diagnosis, parents are often confused about how to find the best doctors and treatment plan for their child. The best care available in the US and Canada is obtained from institutions that are part of the Children's Cancer Group or the Pediatric Oncology Group. These study groups, composed of pediatric oncologists and surgeons, urologists, radiation oncologists, researchers, and nurses, establish the standard of care for patients in the US and Canada, conduct new studies to discover better therapies or fine tune the old ones, and establish follow-up for survivors. They are in the process of merging into one entity called the Children's Oncology Group (COG). If the treatment center you are referred to is a member of one of these groups, you can rest assured that your child will have access to the best thinking on the treatment of pediatric cancers.

Types of leukemia

The two broad classifications of leukemia are acute (rapid progression) and chronic (slow progression). The acute leukemias are characterized by abnormal numbers of immature white cells (blasts). In chronic leukemia, mature white cells predominate. Chronic leukemia accounts for less than 5 percent of all childhood leukemia.

Acute leukemia is the most common type of cancer found in children. The two most common types of acute

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leukemia are acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). AML is also known as acute non-lymphoblastic leukemia (ANLL).

Acute lymphoblastic leukemia (ALL)
Seventy-five percent of all children with leukemia have ALL. It is caused by a rapid proliferation of immature lymphocytes, which would normally have developed into mature T cells or B cells. There are several subgroups of ALL based on whether the cancer cells developed from B cells or T cells, or display characteristics of both. The first sample of bone marrow taken from the child is analyzed to identify cellular characteristics to help plan the best therapy as well predict response to treatment. Each different subgroup has a different response to treatment; some require less chemotherapy, while others require aggressive treatment to achieve a cure.

One child's illness didn't look so bleak to another child's parent:

> *I was walking around the hospital looking shell-shocked the day after my daughter had been admitted to Children's Hospital with leukemia. One of the other mothers came up, introduced herself, and asked what we were in for. I told her leukemia. She told me that her son had just relapsed again from a brain tumor. She looked wistful and said how much she wished that her son had ALL. She said, "You might think that's strange, but I see those kids come, get better, and go home. We are still here."*

Acute myeloid leukemia (AML)
AML (also called acute myelogenous leukemia, acute nonlymphocytic leukemia, or ANLL) is cancer of the bone marrow. The cancer cells are those that would otherwise develop into myeloid cells like granulocytes. Because treatments for AML and ALL are very different, it is crucial that sophisticated laboratory studies are performed on the bone marrow samples to determine whether the child has AML or ALL. Eight thousand cases of AML are diagnosed in the US each year, most often in adults over forty. It is also seen in infants or older teens but can strike children at any age. AML accounts for approximately 15 percent of all cases of childhood leukemia. There are eight different classifications or types of AML (M0 to M7) based on appearance of the diseased cells under the microscope.

Chronic myelogenous leukemia (CML)
CML is rare in children, accounting for less than 5 percent of all childhood leukemias. This disease is most common in adults, but occasionally is diagnosed in older boys and girls. It is characterized by a very large spleen, high white count of mostly neutrophils and other types of granulocytes, and high platelet count. Other symptoms of CML are fatigue, weakness, headaches, irritability, fevers, night sweats, and weight loss. Some patients have no symptoms and the cancer is diagnosed after a routine blood test done for other reasons. There is no severe anemia or tendency to bleed.

In over 90 percent of patients with CML, analysis of the cells of the bone marrow shows a genetic abnormality called the Philadelphia chromosome. This chromosome contains a "translocation" or swap of genetic material involving chromosomes 9 and 22, abbreviated as t(9;22).

Symptoms did not initially suggest that this child had CML:

> *Leah, eleven years old, enjoyed participating in basketball, soccer, and gymnastics. She developed severe hip joint pain, and we brought her back to the doctor three times in an unsuccessful attempt to find out what was wrong. The last time, my husband had to carry her in because she couldn't walk. They did blood work, and her white count was 176,000 and her platelets were one million. A bone marrow test confirmed that she had CML.*

Chronic myelomonocytic leukemia (CMML)
Chronic myelomonocytic leukemia (also called juvenile CML or JCML) usually strikes children under five years of age. The symptoms are similar to those of the acute leukemias: pale skin, bruising, fatigue, headaches, sweating, and recurrent infection. Also usually present

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are enlarged lymph nodes, enlarged spleen and liver, and low platelet count. Unlike CML, CMML does not have a chronic phase. Once diagnosed, progressive deterioration usually occurs.

Because chemotherapy is not generally a successful treatment for juvenile CML, bone marrow or stem cell transplantation is the best hope for cure. However, chemotherapy is sometimes used to get the disease under control while preparing for transplant.

This child's bone marrow transplant was successful:

> *My daughter was diagnosed with JCML is 1993 at the age of 27 months. Although it is a chronic leukemia, it is particularly fast moving and there is no treatment besides BMT. It is also vastly different from the adult CML. My daughter had a mismatched (5/6) related (my husband's sister as donor) BMT four months after she was diagnosed. Today, she is six years post-transplant, is in the second grade, and is the absolute joy of my life.*

This fact sheet was adapted from *Childhood Leukemia: A Guide for Families, Friends, and Caregivers, 2nd Edition*, by Nancy Keene, ©1999 by Patient-Centered Guides. For more information, call **(800) 998-9938** or see *www.patientcenters.com*.