

# MASONIC CANCER CENTER NEWS

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Masonic Cancer Center News is presented to the Masons and Eastern Stars of Minnesota, their families and others concerned with the work and developments at the Masonic Cancer Center at the University of Minnesota. We hope through these pages and future issues to bring the note of aspiration and dedication to you as we sense it in the staff and facilities which depend on us all for continued success.

## *Leukemia in Adults*

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### **Introduction**

Leukemia is a family of cancers affecting blood cells. Like many other cancers, leukemia can often be treated effectively with therapy that preserves a person's quality of life and prolongs survival, sometimes for decades. It is easier to understand leukemia if one understands how normal blood cells are made throughout life. In the bone marrow, immature cells divide and then proliferate into red blood cells, white blood cells, and platelets. Red blood cells enter the blood stream and carry oxygen from the lungs to all the organs and tissues in the body. White blood cells protect us from infection, and platelets help our blood to clot.

### **How Leukemia Makes Us Ill**

When leukemia occurs, the orderly process of blood production is disrupted. The number of immature white blood cells often increases. This can cause swelling of lymph nodes and the spleen, clog critical blood vessels in the heart and brain, and lead to infiltration of the gums, skin or even the lining of the brain with leukemia cells. Unfortunately, the white blood cells may not work well, and infections can occur. Even though white blood cells are primarily affected, leukemia can suppress red blood cell production, leading to anemia. Platelet production is also suppressed, and bleeding can be a serious problem. Substances produced by leukemia cells can provoke clotting in blood vessels (thrombosis) or in the lung (pulmonary embolus), while other substances can cause weight loss, fevers, night sweats, and other general symptoms of illness.

### **What Causes Leukemia?**

Most leukemias occur when genes that control the orderly process of blood cell production are defective or disrupted. Environmental factors such as exposure to high doses of irradiation, to organic solvents such as benzene and even to some

chemotherapeutic agents can predispose individuals to the development of leukemia. There is a predisposition to the development of leukemia in some families. Some congenital disorders such as Down Syndrome are also associated with leukemia. Rarely, infectious agents have been associated with leukemia. In most cases, no obvious cause for the occurrence of leukemia in an individual can be determined.

### **How the Diagnosis is Made**

A physician suspecting leukemia will listen carefully to a patient's complaints to identify symptoms of leukemia, predisposing factors, and the tempo of the illness. A "baseline" evaluation is important to verify the diagnosis of leukemia, identify other secondary effects of the leukemia, guide appropriate therapy and supportive care, and educate the patient and family. The physician will perform an exam looking for enlarged lymph nodes, spleen or other abdominal organs, rash or bruises, gum swelling or bleeding, visual disturbances, and neck stiffness. Laboratory tests will include a complete blood count (CBC) to determine white blood cell number, hemoglobin concentration, and platelet count. The blood will be spread on a glass slide and this "smear" will be examined carefully to look for blood cells with an abnormal appearance. If leukemia is suspected, a bone marrow biopsy and aspirate may be performed. In experienced hands, this test is usually not very painful and provides many clues to abnormal blood cell production. The physician will look at the marrow sample for the characteristic appearance of abnormal cells ("morphology"). Samples will also be analyzed for the presence of chromosome abnormalities ("cytogenetics") by standard techniques or by very sensitive molecular methods. If leukemia involving the brain is suspected, a lumbar puncture may be performed. Skin infiltrates or swollen lymph nodes suspected of harboring leukemia may be biopsied. If spleen, liver or internal lymph node involvement is suspected, CT

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(computerized tomography) scans or other diagnostic imaging techniques may be used to determine the extent of disease involvement. Since leukemia can have indirect but important effects on other systems of the body, routine blood tests reflecting coagulation, renal function, liver function, and electrolyte balance may also be obtained.

## Treatment of Leukemia

When leukemia is diagnosed, the choice of treatments depends on the type of leukemia, physical condition of the patient, and the wishes and expectations of the patient and family. Options range from no treatment through outpatient-based therapy to the use of high-intensity combination chemotherapy requiring extensive hospitalizations and sometimes complicated by significant side effects. Such therapy can be "conventional" or can involve the testing of novel agents used alone or in combination with conventional therapy and intended to improve outcome. A brief discussion concerning the clinical testing of novel therapy is provided below.

## Cancer Clinical Trials

Cancer Centers such as the University of Minnesota provide not only supportive care and conventional therapy for cancer, but test newly developing therapies as well. This testing process is called a "cancer clinical trial", and such trials are performed using very strict guidelines. Investigators first perform "preclinical" testing to determine the properties and potential therapeutic effect of a promising anti-cancer drug. In "Phase 1 trials", the best dose of the new agent is determined. In "Phase 2 trials", the agent is tested at this best dose to determine if it has a beneficial effect on the cancer. In "Phase 3 trials", the new cancer treatment is tested against the best established therapy.

In order to initiate a clinical trial, the investigator writes a protocol describing the methods which will be used to test the promising agent in the clinic. This protocol is reviewed by an "Institutional Review Board" which is primarily concerned with the safety of people who will be enrolled in the clinical trial. Individuals participating in the clinical trial sign "informed consents" which signify that they understand the goals, expectations, and risks associated with the trial. Patients participating in clinical trials are

followed carefully to determine the effectiveness and safety of the therapy, and to identify any side effects or toxicity which might occur.

## Leukemias in Adults

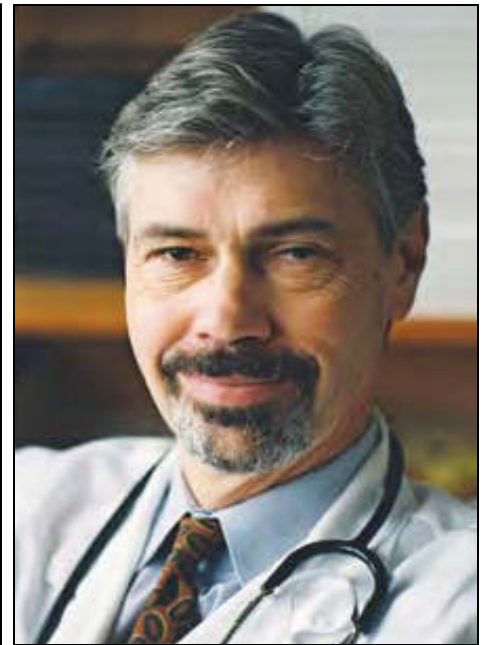
Leukemias can be divided into two major categories including "acute leukemias" and "chronic leukemias." Here we will discuss briefly the features of some of the more common adult leukemias.

### Acute Leukemias

Acute leukemias occur when a "clone" of relatively immature white blood cells grows in a poorly regulated fashion. As discussed above ("How leukemia makes us ill"), patients with acute leukemia experience the relatively sudden onset of symptoms and signs related to infiltration of tissues with an excess of leukemia cells and a decrease in numbers of circulating normal cells. These clinical problems include headache, rash, inflamed gums, enlarged lymph nodes, spleen, liver or testes; abnormal bruising and bleeding, infection, fatigue, weight loss, and fevers. Acute leukemia in adults falls into two categories determined by the type of white blood cell which is affected by the malignant process. In acute myelogenous leukemia (AML) there is an abnormal proliferation of immature "myeloid" cells such as granulocytes, red blood cells, or megakaryocytes (the cells which make platelets). In acute lymphocytic leukemia (ALL) there is an abnormal proliferation of immature lymphocytes.

Acute myelogenous leukemia (AML) can be divided into a number of subtypes based on the appearance of the cells under a microscope. In some cases, treatment is guided by the subtype of AML. In most cases, however, identification of the chromosome abnormality found in the malignant clone of leukemia cells is helpful to determine whether a given leukemia patient falls into "low, intermediate or high risk" categories predicting the likelihood of response to therapy. Patients usually receive one or more courses of intensive intravenous chemotherapy given with a combination of agents (e.g. daunomycin and cytosine arabinoside) in an attempt to "induce" a complete remission.

This "induction" therapy is usually administered in the hospital and is designed to produce a "remission." As a generalization, nausea and vomiting can be controlled by administration of drugs designed to minimize these side effects. Chemotherapy is associated with a drop in blood counts requiring close medical



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monitoring, use of antibiotics to prevent infection (prophylactic antibiotic therapy) or to treat suspected infections (empiric antibiotic therapy), and support with platelet and red blood cell transfusions as well as treatment of a variety of other possible medical complications. Medical complications often resolve as normal blood production occurs.

Remission is "consolidated" with several additional courses of therapy. Persistent or relapse leukemia may be treated with further intensive therapy, with "palliative" therapy designed to control signs and symptoms of leukemia, or with no therapy at all. Chemotherapy may be placed in the spinal cord by lumbar puncture ("intrathecal therapy") to prevent or to treat leukemic involvement of the central nervous system. Radiation may also be used to treat concentrated areas of leukemia in "extramedullary" tissue such as bone or other tissue.

Acute lymphocytic leukemia (ALL) is less common than AML in adults. Again, treatment is guided to some extent by the subtype of cell involved based on identification of receptors on the cell surface ("B cells or T cells"). Identification of the chromosome abnormality underlying the leukemia is important to determine therapy and likelihood of success. Acute lymphocytic leukemia is also treated with

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intensive intravenous therapy; however, combinations of five or more drugs are commonly used for induction therapy. Consolidation therapy is routine, and patients commonly receive extended courses of "maintenance" therapy. Patients are at increased risk of developing central nervous system involvement, and "prophylactic" intrathecal chemotherapy is often part of the induction regimen.

Choosing therapy in the elderly. The chances of developing either AML or ALL increases greatly as adults mature from middle age to elderly.

Unfortunately, the likelihood of success with leukemia therapy falls as patients age. While some elderly patients with acute leukemia may benefit from intensive induction chemotherapy as described above, others may benefit more from alternative approaches such as reduced doses of induction therapy, the use of palliative therapy to control symptoms or signs, or with the use of new agents designed to target the molecular abnormality underlying the leukemia without undue toxicity. In other cases, the choice to proceed without leukemia therapy, but with intensive medical and social support, may be the right one. These choices and their bearing on control of leukemia, life-span, and quality of life should be discussed with the treating physician, patient, and family.

## **Chronic Lymphocytic Leukemia**

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia in the United States and usually affects middle-age or elderly individuals. In this disorder, mature malignant lymphocytes accumulate in the blood, marrow, lymph nodes, and spleen over several years. Symptoms and signs are usually of gradual onset and include fatigue, weight loss, lymph node swelling, recurrent infections, or bleeding. The diagnosis is usually made by examining a blood smear and confirmed by the identification of characteristic receptors on the surface of the abnormal lymphocytes. Identification of chromosome abnormalities and of abnormal cell products is also very useful in determining prognosis. Determination of the "stage" of disease ranging from detection of increased numbers of abnormal lymphocytes in the blood alone (stage 0) to the presence of

low platelets (stage IV) is also important for prognosis and for determining the need for therapy.

Unlike the case with the acute leukemias, no therapy may be required when CLL is diagnosed, and there is little evidence that early treatment of low or intermediate-stage disease prolongs survival. Signs and symptoms prompting

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therapy include increasing lymph node or spleen size, anemia, low platelet count, or recurrent infections. Approaches to therapy include the use of a single drug, combinations of drugs, or drug therapy combined with the administration of antibodies targeting leukemia cells ("chemoimmunotherapy"). This is an exciting era for the development of safe and effective treatments for CLL and it is important to discuss the indications for therapy and the therapy options available through clinical trials.

Although patients with CLL may not require therapy, they do require support-

***“Treatment of adult leukemia has changed radically over the last few decades.”***

ive care and counseling. Patients with CLL are at increased risk for developing other cancers and should receive cancer screening. These individuals may also suffer from anxiety or depression related to a chronic illness and may benefit from a thorough explanation of the natural history of CLL, as well as ongoing psychological counseling.

## **Chronic Myeloid Leukemia**

Chronic myeloid leukemia (CML) occurs because of a specific gene abnormality ("the Philadelphia Chromosome") resulting from the abnormal crossing ("translocation") of two genes. This results in the poorly regulated proliferation of a white blood cell subtype called "granulo-

cytes." Chronic myelogenous leukemia may present as a chronic process with an excess of white blood cells in the blood. At the other extreme, patients may present in "blast crisis" with increased numbers of very immature cells ("blasts") in the blood, anemia, low platelet count, enlarged spleen or other abdominal organs, fever, weight loss and fatigue. When patients present in blast crisis, they may require intensive therapy with hydration, reduction of white blood cell number by reirculation of blood through a machine ("leukapheresis"), and chemotherapy to reduce the risk of clogging cerebral and coronary vessels. When a "chronic phase" has been reestablished, or in the case of patients presenting in chronic

phase, "targeted" therapy is now commonly used to reduce the number of malignant cells. This therapy with the agent "imatinib" (Gleevec) targets an abnormal enzyme produced by the Philadelphia Chromosome, suppresses production of malignant cells, and allows repopulation with normal white blood cells. Imatinib is taken orally and has relatively few side effects. Patients usually experience a rapid return to normal blood counts. In those cases where molecular evidence of the abnormal Philadelphia Chromosome disappears, the likelihood of long-lasting remission with continued imatinib therapy is high. Patients who fail imatinib therapy may respond to a very recently developed "second generation" of agents targeting the Philadelphia Chromosome or may, occasionally, require hematopoietic cell transplantation. Although the curative potential of imatinib and similar agents is not yet known, many patients remain in complete remission with little or no evidence of CML for over

five years on imatinib therapy.

## **Conclusion**

Treatment of adult leukemia has changed radically over the last few decades, and new therapies with increased effectiveness and reduced toxicities are just around the corner. A careful baseline characterization of the leukemia is important to determine prognosis and to plan the timing and type of therapy. Physicians are no longer simply interested in eradicating leukemia, but in sustaining the highest possible quality of life and in providing both physical and psychological support.

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# PERIODICAL

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For further information concerning

make an appointment contact the Masonic Oncology Clinic at 612-625-5411.)

Dr. McGlave has also served for the last eight years as the contact person and coordinator for discussions and negotiations between the University of Minnesota and the Board of Directors of your Masonic Cancer Center Fund. His pleasant demeanor and his commitment to our

common goals have gone far in magnifying your fund's impact on the war against cancer.

***"For further information concerning cancer research visit the University of Minnesota Cancer Center, [www.cancer.umn.edu](http://www.cancer.umn.edu) or the HOT Division, [www.med.umn.edu/hot](http://www.med.umn.edu/hot)."***

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