

Myeloma

LEUKEMIA

LYMPHOMA

MYELOMA

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Introduction

This booklet provides information about myeloma for patients and their families. We hope this information is helpful, and we welcome comments.

This year, about 16,570 persons in the United States will learn that they have myeloma (SEER Cancer Statistics Review, 1975-2003 [Surveillance Epidemiology and End Results data, 2006]). Myeloma may be called by several names, including plasma cell dyscrasia, plasma cell myeloma, myelomatosis and multiple myeloma.

A brief description of normal blood and marrow is provided for background to help readers better understand the myeloma-specific information in the booklet.

This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is distributed as a public service by The Leukemia & Lymphoma Society, with the understanding that The Leukemia & Lymphoma Society is not engaged in rendering medical or other professional services.

Normal Blood and Marrow

Blood is composed of plasma and cells suspended in plasma. The plasma is largely made up of water in which many chemicals are dissolved. These chemicals include:

- Proteins (such as albumin)
- Hormones (such as thyroid hormone)
- Minerals (such as iron)
- Vitamins (such as folate)
- Antibodies, including those we develop from our vaccinations (such as poliovirus antibodies).

The cells suspended in plasma include red cells, platelets and white cells (neutrophils, eosinophils, basophils, monocytes and lymphocytes).

- The red cells make up half the volume of the blood. They are filled with hemoglobin, the protein that picks up oxygen in the lungs and delivers it to the cells all around the body.
- The platelets are small cells (one-tenth the size of red cells) that help stop bleeding at the site of an injury in the body. For example, when a person has a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together and plug up the bleeding site. Later, a firm clot forms. The vessel wall then heals at the site of the clot and returns to its normal state.
- The neutrophils and monocytes are white cells. They are called phagocytes (eating cells) because they can ingest bacteria or fungi and kill them. Unlike the red cells and platelets, the white cells leave the blood and enter the tissues, where they can attack the invading organisms and help combat infection. Eosinophils and basophils are types of white cells that respond to allergens.
- Most lymphocytes, another type of white cell, are found in the lymph nodes, the spleen and the lymphatic channels, but some enter the blood. There are three major types of lymphocytes: T cells, B cells and natural killer cells. These cells are a key part of the immune system.

Marrow is a spongy tissue where blood cell development takes place. It occupies the central cavity of bones. In newborns, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have functioning marrow. The spine (vertebrae), hip and shoulder bones,

ribs, breastbone and skull contain the marrow that makes blood cells in adults. Blood passes through the marrow and picks up formed red and white cells and platelets for circulation.

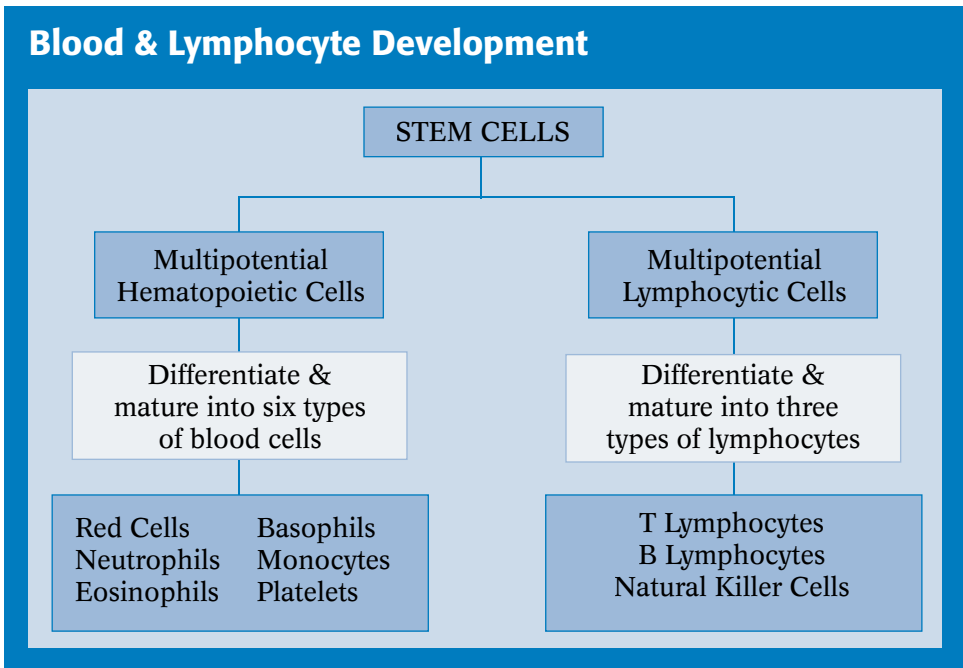


Figure 1. This figure depicts an abbreviated diagram of the process of hematopoiesis. This process involves the development of functional blood and lymphatic cells from stem cells.

The process of blood cell formation is called hematopoiesis. A small group of cells, the stem cells, develop into all the blood cells in the marrow by the process of differentiation (see Figure 1).

When the fully developed and functional cells are formed, they leave the marrow and enter the blood. In healthy individuals, there are enough stem cells to keep producing new blood cells continuously.

Some stem cells enter the blood and circulate. They are present in such small numbers that they cannot be counted or identified by standard blood count tests. Their presence in the blood is important because they can be collected by a special technique. If enough stem cells are harvested from a compatible donor, they can be transplanted into a recipient.

Stem cell circulation, from marrow to blood and back, also occurs in the fetus. After birth, placental and umbilical cord blood can be collected, stored and used as a source of stem cells for transplantation.

In summary, blood cells are made in the marrow. When the cells are formed and functional, they leave the marrow and enter the blood. The red cells and the platelets carry out their respective functions of delivering oxygen and plugging up injured blood vessels throughout the body. The white cells (neutrophils, eosinophils, basophils, monocytes and lymphocytes) enter the tissues (for example, the lungs) to combat infections, such as pneumonia, and perform other immune functions.

Myeloma

The earliest clinical observations of myeloma date back to the mid-19th century. In the late 19th century, the term “myeloma” was used to indicate the disease; this term is derived from “myel,” the Greek word for “marrow,” and “oma,” a Greek suffix denoting a tumor. By the turn of the 20th century, physicians had described the essential features of the disease: its appearance in the marrow as malignant plasma cells; its involvement in multiple sites in marrow; its destruction of bone; and its association with abnormal proteins in the urine and the blood.

Types of Myeloma

Myeloma can be divided into several categories and subtypes based on the distribution of clinically apparent disease and other clinical findings. About 90 percent of patients have disease involving multiple sites at the time of their diagnosis. The term “multiple” is sometimes used in the name of the disease in its most common form. Various other terms are used to describe myeloma in patients who appear to have a different distribution of disease. These include “solitary myeloma” (only one site evident), “localized myeloma” (a few neighboring sites evident) or “extramedullary myeloma” (involvement of tissues other than the marrow, such as skin, muscle or lung). Tumors of plasma cells outside the marrow are referred to as “plasmacytomas.”

Some cases of myeloma progress very slowly, and they may be referred to as “smoldering” or “indolent” myeloma. Myeloma may also be described as “asymptomatic” or “symptomatic.” The term “asymptomatic myeloma” indicates that a patient has the disease but no disease-related symptoms. Patients with “symptomatic myeloma” have the disease as well as disease-related problems such

as anemia, elevated blood calcium, kidney damage or bone disease or frequent infections. Determining the particular type of disease presentation enables the physician to recommend the treatment that is most appropriate for a patient.

Populations at Risk

Myeloma is uncommon in people under the age of 40 years. Eighty percent of cases occur after age 60 (see Figure 2). Americans of African descent have a significantly higher rate of myeloma.

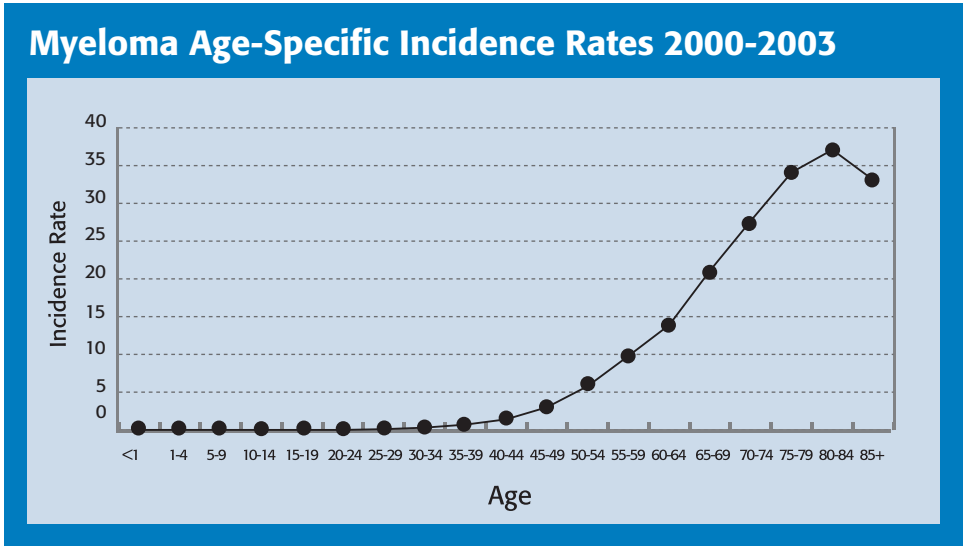


Figure 2. The horizontal axis shows the age at diagnosis, in five-year increments, of Americans who develop myeloma. The vertical axis represents the number of new cases of myeloma per 100,000 people in a particular five-year age grouping. Thus, the risk of myeloma is about 10 times greater in those 75 to 79 years of age (34 cases/100,000 persons) compared to those 45 to 49 years of age (3 cases/100,000 persons). (SEER Cancer Statistics Review, 1975-2003 [Surveillance Epidemiology and End Results data, 2006].)

Onset of the Disease

Myeloma results from an acquired injury to the DNA of a single cell in the lymphocyte development sequence that is intended to form plasma cells, as shown in Figure 3. The cause or causes of injury to the DNA that results in myeloma are unknown.

Although myeloma incidence increased somewhat in people who were exposed to the highest doses of radiation after the atomic bomb blasts in Hiroshima and Nagasaki,

Japan, exposure to radiation from diagnostic or therapeutic medical procedures is not associated with an increased incidence of myeloma.

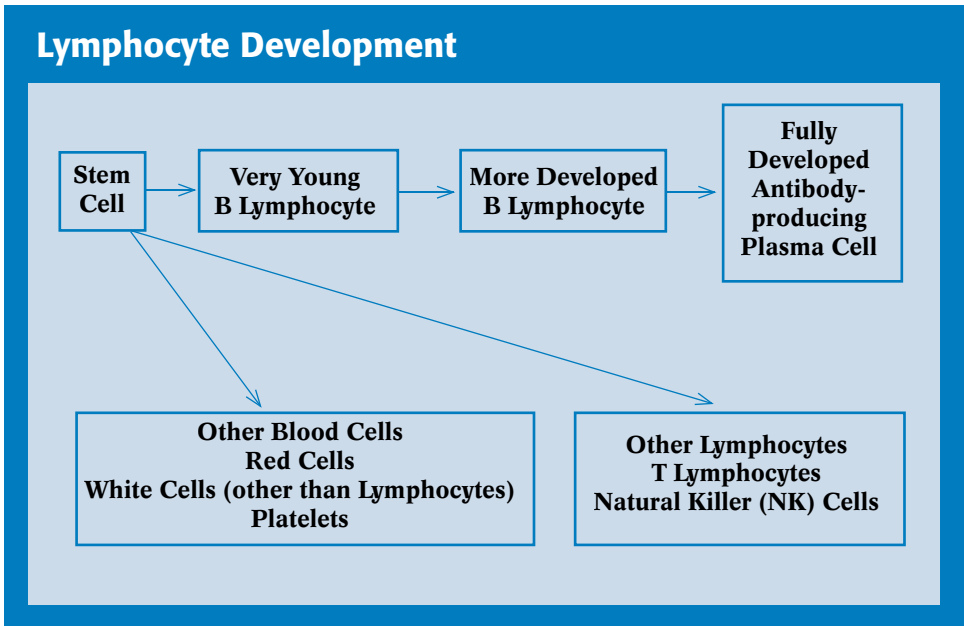


Figure 3. Early lymphocyte development in adults takes place principally in the lymph nodes. The lymphocyte then migrates to the marrow (a major site of plasma cell development and function), where further development occurs. The malignant transformation in myeloma occurs in a B lymphocyte. The affected lymphocytes transform into malignant cells that have the appearance of plasma cells. Plasma cells, including malignant forms such as myeloma cells, have an affinity for the marrow.

Myeloma occurs in lymphocytes that are B cells, as opposed to T cells. As part of their normal function, B lymphocytes transform into plasma cells, which produce proteins called antibodies. The B lymphocyte, if stimulated by a foreign antigen such as an infectious agent, transforms to a plasma cell. The latter produces antibodies that can attach to the infectious agent and predispose it to removal by other cells. In myeloma, even though the malignant transformation takes place in a B lymphocyte, the change leads to an accumulation of malignant cells that have the appearance of plasma cells. In most cases these malignant plasma cells are confined to the marrow. Their accumulation often interferes with normal blood cell production in the marrow.

The cells resulting from the malignant transformation sometimes look like normal plasma cells under the microscope. They may have structural abnormalities that suggest they are malignant (cancer) cells. Special tests described on the following pages can identify them as malignant plasma cells.

Clinical Findings

Marrow There are relatively few plasma cells in normal marrow. Plasma cells are often present in abnormally large numbers in patients with myeloma (see Figure 4). The myeloma cells accumulate in an uncontrolled manner, which is a sign of cancer, and form tumors in the marrow. Sometimes, the myeloma cells collect in tissue and form a single tumor called a plasmacytoma. However, in most cases, the tumor (also called a “mass”) spreads, usually in the marrow of many bones, including the ribs, spine, pelvis, shoulders, breastbone and skull.

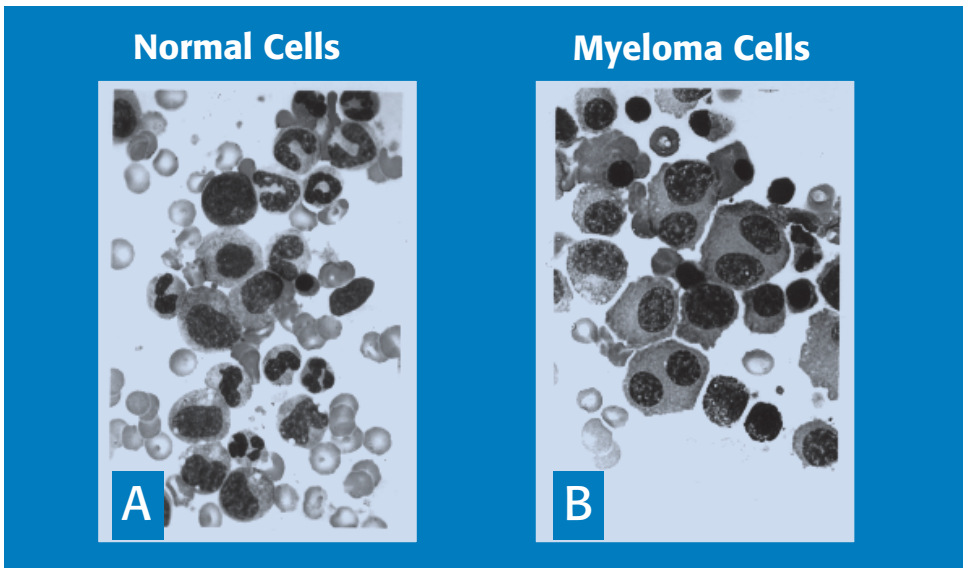


Figure 4. Panel A is a photograph of normal marrow cells. The variations in the shape and appearance of the cells are characteristic of the developmental stages of normal cells. Panel B is a photograph of marrow cells from a patient with myeloma. The normal marrow cells are replaced by plasma cells. Several cells have two nuclei, which may be one sign of abnormal plasma cells (myeloma cells).

Abnormal Proteins (Monoclonal Immunoglobulins) In myeloma, large amounts of a single type of protein, called “monoclonal immunoglobulin” (also called “M protein” or “M spike”), is made and secreted into the blood. The term “monoclonal” indicates that the protein is derived from one cell population, the malignant plasma cells.

The body's normal process is for plasma cells to produce many types of proteins, called "polyclonal immunoglobulins;" these are antibodies, which protect the body against infection caused by invading viruses, bacteria or other agents. By contrast, the production of M protein does not take place in response to an antigen such as an infectious agent.

M protein can be measured in the blood, and the amount generally correlates with the extent of the myeloma. Increasing M protein levels in the blood usually indicate progression of disease, and decreasing levels usually reflect regression of disease. Decreasing levels are usually associated with successful therapy. The intact immunoglobulin is composed of two larger pieces (heavy chains) and two smaller pieces (light chains) attached to each other (see Figure 5).

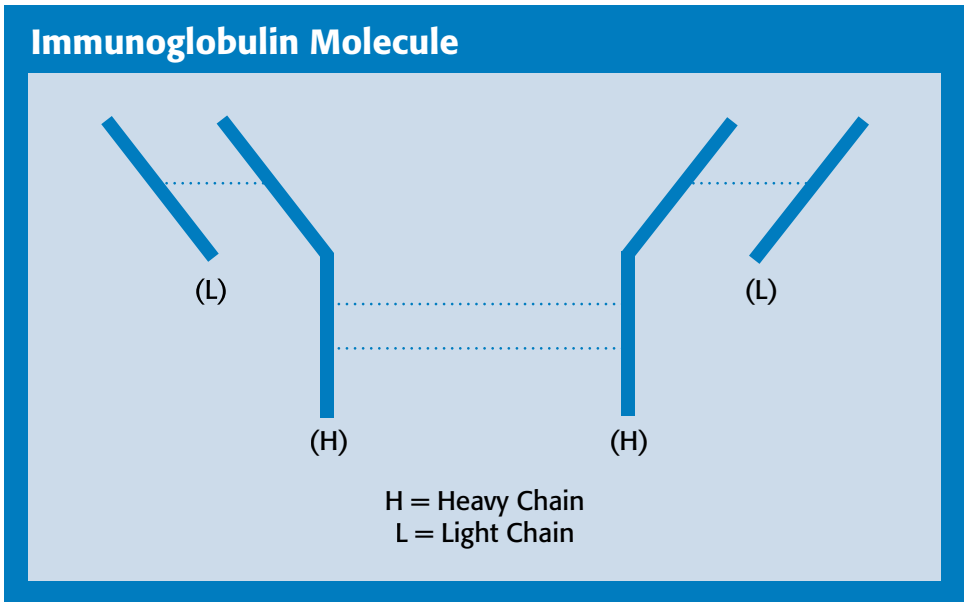


Figure 5. The M protein in myeloma, like normal immunoglobulin, is made up of two heavy chains and two light chains attached to each other. In many cases the coordination of making and attaching light chains and heavy chains in the malignant plasma cells is lost, and light chains leave the cell unattached. They are small enough to pass through the kidney and enter the urine, where they can be detected. Light chains in the urine are also referred to as "Bence Jones protein."

This whole immunoglobulin, made of the four chains, is too large to pass through the filtering apparatus of the kidney; it is present in the blood but not the urine. In many cases the coordination of making and attaching light chains and heavy chains in the malignant plasma cells is lost. An unattached light chain of immunoglobulin enters the blood and is excreted rapidly in the urine. This light chain is often called "Bence Jones

protein,” for the English physician Henry Bence Jones, who studied its characteristics after isolating it from the urine of a patient with myeloma. When excreted in large amounts, Bence Jones protein (immunoglobulin light chains) can cause injury to the kidney and kidney failure.

Bone Destruction Another special feature of myeloma cells is that they secrete chemicals (cytokines) that stimulate other cells that dissolve bone. Bone is remodeled continuously. This remodeling is a coordinated effect of cells that dissolve bone (osteoclasts) and cells that lay down new bone (osteoblasts). The chemicals secreted by plasma cells stimulate the bone-dissolving cells into marked overactivity. The bone-forming cells cannot keep up. Holes (lytic spots) develop in the bone. Bone is thinned (osteoporosis) and can be weakened enough to break (fracture) with normal stresses such as walking or lifting. Slightly increased stresses of coughing and minor falls or injuries can also break the bones when they are thinned by the effects of myeloma.

Symptoms and Signs

Bone pain is the most common early symptom of myeloma. Most patients feel pain in their back or ribs, but it can occur in any bone. The pain is usually made worse by movement. Patients fatigue more easily and often feel weak. They may have a pale complexion from anemia, which is a common medical problem for patients with myeloma and may contribute to the fatigue. If the disease progresses, the concentration of other normal cells in the blood, e.g., the white cells and platelets, may also decrease. Patients may have repeated infections because antibodies to invading viruses, bacteria or other disease agents are not made efficiently or in adequate amounts. A urinary tract, bronchial, lung, skin or other site of infection may be the first sign of the disease. In addition, recurrent infections may complicate the course of the disease.

Diagnosis

Laboratory reports that accompany some periodic medical examinations, especially in older patients, include a measurement of plasma proteins. A report of an elevated globulin fraction may lead to further tests and the diagnosis of myeloma in an asymptomatic patient. The diagnosis of myeloma depends on three principal findings:

- 1) Increased numbers of malignant plasma cells (myeloma cells) are found when a bone marrow aspiration and biopsy are performed (usually from the hipbone).
- 2) Intact monoclonal immunoglobulins or immunoglobulin light chains (Bence Jones

protein) are found in the blood or urine, respectively (see Figure 6). 3) Imaging studies of the bones identify the thinning, holes or fractures of the bones that characterize myeloma. Magnetic resonance imaging (MRI) can detect bone changes earlier than conventional x-ray studies. Taken together, these three findings make it possible for physicians to diagnose myeloma in patients.

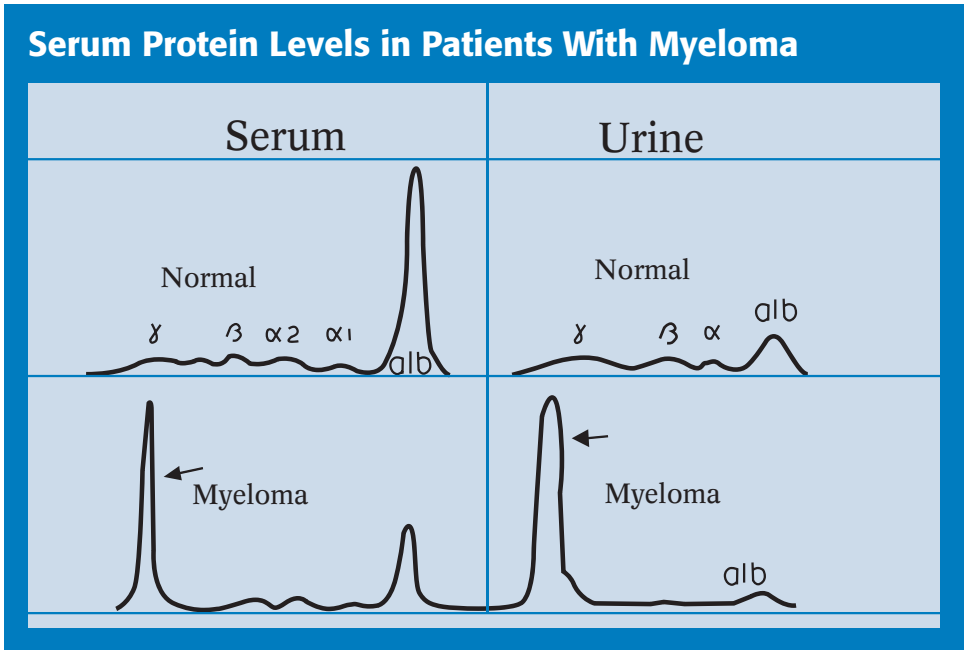


Figure 6. This figure represents the graphs of the readout of the serum blood protein measurement as performed in a clinical laboratory. The differences between normal serum and urine and those of a patient with myeloma are shown. The upper left panel displays the distribution of normal human serum proteins. There are two major types of proteins: albumin (alb) and globulin. The Greek symbols alpha (α), beta (β) and gamma (γ) are used to denote the different types of globulins. The lower left panel is the serum protein readout of a patient with myeloma. The characteristic findings are the lower amount of albumin in the far right peak and the markedly increased amount of gamma globulin in the far left peak (see arrow). The upper right panel displays the proteins in concentrated urine. Usually, only small amounts of protein are detected. The amounts are magnified here since the urine was concentrated 100-fold before the proteins were measured. The lower right panel is the urine readout from a patient with myeloma with a very large excretion of light chains (Bence Jones protein) shown by the far left peak (see arrow). Virtually all patients with myeloma have a protein peak in serum or urine, or in both.

Light chains can often be detected in the blood and urine of patients with myeloma. In some patients, the myeloma cells are so disordered that they do not make a complete monoclonal immunoglobulin molecule with two heavy and two light chains (see **Clinical Findings**, page 8 and Figure 5, page 9); their myeloma cells make only light chains. In these cases of myeloma, referred to as “light chain disease,” the examination of serum will not show the characteristic increase of M protein, but the urine will have large amounts of monoclonal light chains.

Physicians will also order other blood tests that measure red cell, white cell and platelet concentrations in the blood (complete blood count). These measurements indicate the degree to which the myeloma cells in the marrow are affecting normal blood cell development.

Blood calcium is measured because the bone destruction causes calcium to leave bone and reach elevated levels in the blood. High calcium levels can injure the kidneys.

The serum (blood) concentration of three proteins, lactic dehydrogenase, beta 2-microglobulin and C-reactive protein, is measured. The increase in each of these proteins is an indirect measure of the size and growth rate of the myeloma tumors.

Tests that reflect kidney function (urea nitrogen and creatinine) and a urine examination (urinalysis) are usually performed, since impaired kidney function can result from both the effects of the abnormal protein on the kidney as well as metabolic changes, such as elevated blood calcium.

G-banding karyotyping and FISH (fluorescence in situ hybridization) are cytogenetic tests that are used to identify specific chromosome abnormalities. Deletion of chromosome 13 is associated with more progressive disease. Other chromosome abnormalities, including translocations involving chromosome 14 (the site of a gene for the immunoglobulin heavy chain), are common findings. These alterations can suggest how rapidly the disease is progressing and may contribute to the decision on the best approach to treatment.

Treatment

There are several treatment options for myeloma. Several drugs in various combinations may be used: hematopoietic stem cell transplantation of three types (autologous, allogeneic and nonmyeloablative allogeneic transplantation) may be appropriate; and there is sometimes a role for local radiotherapy. A procedure to stabilize damaged bones is another treatment option for some patients.

Staging

Physicians determine the stage or extent of a patient's myeloma to help them decide which of several treatment approaches to take. For decades, a system of staging was in use that considered the patient's blood hemoglobin concentration, the amount of the M protein in blood and urine, the level of blood calcium, and the presence of bone lesions on imaging studies to determine the extent of the myeloma. The degree of increase in the beta 2-microglobulin and the degree of decrease in serum albumin – two serum measurements done on virtually all patients – can be used as a means for estimating disease stage. In an individual patient, a physician will consider many factors in deciding how to use staging information.

Some patients have minimal disease and little evidence of progression at the time of diagnosis. This circumstance has been referred to as “smoldering myeloma.” In such cases, watchful waiting may be preferable to early chemotherapy. However, in most cases, therapy will eventually be required.

Since myeloma usually occurs in the sixth through eighth decade of life, physicians also consider other factors in deciding whether to treat and what approach to take. The general health of the patient, the presence of other significant diseases such as heart disease or diabetes, the presence of myeloma renal disease, and other findings that influence the tolerance of patients to treatment and the risk of treatment-induced difficulties are considered in deciding on a treatment approach.

Drug Therapy

Chemotherapy has been the mainstay of treatment for myeloma. Chemotherapy uses drugs to kill the myeloma cells. Generally, people with symptomatic disease would be treated with chemotherapy. Table 1, page 14 lists the drugs most commonly used. Often, two or three drugs are used simultaneously. As many as six drugs are combined in some intensive treatment programs.

Table 1. Some Drugs Used in Treatment of Myeloma

- Arsenic trioxide (Trisenox[®])
- Bortezomib (Velcade[®])
- Carmustine (BiCNU[®], BCNU[®])
- Cyclophosphamide (Cytosan[®])
- Dexamethasone (Decadron[®])
- Doxorubicin (Adriamycin[®])
- Idarubicin (Idamycin[®])
- Interferon alfa (Roferon[®]-A, Intron[®] A)
- Lenalidomide (Revlimid[®])
- Melphalan (Alkeran[®])
- Pamidronate (Aredia[®])
- Prednisone
- Thalidomide (Thalomid[®])
- Vincristine (Oncovin[®])
- Zoledronic acid (Zometa[®])

Chemotherapy for myeloma has led to sustained remissions in some patients. Temporary cessation or marked slowing of the disease may occur for a time. Achieving complete remission for long periods has been infrequent. Thus, conventional chemotherapy with one, two or three drugs has given way to more intensive treatment. Since myeloma occurs principally in individuals between 60 and 80 years of age, the ability to tolerate intensive therapy must be judged on an individual basis.

Several approaches to drug therapy can be used depending on the individual patient's circumstances, including age, extent of disease, rate of progression of disease and other accompanying conditions, such as heart disease or diabetes.

Drug combinations include longstanding drugs such as melphalan, prednisone and others, shown in Table 1. Several newer agents are being used in treatment. They are also being studied (either with or in place of standard treatments) as initial therapy and as therapy for relapsed or refractory disease. Some of the newer agents include:

- **Thalidomide** (Thalomid®) This drug, in combination with dexamethasone, is indicated for the treatment of patients with newly diagnosed myeloma. Its use in combination with other drugs in addition to dexamethasone is under study. Study combinations include melphalan, prednisone and thalidomide, or bortezomib (Velcade®) and thalidomide.
- **Lenalidomide** (Revlimid®) This drug is a more potent form of thalidomide and may have broader anti-myeloma effects. Revlimid® in combination with dexamethasone is indicated for the treatment of myeloma patients who have received at least one prior therapy. Revlimid® in combination with melphalan and prednisone or with Velcade® is also under study.
- **Bortezomib** (Velcade®) This drug interferes with the growth of cancer cells and is approved to treat myeloma in patients who have not responded to or have relapsed after receiving at least one other treatment. It is given by injection. Velcade® is also being studied as first-line treatment alone, and in combination with other agents, for advanced disease.
- **Bisphosphonates** These are potent inhibitors of bone resorption. Pamidronate (Aredia®) and zoledronic acid (Zometa®) are bisphosphonates that can alleviate bone disease, decreasing pain, the likelihood of fracture and the high blood calcium levels associated with bone destruction. Studies indicate that a secondary effect of bisphosphonates includes the inhibition of myeloma cell growth.
- **Arsenic trioxide** (Trisenox®) Arsenic trioxide produces a variety of anti-tumor effects. It is being studied in clinical trials with melphalan and vitamin C (MAC therapy) in patients with relapsed or nonresponsive disease.

Stem Cell Transplantation

Treatment with allogeneic stem cell transplantation may be considered for a myeloma patient who has an HLA-matched donor. There are other key eligibility factors including patient age (usually about age 50 or younger) and the absence of complicating medical conditions, such as diabetes, kidney disease or heart disease. Low-intensity or nonmyeloablative allogeneic stem cell transplantation is under study to see if older patients with myeloma benefit from such an approach.

Most patients with myeloma are older, and if they are treated with stem cell transplantation, they receive an autologous transplant, which is a less difficult procedure. Two successive autologous transplants are done if they can be tolerated. This tandem autologous transplant can produce long-term remissions in some patients.

New options for drug therapy may prove as effective as autologous transplantation, and clinical trials comparing these choices should answer that question. Some physicians favor using drug treatment as the first option. Much depends on the circumstances of an individual patient in determining the best initial treatment after diagnosis.

A modified form of allogeneic transplant – nonmyeloablative or “mini transplant” – is being studied to determine its effectiveness compared with a standard allogeneic transplant. Such an approach could also expand this form of therapy to older patients who are not now eligible for allogeneic transplant.

Maintenance Therapy Myeloma patients who have had one or two autologous transplants are likely to require maintenance therapy. There is no standard maintenance treatment at present; research on the outcomes of various approaches is under way. There are several ongoing maintenance therapy trials, including several different phase III studies evaluating the effectiveness of treatment with thalidomide, lenalidomide and other drugs before and after autologous stem cell transplantation.

Radiation Therapy

This is a treatment that uses high-energy rays (x-rays) to kill malignant plasma (myeloma) cells and may be used to treat myeloma patients in select circumstances. Radiation therapy is the main treatment for localized myeloma, such as a solitary myeloma or an accumulation of myeloma cells outside the marrow (plasmacytoma). Patients sometimes receive radiation therapy in preparation for stem cell transplantation. Carefully selected patients whose bone pain does not respond to chemotherapy may receive radiation therapy as well. Because the disease may be widespread, radiation therapy may be impractical if there are widely distributed sites of painful bone involvement.

Supportive Care

Treating Anemia In some patients with severe anemia, the administration of an engineered form of the red cell growth factor, erythropoietin, may improve the anemia or decrease the need for blood transfusions.

Stabilizing Damaged Bones Vertebroplasty and kyphoplasty are surgical techniques that may be used to help myeloma patients who have disabling back pain. With vertebroplasty, a chemical cement is inserted into the damaged vertebrae via a catheter. Kyphoplasty involves inflating a balloon before stabilizing the area with the chemical cement. These procedures relieve nerve compression and may alleviate pain and reduce the amount of pain medication that the patient needs. In some cases, height lost due to vertebral collapse is restored.

The usefulness of either of these procedures for any individual patient is a matter that should be carefully discussed by patients and their physicians.

Disease Complications and Treatment Side Effects

Infections Infections are one of the most troublesome medical problems for patients with myeloma. Patients with myeloma may not be able to fight infections efficiently because their B lymphocytes do not make antibodies in response to microbes that enter the body. The effects of chemotherapy or radiation therapy on blood cell production also cause further deficits in white cells, which contributes further to the risk of infection.

Pain Bone pain may occur because of the expansion of myeloma tumors. Successful treatment may relieve bone pain. Patients may also experience pain that radiates from the back when the back bones (vertebrae) collapse and impinge on nerves. Fractures of bones may also result in pain.

Kidney Impairment Myeloma patients may have serious problems with their kidney function for two principal reasons. One reason is the excretion of large amounts of Bence Jones protein in the urine. This excess protein can damage the kidney filtration apparatus and the channels or tubules that are important in urine formation. Another reason is that patients with myeloma often have high levels of calcium in the blood (hypercalcemia). When bones are damaged, calcium is released into the blood. High blood concentration of calcium can damage the kidneys.

Masses of Myeloma Cells (Plasmacytomas) “Extramedullary myeloma” is the term applied to masses of myeloma cells that develop outside the marrow. These may involve organs like lymph nodes, the respiratory tract, the gastrointestinal tract or the skin. In the skin, the masses are evident as small tumors, often with a purple discoloration. In some cases, the spinal cord may be injured due to myeloma masses that extend from bone and press on the cord.

Impaired Blood Flow Occasionally, the abnormal protein (monoclonal immunoglobulin) concentration in the blood is so great that it interacts with the red cells to produce a sludging of blood flow, which is referred to as “hyperviscosity.” The circulation of the oxygen-carrying red cells is slowed, and the work of the heart is increased by the resistance of the blood to being pumped through the circulation. This complication can lead to headaches, dizziness, weakness, fatigue, sleepiness, oozing from cuts and other symptoms. Rarely, some myeloma monoclonal immunoglobulins may congeal in the cold and lead to poor circulation, especially if the body is exposed to cold temperatures. These immunoglobulins are referred to as “cryoglobulins” (from the Greek word “kryos,” meaning “cold”). Hyperviscosity is much less common in myeloma than in Waldenström macroglobulinemia (see page 21).

Acute Myelogenous Leukemia There is a heightened risk among myeloma patients of developing acute myelogenous leukemia, especially after treatment with certain cytotoxic drugs. This complication occurs in a small proportion of patients.

Osteonecrosis of the Jaw (ONJ) This is an uncommon but serious condition that has occurred in some patients receiving bisphosphonates such as pamidronate (Aredia®) or zoledronic acid (Zometa®). Although no cause-and-effect relationship between bisphosphonate therapy and osteonecrosis has been established, it is suspected.

ONJ may develop when the jaw fails to heal after minor trauma such as a tooth extraction that results in bone exposure. Symptoms include pain, swelling, poor healing or infection of the gums, loosening of teeth, or numbness or a feeling of heaviness in the jaw. Some factors that may increase the risk of osteonecrosis are radiation therapy to the head or neck, chemotherapy, steroid therapy, anemia (low red cell count), infection, poor dental health, alcohol abuse or cigarette smoking, poor nutrition, poor blood circulation or clotting problems.

Treatment with bisphosphonates should be managed by an experienced oncologist, with close coordination between the oncologist and oral surgeon and/or a dental specialist. A dental examination before patients begin therapy with intravenous

bisphosphonates is advisable if possible. Dental treatments and procedures that require bone healing should be completed before initiating intravenous bisphosphonate therapy. Patients should receive and follow instructions on maintaining good oral hygiene and having regular dental assessments. For patients currently receiving bisphosphonates who require dental procedures, there is no current evidence to suggest that interrupting bisphosphonate therapy will prevent or lower the risk of ONJ. Frequent clinical assessments and conservative dental management are suggested for these patients. Treatment of patients who develop ONJ may include frequent clinical assessments, antibiotics, oral rinses and removable mouth appliances. Minor dental work may be necessary to remove injured tissue and reduce sharp edges of the bone. Surgery is typically avoided because it may make the condition worse.

Peripheral Neuropathy This is the term for damage to nerves of the peripheral nervous system, which transmits information from the brain and spinal cord to every other part of the body. There are several causes for this condition. It can be a result of the disease, or it can be a side effect of certain anticancer drugs, including vincristine, thalidomide and lenalidomide. Symptoms may include temporary or ongoing numbness, tingling, burning, coldness or weakness in arms or legs.

Thrombosis and Embolism “Deep venous thrombosis” (DVT), the term for a blood clot, forms in the deep veins of the body, usually in the legs. It can cause obstruction to blood flow and pain and swelling below the obstruction. Pulmonary embolism occurs when a blood clot in a deep vein breaks off, travels through the circulation and lodges in the pulmonary arteries. Depending on the size and number of the emboli that reach the pulmonary arteries, a patient may have chest pain, shortness of breath and potentially other severe effects. Thalidomide and Revlimid® are associated with an increased incidence of DVT and pulmonary embolism. Revlimid® may have a lower frequency of these side effects as compared to thalidomide. Some physicians have observed that taking either thalidomide or Revlimid® and dexamethasone in combination with erythropoietin (Procrit® or Aranesp®) further increases a patient’s risk for DVT.

Clinical Trials

New approaches to treatment are under study in clinical trials to determine their potential benefits and what, if any, adverse effects they have. New treatments have the potential to both extend patients' lives and improve the quality of life. Some treatments are used sequentially; others are used in combination with current agents.

Myeloma cells are inherently resistant to current drug therapies. In part, this is related to the presence of multidrug resistance factors in the cell that prevent drugs from acting on the cell. Several new approaches to counteracting these drug-resistance factors are under study and could be used in the future to enhance the effectiveness of drugs.

Examples of *types* of therapy under study are:

Immunotherapy Various forms of immunotherapy are being studied. Myeloma cells express highly specific targets for immune attack. Vaccines are being studied that could employ a patient's immune cells to attack his or her own myeloma cells. These vaccines and other types under study do not prevent the disease, as in the case of most vaccines for infectious diseases. They would reduce the myeloma tumors or suppress the growth of residual myeloma tumors after other forms of therapy have reduced their size.

Targeted Radiotherapy A radioactive isotope that attaches to bone is being studied to determine if its myeloma-killing radiation can be used to treat the disease prior to autologous transplantation.

Antisense Oligodeoxynucleotides These agents may have therapeutic activity in myeloma. In particular, antisense oligonucleotides to Bcl-2 have been tested as myeloma treatment in phase III clinical trials in myeloma. The Bcl-2 protein is highly expressed in myeloma patients, and in vitro studies have shown its role in the regulation of chemosensitivity, which makes Bcl-2 an attractive target for treatment.

Statins These agents, which are widely used for the treatment of hypercholesterolemia, kill myeloma cells. Lovastatin has been shown to induce cell death in myeloma cells by inhibition of anti-cell death proteins in myeloma cells. Phase II studies have been performed coupling Bcl-2 antisense oligonucleotides and high-dose simvastatin in combination with chemotherapy in heavily treated myeloma patients. Encouraging results from these studies may provide the framework for the future application of new treatment strategies for myeloma.

Specific *agents* that have shown antimyeloma activity and are under study include:

- CHIR-258, which inhibits fibroblast growth factor receptor 3
- NVP-ADW742, which inhibits insulin-like growth factor receptor 1
- PTK787, which inhibits vascular endothelial growth factor
- Histone deacetylase inhibitors, which are aimed at switching on silenced genes.

These and other new approaches, some of which are being supported by the research programs of the Society, hold the promise of increasing the rate of remission and finding a cure for myeloma.

The Society's Information Resource Center offers guidance on how patients can work with their physicians to find out if a specific clinical trial is an appropriate treatment option. Information Specialists will conduct clinical trials searches for patients, family members and healthcare professionals. Information Specialists can be called at (800) 955-4572. The service is also available on the Society's Web site at www.LLS.org.

Related Diseases

Essential Monoclonal Gammopathy (also called “benign monoclonal gammopathy,” “monoclonal gammopathy of unknown significance” [MGUS] and other names). This common condition is usually found in older persons and increases in frequency in the sixth through ninth decades of life. It is manifested by the appearance of a pathological (monoclonal) protein in the blood analogous to that which characterizes myeloma (see Figure 6, page 11). However, an increase in plasma cells is not apparent in the marrow, and anemia, bone damage, recurrent infections and other features of myeloma are not present. The disorder usually does not affect the well-being of the patient, although occasionally the monoclonal protein may interact with normal tissues and lead to symptoms, depending on the tissue affected. The significance of the disorder is that it evolves into a progressive B lymphocyte malignancy such as myeloma or lymphoma in about 30 percent of those affected over 20 years of observation.

Waldenström Macroglobulinemia This disease has similarities to myeloma in that it is a malignancy of B lymphocytes that produce a monoclonal immunoglobulin that can be measured in the blood. The malignant B lymphocytes replace the normal marrow cells and may cause anemia and other blood cell deficiencies by preventing the normal marrow cells from making blood cells efficiently. Macroglobulinemia also

occurs in older individuals, as does myeloma. It differs from myeloma in that it usually does not progress as rapidly and does not lead to bone destruction and fractures. The monoclonal immunoglobulin produced by the malignant B lymphocyte is a very large type, referred to as “macroglobulin” (large globulin). One of the effects of the macroglobulin is to increase the viscosity of the blood, leading to impaired blood flow. This immunoglobulin may also result in kidney damage. Although successful drug therapy decreases the level of this harmful protein, in some cases reduction requires removal through a process called “plasmapheresis,” which lowers the plasma macroglobulin level more quickly for a time.

Primary Amyloidosis An uncommon disease process is associated with the deposit of the material called “amyloid” (from the French word meaning “starch”) in tissues such as the heart, the gastrointestinal tract, the nerves, the skin and other sites. Although there are several types of amyloid, one type is caused by the deposit of immunoglobulin light chains (see Figure 5, page 8) in the tissues. In some patients with myeloma, the light chains made by their plasma cells can result in the formation of amyloid and its deposition in tissues. This type of amyloidosis can occur with or without overt myeloma. In patients with myeloma-associated amyloid, the involvement of the heart, intestines or nerves can produce dysfunction in those organs, significantly complicating the management of the myeloma. In other patients, the marrow may not have increased numbers of plasma cells and the bones may not be affected. The malignant B cells, which make the light chains that deposit themselves in the tissues and form the amyloid, are too few to be identified by a marrow biopsy.

Heavy Chain Disease Heavy chain disease is a rare disease of B lymphocytes, so named because the protein made by the malignant lymphocytes is an incomplete immunoglobulin (the heavy chain of the immunoglobulin; see Figure 5, page 8). It is similar to myeloma in that it is a malignancy of B lymphocytes that secrete a characteristic immunoglobulin, but its clinical features are quite different. For example, there is no bone disease.

POEMS Syndrome POEMS syndrome is a very uncommon marrow disorder related to myeloma. The name of the syndrome is derived from its five most common features: P (peripheral neuropathy), O (organ enlargement), E (endocrine gland dysfunction), M (monoclonal plasma cell tumors and monoclonal immunoglobulin), S (skin changes). The nerve injury is often the most disabling element and can include progressive weakness of arms or legs. The bone alterations related to the marrow accumulation of plasma cells take on a different character than that in classic

myeloma. The marrow looks more dense rather than less dense than normal. Thyroid or sex hormone deficiencies may require replacement therapy. Therapy can benefit several features of the disease.

Social and Emotional Effects

A myeloma diagnosis may provoke a strong emotional response in patients, family members and friends. Denial, depression, hopelessness and fear are a few of the feelings or emotions people may experience. No one response is either universal or unexpected.

Most people with myeloma are able to cope with what at first may seem too hard to accept. This adjustment usually takes time. Patients may first want to focus on learning about their disease and its treatment. Knowing more about the disease and its treatment helps many individuals to cope. Patients and caregivers are advised to discuss the disease and its treatment with the physician to ask questions and convey fears or concerns. The beginning of treatment helps many people shift their focus to the therapy process ahead and the prospect of recovery.

Patients may want to have a friend, family member or caregiver accompany them to treatments, especially for the first several times. The presence of another individual may help ease the patient's stress. This person can also help the patient ask questions and retain treatment information. While it is not always possible to have this type of support, patients can reach out in other ways – for example, local or Internet support groups can provide a forum for discussing healthcare appointments and other aspects of treatment. Often, patients with cancer become acquainted with one another, and these friendships provide support. Over time, some patients form supportive relationships with their healthcare team.

A change in lifestyle occurs for many patients with cancer, at least for a time. Daily routines for the patient (and his or her family, if applicable) may have to be adjusted to accommodate treatment schedules. Disease and treatment side effects sometimes cause a person to question his or her self-worth, identity and appearance. These issues may affect relationships, including sexual relationships. Sexual desire may decrease for a period of time, then return. Recognition that these feelings are normal and knowing that many side effects are temporary may be reassuring. Open, honest communication regarding fears and concerns can be very helpful.

It is important to seek medical advice if a patient's mood does not improve over time — for example, if a patient is feeling depressed every day for a two-week period. Depression is an illness that should be treated even when a person is undergoing treatment for myeloma. Treatment for depression has proven benefits for people living with cancer. (The National Institute of Mental Health fact sheet at www.nimh.nih.gov/publicat/NIMHdepcancer.pdf has more information about depression and cancer.)

There are many sources of help available to patients and caregivers. Aspects of care such as making treatment choices, finding the time and money for medical care and communicating with family members and friends can be stressful. Contact the Society or ask the healthcare team for guidance and referrals to other sources of help such as support groups, counseling services or community programs.

For more support information, see the Society's free booklets.

Emotional Aspects of Childhood Blood Cancers: A Handbook for Parents.
The Leukemia & Lymphoma Society; 2006.

Coping: Support for People Living with Leukemia, Lymphoma or Myeloma.
The Leukemia & Lymphoma Society; 2005.

Each New Day: Ideas for Coping with Leukemia, Lymphoma or Myeloma.
The Leukemia & Lymphoma Society; 2006.

Touching Lives: A Directory of Patient Services Programs. The Leukemia & Lymphoma Society; 2005.

The Leukemia & Lymphoma Society also offers programs through its local chapters to help ease the emotional and economic pressure that comes with a blood cancer diagnosis. Visit the Society's Web site at www.LLS.org or contact the Society's Information Resource Center at (800) 955-4572 to locate a chapter in your area, order free publications or speak directly to an Information Specialist.

Glossary

Allogeneic Stem Cell Transplantation

A treatment that uses donor stem cells to restore a patient's marrow and blood cells. First, the patient is given "conditioning therapy" (high-dose chemotherapy or high-dose chemotherapy with total body radiation) to treat the leukemia and to "turn off" the patient's immune system so that the donor stems will not be rejected. A type of transplant called a "nonmyeloablative" transplant (or "mini transplant") is under study. It uses lower doses of conditioning therapy and may be safer, especially for older patients.

Amyloid

In myeloma, an abnormal protein made by malignant plasma cells. An amyloid develops when parts of the immunoglobulin molecule, referred to as "light chains," deposit in tissues. In the type of amyloid that occurs in myeloma or closely related diseases, organ failure can occur as a result of amyloid deposits in the heart, gastrointestinal tract and other systems.

Anemia

A decrease in the red cells and, therefore, the hemoglobin concentration of the blood. This results in a decreased capacity of the blood to carry oxygen. If severe, anemia can cause a pale complexion, weakness, fatigue and shortness of breath on exertion.

Antibodies

Proteins released by plasma cells that recognize and bind to specific foreign substances called antigens. Plasma cells are derived from B lymphocytes. Antibodies coat, mark for destruction or inactivate foreign particles like bacteria, viruses or certain chemicals such as harmful toxins. Antibodies can also be made in the laboratory. These can be polyclonal antibodies (derived from different B-lymphocyte lines) or monoclonal antibodies (derived from a single B-lymphocyte line). Monoclonal antibodies produced in the laboratory can be used to target and destroy specific types of cancer cells.

Apheresis (see Hemapheresis)

Autologous Stem Cell Infusion

A technique, often referred to as "autologous stem cell transplantation," involving 1) harvesting the patient's stem cells from blood or marrow, 2) freezing them for later use and 3) thawing and infusing them via an indwelling catheter after the patient has been given intensive chemotherapy or radiation therapy. The blood or marrow may be obtained from a patient with a disease of the marrow, such as myeloma, when in remission or when the marrow and blood are not overtly abnormal (for example,

in lymphoma). Technically, this procedure is not transplantation, which implies taking tissue from one person (donor) and giving it to another person (recipient). The purpose of this procedure is to restore blood cell production from the preserved and reinfused stem cells after intensive therapy has severely damaged the patient's remaining marrow. This procedure can be performed using marrow or blood stem cells. The latter can be harvested by hemapheresis.

Basophil

A type of white cell that participates in certain allergic reactions.

Bence Jones Protein

An abnormal protein made by the malignant plasma (myeloma) cells, which enters the blood but is excreted rapidly in the urine. This protein can cause injury to the kidney or kidney failure when excreted in large amounts. By contrast, normal immunoglobulin is too large to pass through the filtering apparatus of the kidney, so it is present in the blood but not in the urine. Bence Jones proteins are also called "immunoglobulin light chains."

Beta 2-microglobulin

A cell protein that can be measured in the plasma. The amount of beta 2-microglobulin is used to estimate the extent of the patient's myeloma. A very low level is better than a very high level.

Bisphosphonates

A class of drugs, including pamidronate and zoledronic acid, which have been helpful in preventing or minimizing bone loss. Bisphosphonates probably act by preventing cells called "osteoclasts" from dissolving bone. In myeloma, bone thinning (osteoporosis) and fracture are major problems.

Bone Marrow

A spongy tissue that is the site of blood cell formation in the central cavity of the bones. By puberty, the marrow in the spine, ribs, breastbone, hip, shoulders and skull is most active in blood cell formation. In the adult, the bones of the hands, feet, legs and arms do not contain marrow in which blood cells are made. In these sites, the marrow is filled with fat cells. When marrow cells have matured into blood cells, they enter the blood that passes through the marrow and are carried throughout the body.

Bone Marrow Aspiration

A test to examine marrow cells to detect cell abnormalities. A marrow sample is usually taken from the patient's hipbone. After medication is given to numb the skin, the sample is removed using a special needle inserted through the bone into the marrow. The sample is viewed under a microscope to identify abnormal cells such

as myeloma cells. The cells obtained can also be used for cytogenetic analysis, flow cytometry and other tests.

Bone Marrow Biopsy

A test to examine marrow cells to detect cell abnormalities. This test differs from a marrow aspiration (defined above) in that a small amount of bone filled with marrow is removed, usually from the hipbone. After medication is given to numb the area, a special biopsy needle is used to remove a core of bone containing marrow. The marrow is examined under a microscope to determine if abnormal cells such as myeloma cells are present.

Bone marrow aspiration and biopsy may be done in the doctor's office or in a hospital. The two tests are almost always done together. Both tests are also done after treatment to determine the proportion of blood cancer cells that have been killed by therapy.

Chemotherapy

The use of chemicals (drugs or medications) to kill malignant cells. Numerous chemicals have been developed for this purpose, and most act to injure the DNA of the cells. When the DNA is injured, the cells cannot grow or survive. Successful chemotherapy depends on the fact that malignant cells are somewhat more sensitive to the chemicals than normal cells. Because the normal cells of the marrow, the intestinal tract, the skin and the hair follicles are most sensitive to these chemicals, injury to these organs causes the most common tissue effects of chemotherapy (i.e., mouth sores, diarrhea and hair loss).

Computed Tomography (CT) Scan

This is a technique for imaging body tissues and organs. X-ray transmissions are converted to detailed images using a computer to synthesize x-ray data. The images are displayed as a cross-section of the body at any level from the head to the feet. A CT scan of the chest or abdomen permits detection of an enlarged lymph node, liver or spleen. A CT scan can be used to measure the size of these and other structures during and after treatment.

Cytokines

Cell-derived chemicals that are secreted by various types of cells and act on other cells to stimulate or inhibit their function. Chemicals derived from lymphocytes are called "lymphokines." Chemicals derived from lymphocytes that act on other white cells are called "interleukins;" that is, they interact between two types of leukocytes. Some cytokines can be made commercially and used in treatment. Granulocyte colony-stimulating factor (G-CSF) is one such cytokine. It stimulates the production of neutrophils and shortens the period of low neutrophil counts in the blood after chemotherapy. Cytokines that stimulate cell growth are sometimes referred to as "growth factors."

Differentiation

The process by which stem cells transform from cells without specific structural or functional characteristics into functional cells of a single blood cell line. The process of stem cell differentiation forms the red cells, platelets, neutrophils, monocytes, eosinophils, basophils and lymphocytes.

Eosinophil

A type of white cell that participates in allergic reactions and helps to fight certain parasitic infections.

G-banding Karyotyping

A “karyotype” is the systematic arrangement, using images, of the 46 human chromosomes of a cell. Karyotypes are examined for deviations from the expected arrangement, number, size, shape or other characteristics of the chromosomes. Each chromosome pair has a characteristic banding pattern. To make the banding pattern easier to see, a dye called Giemsa may be used as a stain. This is also referred to as “G-banding.” Certain chromosomal abnormalities are associated with specific myeloma subtypes. G-banding karyotyping and other cytogenetic tests provide physicians with information that contributes to determining the best treatment approach for an individual patient.

Growth Factors (see Cytokines)

Hemapheresis (Apheresis)

The process of removing a donor’s blood to extract a specific blood component and returning the remaining parts to the donor. The process uses continuous circulation of blood from a donor through an apparatus and back to the donor. This process makes it possible to remove desired elements from large volumes of blood. Platelets, red cells, white cells or plasma can be removed separately. For example, this technique permits the harvest of enough platelets for a platelet transfusion from one donor (rather than six to eight separate donors). In so doing, the recipient of the platelets is exposed to the blood of fewer donors or can be given HLA-matched platelets from a single related donor. This technique is also used to remove circulating blood stem cells that can be frozen, stored and later used instead of marrow stem cells for transplantation. The system of hemapheresis is closed and sterile.

Hematologist

A physician who specializes in the treatment of blood diseases. This person is either an internist who treats adults or a pediatrician who treats children. Hematopathologists are pathologists who specialize in the diagnosis of blood cell diseases and who perform the specialized laboratory tests often required to make a conclusive diagnosis.

Hematopoiesis

The process of blood cell development in the marrow. The most undeveloped cells in the marrow are stem cells. They start the process of blood cell development. The stem cells begin to develop into young or immature blood cells like red cells or white cells of various types. This process is called “differentiation.” The young or immature blood cells then further develop into fully functional blood cells. This process is called “maturation.” Mature cells leave the marrow and enter the blood and circulate throughout the body. Hematopoiesis is a continuous process that is active normally throughout life. The reason for this continuous activity is that most blood cells live for short periods and must be continuously replaced. After release from the marrow, red cells are removed in four months, platelets in 10 days and most neutrophils in one to three days. About five hundred billion blood cells are made each day. This requirement for very rapid replacement explains the severe deficiency in blood cell counts that occurs when the marrow is injured by replacement with leukemia, lymphoma or myeloma cells.

HLA

The acronym for human leukocyte antigens. These proteins are on the surface of most tissue cells and give each individual his or her unique tissue type. Hence, the testing for HLA antigens is referred to as “tissue typing.” There are four major groups of HLA antigens: A, B, C, and D. These proteins act as antigens when donated (transplanted) to another individual, e.g., a bone marrow or stem cell recipient. If the antigens on the donor cells are identical (e.g., identical twins) or very similar (e.g., HLA-matched siblings), the transplant (donated marrow or cells) is more likely to survive in the recipient (engraft). In addition, the recipient’s body cells are less likely to be attacked by the donated cells (graft versus host disease).

Hypercalcemia

An abnormally high concentration of calcium in the blood. In myeloma, the breakdown of bone, which is rich in calcium, is the main cause of high blood and urine calcium. The high calcium can contribute to weakness, loss of appetite, nausea, confusion, lethargy and other symptoms.

Karyotype

The systematic arrangement, using images, of the 46 human chromosomes of a cell in 22 matched pairs (maternal and paternal members of each pair) ordered by length (from longest to shortest) and other features. These 22 pairs are referred to as “autosomes.” The sex chromosomes are shown as a separate pair (either XX or XY).

Lymph Nodes

Small structures, the size of beans, which contain large numbers of lymphocytes and are connected with each other by small channels called “lymphatics.” These nodes are distributed throughout the body. In patients with lymphoma and some types of lymphocytic leukemia, the malignant lymphocytes grow and expand the lymph nodes, so they may be enlarged. This enlargement of lymph nodes can be seen, felt or measured by computed tomography (CT) scan or magnetic resonance imaging (MRI), depending on the degree of enlargement and the location.

Lymphocyte

A type of white cell that is the essential cell type in the body’s immune system. There are three major types of lymphocytes: B lymphocytes that produce antibodies to help combat infectious agents such as bacteria, viruses and fungi; T lymphocytes that have several functions, including assisting B lymphocytes to make antibodies; and natural killer (NK) cells that can attack virus-infected cells or tumor cells.

Macrophage (see Monocyte)

Magnetic Resonance Imaging (MRI)

This technique provides detailed images of body structures. It differs from CT scanning in that the patient is not exposed to x-rays. The signals generated in the tissues in response to a magnetic field produced by the instrument are converted by computer into images of body structures. Thus, the size and a change in size of organs – such as the lymph nodes, liver and spleen – or tumor masses can be measured.

Mini-transplant (see Nonmyeloablative Allogeneic Stem Cell Transplant)

Monocyte (Macrophage)

A type of white cell that represents about 5 to 10 percent of the cells in normal human blood. The monocyte and the neutrophil are the two major microbe-eating and microbe-killing cells in the blood. When monocytes leave the blood and enter the tissue, they are converted to macrophages. The macrophage is the monocyte in action and can combat infection in the tissues, ingest dead cells and assist lymphocytes in their immune functions.

M Protein (M Spike)

A term for “monoclonal immunoglobulin,” a type of protein made in large amounts by malignant plasma cells and secreted into the blood. The term “monoclonal” indicates that the protein is derived from one cell population. Normal plasma cells produce many types of proteins, called “polyclonal immunoglobulins” (antibodies), to protect the body against infection caused by invading viruses, bacteria or other agents. The production of M protein does not take place in response to an antigen, such as an

infectious agent. M protein can be measured in the blood, and the amount generally correlates with the extent of the myeloma progression. Increases in the amount of the protein usually parallel increasing M-protein concentration in the blood, and decreasing M-protein concentration in the blood usually reflects regression of the myeloma. M protein is also referred to as “M spike.”

Myeloma Cells

Malignant plasma cells that are the hallmark of myeloma. Their appearance may be similar to normal plasma cells, but they are present in increased numbers.

Neutrophil

The principal phagocyte (microbe-eating cell) in the blood. This blood cell is the main cell that combats infections. Often, it is not present in sufficient quantities in patients with acute leukemia or after chemotherapy. A severe deficiency of neutrophils increases the patient’s susceptibility to infection. A neutrophil may be called a “poly” (polymorphonuclear neutrophil) or “seg” (segmented neutrophil) because its nucleus has several lobes.

Nonmyeloablative Allogeneic Stem Cell Transplant

A type of stem cell transplant, also called “mini transplant,” that uses less induction chemotherapy and radiation. The theory being tested with a mini-allogeneic transplant is that by using less toxic methods prior to the transplant, the body is better able to withstand the transplant.

Phagocytes

Cells that readily eat (ingest) microorganisms such as bacteria or fungi and can kill them as a means of protecting the body against infection. The two principal types of phagocytes are neutrophils and monocytes. They emigrate out of the blood and into tissues in which an infection has developed. A severe decrease in the blood level of these cells is the principal cause of susceptibility to infection in patients treated with intensive radiotherapy and/or chemotherapy. The latter treatments suppress blood cell production in the marrow, resulting in deficiencies of phagocytes.

Plasma Cell

A cell that is derived from the antigen-induced activation and maturation of B lymphocytes. It is the principal antibody producing form of B cells. In myeloma, the tumor cell has the appearance of plasma cells, that is, they are malignant plasma cells, sometimes referred to as myeloma.

Plasmacytoma

A localized tumor of malignant plasma cells either in a bone or in the other tissues of the body. If there is only one such area of bone involved, it is called “solitary plasmacytoma.” An area outside of bone may be referred to as “extramedullary plasmacytoma.”

Platelets

Small blood cells (about one-tenth the volume of red cells) that stick to the site of blood vessel injury, aggregate with each other and seal off the injured blood vessel to stop bleeding. “Thrombocyte” is a synonym for platelet and is often used as the prefix in terms describing disorders of platelets, such as thrombocytopenia or thrombocytopenia.

Red Cells

Blood cells that contain hemoglobin. Hemoglobin binds oxygen when red cells pass through the lungs and releases it to the tissues of the body. The red cells make up a little less than half the volume of blood in healthy individuals.

Refractory Disease

Disease that has not responded to initial therapy or relapsed disease that does not respond to subsequent treatment. The latter instance is also called “relapsed and refractory disease.” Refractory disease may be nonresponding progressing refractory disease or nonresponding nonprogressing refractory disease.

Relapsed Disease

Disease that initially responded to therapy but has begun to progress.

Remission

A disappearance of evidence of a disease, usually as a result of treatment. The terms “complete” and “partial” are used to modify the term “remission.” Complete remission means all evidence of the disease is gone. Partial remission means the disease is markedly improved by treatment, but residual evidence of the disease is present. Remission may also be discussed in terms of a complete hematologic response. This term refers to a marked decrease of myeloma cell numbers in marrow and abnormal immunoglobulin in blood and urine; also, the hemoglobin concentration, white cell count and platelet count are at or near normal. In a complete cytogenetic response, sensitive laboratory tests reveal no myeloma cells in the marrow and no detectable abnormal immunoglobulin in blood and urine.

Serum

The liquid portion of the blood after it clots. A blood sample is collected in sterile tubes without an anticoagulant and allowed to clot. The liquid portion or serum is removed after the clot forms. Most chemical tests are performed using serum.

Spleen

An organ of the body located in the left upper portion of the abdomen under the left side of the diaphragm. It contains clusters of lymphocytes and also filters the blood of old or worn-out cells. Enlargement of the spleen is referred to as “splenomegaly.” Removal of the spleen by surgery is referred to as “splenectomy.” Removal of the spleen is used to treat certain diseases. Other organs, such as the lymph nodes and liver, can perform most of the functions of the spleen.

Stem Cell

A primitive cell found mainly in marrow that leads to the development of red cells, white cells and platelets (see Hematopoiesis). Some stem cells leave the marrow and circulate in the blood. Using special techniques, the stem cells in blood can be collected, preserved by freezing and later thawed and used for stem cell therapy.

Stem Cell Transplantation (see Allogeneic Stem Cell Transplantation, Autologous Stem Cell Infusion, Nonmyeloablative Allogeneic Stem Cell Transplantation)

White Cells

A synonym for leukocytes. There are five major types of white cells in the blood: neutrophils, eosinophils, basophils, monocytes and lymphocytes.

Resources

The Leukemia & Lymphoma Society Patient Publications

Acute Myelogenous Leukemia; 2006.

Blood and Marrow Stem Cell Transplantation; 2005.

Choosing and Communicating With a Cancer Specialist Fact Sheet; 2002.

Myeloma: A Guide for Patients and Caregivers; 2006.

Understanding Clinical Trials for Blood Cancers; 2006.

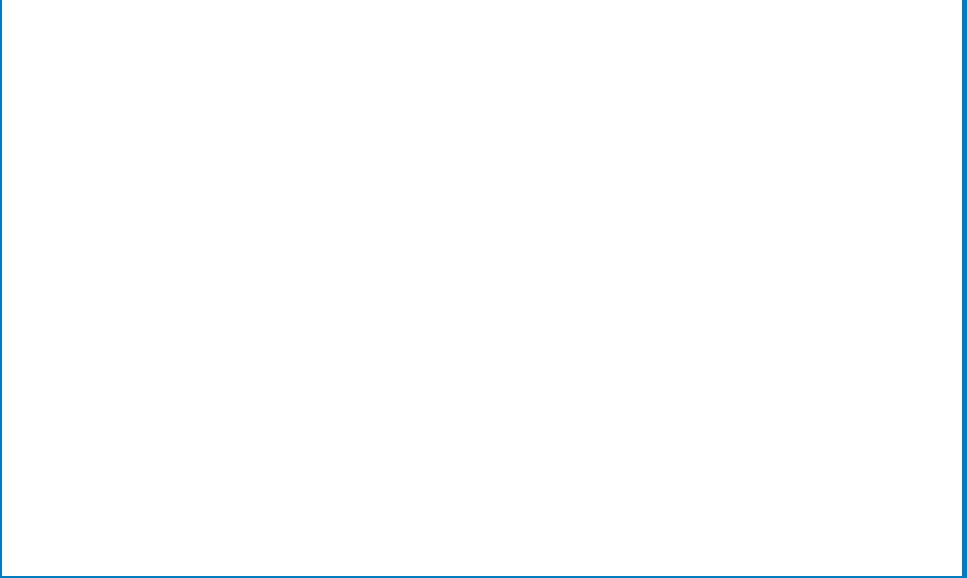
Understanding Drug Therapy and Managing Side Effects; 2006.

Waldenström Macroglobulinemia Fact Sheet; 2004.

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*Our Mission: Cure leukemia, lymphoma,
Hodgkin's disease and myeloma, and improve the
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