

“Until There is a Cure... There is the IMF.”

Published by the International Myeloma Foundation (IMF)

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Dedicated to improving the quality of life of myeloma patients while working towards prevention and a cure.



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Patient Handbook



International Myeloma Foundation

Multiple Myeloma

Cancer of the Bone Marrow



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2007 Edition

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INTRODUCTION

Multiple myeloma is a bone marrow cancer. Despite periodic media attention, general public awareness about myeloma is low. The intent of this booklet is to provide basic information and suggestions about how to cope with this disease.

The International Myeloma Foundation (IMF) is committed to providing education and support for patients and families. This handbook provides a basic understanding of myeloma sufficient to allow patients to make informed decisions about treatment choices. The handbook is supplemental to the information given by the doctor. Caregivers, family, and friends may also find the information useful.

Although there is currently no cure for myeloma, it is an eminently treatable disease. Many patients go on to lead full lives for years, even decades, after diagnosis. With increasing research, the overall outlook for patients is improving steadily. Knowing more about the disease, and understanding what can be done to help, reduces anxieties and makes it easier to come to terms with the diagnosis.

Myeloma is a very individual disease. Myeloma is often slow moving, but can sometimes be more aggressive. While the doctor assesses each particular situation and recommends the best approach, the patient plays a central role in helping make these individual treatment decisions. It is important that patients and their families be well informed, ask questions, and give serious thought to alternative strategies or options.

WHAT IS MYELOMA?

Myeloma is literally an “oma,” or tumor, involving the “myelo,” or blood-producing cells in the bone marrow. The cells that are affected are plasma cells (a type of white blood cell), which are our antibody- (immunoglobulin-) producing cells. A malignant or cancerous plasma cell is called a myeloma cell. Myeloma is called “multiple” since there are frequently multiple patches or areas in the bones where tumors or lesions have developed. A single lesion is called a solitary plasmacytoma.

Myeloma affects the places where bone marrow is normally active in an adult. This marrow is in the hollow area within the bones of the spine, skull, and pelvic bones, the rib cage, and the areas around the shoulders and hips. The areas usually not affected are the extremities: that is the hands, feet, and lower arm/leg regions. This is very important since the function of these critical areas is usually fully retained.

Myeloma can be discovered at a precancerous stage (see Table 1). In some cases the myeloma cells build up very slowly in the bone marrow. The very earliest stage is called **MGUS**. This is not a cancer, but a condition called **Monoclonal Gammopathy of Undetermined Significance**. In MGUS, the myeloma cells constitute fewer than 10% of the bone marrow cells. The risk of transition from MGUS to active myeloma is very low: only a 1% chance each year of follow-up. Even if the myeloma cells are at a higher level of 10–30% of the total bone marrow, the growth rate can be very slow and represent **indolent/smoldering or asymptomatic myeloma**. Both MGUS and indolent myeloma can change very slowly over a period of years and do not require active treatment. It is very important to establish the correct diagnosis distinguishing MGUS and indolent myeloma from active or symptomatic myeloma, which does require treatment.

TABLE 1: DEFINITIONS OF MGUS AND MYELOMA

<i>STANDARD NAME</i>	<i>PROPOSED NEW NAME</i>	<i>DEFINITION</i>
MGUS (Monoclonal Gammopathy of Undetermined Significance)	MGUS (i.e., no change in name)	<ul style="list-style-type: none"> • Monoclonal protein present • No underlying disease state.
SMOLDERING OR INDOLENT MYELOMA	ASYMPTOMATIC MYELOMA	<ul style="list-style-type: none"> • Higher level of disease than MGUS, but still no symptoms or organ damage.*
MYELOMA	SYMPTOMATIC MYELOMA	<ul style="list-style-type: none"> • Monoclonal protein present, and • One or more “CRAB” features of organ damage.*

*ORGAN DAMAGE CLASSIFIED AS “CRAB”

C – calcium elevation (>10 mg/L)

R – renal dysfunction (creatinine >2 mg/dL)

A – anemia (hemoglobin <10 g/dL)

B – bone disease (lytic lesions or osteoporosis)

ONE OR MORE required for diagnosis of SYMPTOMATIC MYELOMA

BASIC FACTS ABOUT MYELOMA

Although several things appear capable of causing or triggering myeloma, all of the details are not known. Things associated with an increased risk of myeloma and related diseases are toxic chemicals (for example, agricultural chemicals and Agent Orange used in Vietnam), radiation (including atomic radiation), and several viruses including human immunodeficiency virus (HIV), hepatitis viruses, human herpes virus 8 (HHV-8), and others. There is not a strong family tendency for myeloma; a few families do, however, have an increased predisposition to the disease.

Myeloma occurs in adults. The average age of onset of myeloma is in one’s early 60s. Only 5–10% of patients are under the age of 40 years. It occurs more commonly in men and in some racial groups, such as African-Americans.

There will be an estimated 19,000 new cases of myeloma in the U.S. in 2007. The incidence ranges from ~0.5–1/100,000 among Asians to as high as ~10–12/100,000 among African-American men. At any one time there are over 50,000 myeloma patients undergoing treatment for their disease in the U.S.

WHY MYELOMA HAS TO BE TREATED

Myeloma, if left untreated, can cause bone damage, elevated blood calcium, low blood counts (especially anemia), predisposition to infection, and kidney damage. Because the bones of the spine are often affected and because myeloma proteins produced by myeloma cells can damage nerves, it is common to have spine and nerve problems that may require urgent attention.

In getting treatment for myeloma, it is important to distinguish between urgent problems such as bone damage, infection, kidney damage, or nerve pressure, which need immediate attention, and overall planning to treat the disease. Sometimes urgent care cannot and should not be delayed. However, early consultation with a hematologist/oncologist familiar with myeloma is encouraged. For example, options of emergency surgery versus radiation therapy can be discussed. Also, making sure that all options are kept open for the future is an important consideration.

Once urgent matters have been dealt with, overall plans can be discussed in more detail. Frequently there is time to seek a second opinion or consultation with an expert to be assured that all options are carefully reviewed. Even if plans seem to be clear, if there are any concerns, questions, or doubts, it is better to have these aired sooner rather than later. Having a mutually agreed-upon plan with your physician for ongoing treatment is tremendously important.

WHAT CAUSES THE MEDICAL PROBLEMS WITH MYELOMA

Healthy plasma cells produce immunoglobulins, which are complex proteins that we call “antibodies.” Myeloma cells cannot make functioning antibodies, but instead produce a clonal protein, or immunoglobulin, that is known as a “monoclonal protein.” **All of the medical problems related to myeloma are caused by the build-up of myeloma cells (see Table 2).** Unlike other types of cancer, myeloma can present patients with many strange complications because **myeloma cells do not just produce tumors, they release many proteins and other chemicals** into the local micro-environment of the bone marrow and directly into the blood stream.

- **Local effects in the bone marrow.** The effects in the bone marrow include a reduction in blood cell production and damage to the surrounding bone. The net results are the many common features of myeloma, such as anemia, predisposition to infection, bone pain, bone fractures, and elevated blood calcium.
- **Effects outside the bone marrow.** The effects outside the bone marrow are mostly due to the monoclonal protein produced by the myeloma cells. As the myeloma cells build up in the bone marrow, the immunoglobulin or antibody protein that is specific to the myeloma is released into the blood circulation. This specific immunoglobulin protein or monoclonal protein produced by myeloma cells can cause tissue damage at distant sites; for example, kidney damage is not uncommon. The protein can interfere with blood clotting and/or circulation, and can potentially cause other organ or tissue damage.

Treatment for myeloma reduces tumor growth as well as these diverse effects from myeloma proteins and chemicals.

TABLE 2: MEDICAL PROBLEMS RELATED TO MYELOMA

<i>Effects Of Increased Myeloma Cells In Bone Marrow</i>	<i>Cause</i>	<i>Impact On Patient</i>
Anemia	Decrease in number and activity of red blood cell-producing cells.	<ul style="list-style-type: none"> • Fatigue • Weakness
High protein level (in blood and/or urine)	Abnormal or monoclonal protein produced by the myeloma cells is released into the bloodstream and can pass into the urine (where it is called Bence Jones protein).	<ul style="list-style-type: none"> • Sluggish circulation • Possible kidney damage
Bone Damage: <ul style="list-style-type: none"> • Thinning (osteoporosis) or • Areas of more severe damage cause lytic lesions, fracture or collapse of a vertebra 	The myeloma cells activate osteoclast cells, which destroy bone, and block osteoblast cells, which normally repair damaged bone.	<ul style="list-style-type: none"> • Bone pain • Bone swelling • Fracture or collapse of a bone
High blood calcium	Release of calcium from damaged bone into bloodstream	<ul style="list-style-type: none"> • Mental confusion • Dehydration • Constipation • Fatigue • Weakness
Reduced normal immune system function against infection	The myeloma cells block production of normal antibodies against infection	<ul style="list-style-type: none"> • Susceptibility to infection • Delayed recovery from infection

DIFFERENT TYPES OF MYELOMA

There are different types and subtypes of myeloma. These are based on the type of immunoglobulin (protein) produced by the myeloma cell. Normally, the various immunoglobulins have different functions in the body. Each immunoglobulin protein is made up of two heavy chains and two light chains. (See Figure 1). There are five types of heavy protein chains: G, A, D, E, and M. There are two types of light protein chains: k(K) and l(λ). The typing of myeloma (done with a test called “immunofixation”) identifies both the heavy and light chains. Most myeloma patients, about 65%, have IgG (iG) type myeloma with k or l light chains. The next most common type is IgA (iA) type myeloma, also with either k or l light chains. (See Table 3). IgM, IgD, and IgE myelomas are quite rare.

FIGURE 1: IMMUNOGLOBULIN STRUCTURE



Approximately 30% of patients produce light chains in the urine (such as kappa light chains) as well as heavy and light chains (such as IgG kappa) in the blood. In about 10% of patients, the myeloma cells produce only light chains and no heavy chains. This is called “light chain” or “Bence Jones” myeloma. Rarely (in about 1–2% of patients) the myeloma cells produce very little or no monoclonal protein of any type. This is called “non-secretory” myeloma. However, a recently developed test called the Freelite® test (serum free light chain assay) can detect minute amounts of light chains in the blood of most of these patients.

TABLE 3: TYPES OF MYELOMA

HEAVY CHAIN*	LIGHT CHAIN**	MYELOMA TYPE
IgG: (immunoglobulin G)	kappa (K) or lambda (λ or L)	IgGK or IgGλ immunoglobulin G with kappa or lambda light chains
IgA: (immunoglobulin A)	kappa (K) or lambda (λ or L)	IgAK or IgAλ immunoglobulin A with kappa or lambda light chains

*Rarer types are IgD, IgE and IgM

**There are only 2 light chain types

There are subtle differences in the behaviors of different types of myeloma. IgG myeloma has the usual features of myeloma. The IgA type can sometimes be characterized by tumors outside of the bone. The IgD type can be accompanied by plasma cell leukemia and more frequently causes kidney damage. The light chain or Bence Jones myelomas are the most likely to cause kidney damage and/or lead to deposits of light chains in the kidneys and/or on nerves or other organs. Depending upon the characteristics of the light chain deposits, this condition is called either amyloid or light chain deposition.

STAGING OF MYELOMA

When myeloma is diagnosed, the amount of myeloma in the body varies from patient to patient. This is called the stage of myeloma. The previously most commonly used staging system is shown in Table 4, and shows the correlation between the extent of the myeloma and the damage caused, such as bone disease or anemia. The outlook is better when treatment is started early and bone disease or other complications can be prevented. The most current staging system is shown in Table 5, and is the result of the collaboration of more than twenty research institutions world-wide

TABLE 4: THE DURIE AND SALMON STAGING SYSTEM

STAGE	CRITERIA	MEASURED MYELOMA CELL MASS (myeloma cells in billions/m ²)*
STAGE I (low cell mass)	<i>All of the following:</i> <ul style="list-style-type: none"> • Hemoglobin value >10g/dL • Serum calcium value normal or <0.5mg/dL • Bone x-ray, normal bone structure (scale 0), or solitary bone plasmacytoma only • Low M-component production rates IgG value <5g/dL IgA value <3g/dL • Urine light chain M-component on electrophoresis <4g/24h 	600 billion*
STAGE II (intermediate cell mass)	<i>Fitting neither Stage I nor Stage III</i>	600 to 1,200 billion* *myeloma cells in whole body
STAGE III (high cell mass)	<i>One or more of the following:</i> <ul style="list-style-type: none"> • Hemoglobin value <8.5g/dL • Serum calcium value >12mg/dL • Advanced lytic bone lesions (scale 3) • High M-component production rates IgG value >7g/dL IgA value >5g/dL • Bence Jones protein >12g/24h 	>1,200 billion*
SUBCLASSIFICATION (either A or B)	<ul style="list-style-type: none"> • A: relatively normal renal function (serum creatinine value) <2.0 mg/dL • B: abnormal renal function (serum creatinine value) >2.0 mg/dL <i>Examples: Stage IA (low cell mass with normal renal function) Stage IIIB (high cell mass with abnormal renal function)</i>	

**TABLE 5: INTERNATIONAL STAGING SYSTEM (ISS)
Staging for Multiple Myeloma**

STAGE	VALUES
STAGE 1	$\beta 2M < 3.5$ ALB ≥ 3.5
STAGE 2	$\beta 2M < 3.5$ ALB < 3.5 or $\beta 2M \ 3.5 - 5.5$
STAGE 3	$\beta 2M > 5.5$

Note: $\beta 2M$ = Serum $\beta 2$ microglobulin in mg/dL
ALB = Serum albumin in g/dL

Several tests (assessments of so-called prognostic factors, from the Greek words that mean “knowing ahead”) can be used to assess how aggressive the myeloma is in a given patient. In general, higher or abnormal test results indicate more active myeloma, and possibly, less likelihood of having a long response with treatment (Table 6).

TABLE 6: PROGNOSTIC FACTORS

TEST	SIGNIFICANCE
• Serum $\beta 2$ microglobulin (S $\beta 2M$)	The higher the level the more advanced the stage.
• Serum Albumin (S. Alb)	The lower the level the higher the stage.
• C-reactive protein (CRP)	Increased with active disease
• Serum LDH (lactate dehydrogenase)	Increased with active disease
• Abnormal chromosomes on bone marrow cytogenetics and FISH (Fluorescent In Situ Hybridization)	Chromosome 13 deletions (13 q-) associated with shorter duration of remission as well as other chromosomal abnormalities

TESTING AT DIAGNOSIS

Table 7 summarizes the typical testing required at the time of diagnosis (baseline testing).

TABLE 7: BASELINE TESTING

TEST	PURPOSE
<p>Bone marrow biopsy Special testing is done to assess prognosis (e.g., chromosomes, immune typing, staining for amyloid)</p>	<p>This is the single most critical test to determine the percentage of myeloma cells in the bone marrow. In Stage I disease or for a solitary plasmacytoma, direct biopsy of the tumor mass is performed.</p> <p>Chromosome analysis (cytogenetic testing) can reveal good or poor chromosome features using direct and/or FISH analysis.</p>
<p>Blood Testing</p> <ol style="list-style-type: none"> Complete blood count (CBC) Chemistry panel Special protein testing <ul style="list-style-type: none"> Serum protein electrophoresis (SPEP) Immunofixation FREELITE® test 	<ul style="list-style-type: none"> To assess presence/severity of anemia To assess for low white cell count To assess for low blood platelet count <ul style="list-style-type: none"> Particularly important to assess kidney function (creatinine and BUN), calcium level, and LDH <p>This shows the presence of the monoclonal myeloma protein.</p> <ul style="list-style-type: none"> The amount of the abnormal myeloma protein as well as the normal albumin protein level are measured. Shows the type of myeloma protein [i.e., heavy chain (G, A, D or E), light chain, kappa (K), lambda (L/λ)]. Can be used to measure the amount of free kappa or lambda if no SPEP or UPEP abnormality discovered.

TABLE 7: BASELINE TESTING CONT'D

TEST	PURPOSE
Urine Testing Special protein testing similar to serum above: <ul style="list-style-type: none"> • Urine Protein Electrophoresis (UPEP) • Immunofixation 	Shows the presence, amount, and type of abnormal myeloma protein in urine.
Bone Testing X-Rays MRI CT Scan Nuclear Medicine Scans FDG/PET Scan Bone Density Testing	To assess the presence, severity, and location of any areas of bone damage. X-rays are still the gold standard in searching for myeloma bone damage. A full skeletal survey for myeloma using a series of X-rays is needed to show loss or thinning of bone (osteoporosis or osteopenia caused by myeloma bone destruction), lytic lesions, and/or any fracture or collapse of bone. Used when X-rays are negative and/or for more detailed testing of particular areas such as spine and/or brain. Can reveal the presence and distribution of disease in the bone marrow when X-rays show no bone damage. Can also reveal disease outside of bone, which may be pressing on nerves and/or spinal cord. Used when X-rays are negative and/or for more detailed testing of particular areas. Especially useful for detailed evaluation of small areas of possible bone damage or nerve pressure. Routine bone scans used for other cancers. <i>Not useful in myeloma and should not be performed.</i> A much more sensitive Whole Body scanning technique. Useful for disease monitoring, especially for non-secretory disease Helpful to assess the severity of diffuse bone loss in myeloma and to measure the serial improvement with bisphosphonate therapy.

TREATMENT OF MYELOMA

Deciding about treatment is the most important initial decision. As already emphasized, baseline testing, staging, and prognostic classification are essential. Treatment is recommended for active or symptomatic myeloma. The urgency of treatment depends upon the exact problems faced by an individual patient.

TABLE 8: GOALS OF MYELOMA TREATMENT

TYPE OF TREATMENT	OBJECTIVE	EXAMPLES	TIME TO DECIDE
Stabilizing	Countering the life-threatening disruptions to body chemistry and the immune system	<ul style="list-style-type: none"> • Plasmapheresis to thin the blood and avoid stroke • Hemodialysis when kidney function is impaired • Drugs to reduce hypercalcemia (may include chemotherapy) 	Hours to Days
Palliative	Relieving discomfort and increasing the patient's ability to function	<ul style="list-style-type: none"> • Radiation to stop bone destruction • Erythropoietin to relieve anemia • Orthopedic surgery to repair and/or strengthen bone 	Days to Months
Remission-Inducing	Improving symptoms, slowing or arresting the course of the disease	<ul style="list-style-type: none"> • Therapy to kill malignant cells throughout the body. • Radiation to kill malignant cells at a tumor site 	Weeks to Months
Curative	Permanent remission*	<ul style="list-style-type: none"> • Bone marrow transplants as a means of delivering high-dose chemotherapy 	Weeks to Months

* Although never achieved and confirmed, permanent remission remains the objective of many experimental treatments.

INITIAL OR FRONTLINE THERAPY

It is important for patients to set aside plenty of time to discuss the options with their hematologist or hematologist/oncologist. In addition to the baseline test results, one must consider:

- How much impact does the myeloma have on day-to-day functioning?
- Will the patient be able to work? Are plans in place to be off work as needed to undertake treatment?
- How old is the patient? Are there any other medical problems?
- Can the patient tolerate chemotherapy?
- Is high-dose chemotherapy with stem cell transplant an option?
- How well and how rapidly you respond to treatment varies from patient to patient.
- All treatment decisions do not need to be made on “Day 1.”
- It is generally best to keep the door open for stem cell transplantation if you feel it can be a future option for you.
- Although frontline clinical trials are available, you have to be completely comfortable that you will be randomly assigned to one treatment versus another. You may become “locked in” to future randomization and treatments. Make sure you understand the full scope of the protocol.
- **If one treatment does not work, this does not mean that another treatment cannot work extremely well and give an excellent remission.**

TABLE 9: FRONTLINE TREATMENT OPTIONS

<i>FRONTLINE THERAPY</i>	<i>ADVANTAGES</i>	<i>DISADVANTAGES</i>
Dexamethasone plus Thalidomide	<ul style="list-style-type: none"> • An oral approach producing remissions in 70% of patients • New gold standard for frontline induction 	<ul style="list-style-type: none"> • Neuropathy and deep vein thrombosis (blood clots) are potential concerns
Dexamethasone alone	Pulse dexamethasone alone provides a substantial percentage of the benefit of the full VAD	Dexamethasone on an intensive schedule can be poorly tolerated
MP (Melphalan/ Prednisone)	<ul style="list-style-type: none"> • Taken by mouth • Well tolerated • Produces excellent remissions in about 60% of patients • Physicians very familiar with protocol 	<ul style="list-style-type: none"> • Can cause bone marrow stem cell damage and therefore reduce chances of successful stem cell transplant • Full benefit occurs slowly over several months • Not ideal if prompt response required and/or if stem cell transplant planned
Dexamethasone plus Melphalan	In combination with melphalan, produces more rapid benefit than MP	The use of melphalan up front damages stem cells
VAD (Vincristine/ Adriamycin/ Dexamethasone)	<ul style="list-style-type: none"> • Produces remission in 70% of patients • Doesn't damage normal stem cells • Can be basis for stem cell transplant 	<ul style="list-style-type: none"> • Needs central line catheter for IV administration The catheter can trigger infection and blood clot complications • Vincristine can cause nerve damage
VELCADE® alone, with dexamethasone, and/or other agents, including Revlimid® and Doxil®	Shows remarkable benefit Stem cell transplant still possible	Produces neuropathy that is partially or completely reversible in this setting

TABLE 9: FRONTLINE TREATMENT OPTIONS TABLE CONT'D

<i>FRONTLINE THERAPY</i>	<i>ADVANTAGES</i>	<i>DISADVANTAGES</i>
<p>A variety of other therapies are sometimes used such as Cytosan® (cyclophosphamide) and Etoposide® (VP-16). Potential combinations include:</p> <ul style="list-style-type: none"> • VBMCP (M2 protocol) • VMCP/VBAP (SWOG protocol) • ABCM (UK MRC protocol) • CVAD (pre stem-cell protocol) 	<ul style="list-style-type: none"> • Combinations provide a more aggressive approach, if deemed necessary • Symptoms of active disease may be controlled more rapidly and quality of first remission may be better 	<ul style="list-style-type: none"> • More side effects than simpler regimens • No added longer-term benefit • Side effects may both reduce quality of life and compromise eligibility for new protocols

Further details about treatment options are available in other IMF publications. To order these, please contact the IMF or visit our website at www.myeloma.org.

SUPPORTIVE CARE

Treatments are available to alleviate the physical and emotional impact of the disease. Early use of supportive care measures is just as important as initiating frontline therapy.

TABLE 10: SUPPORTIVE CARE

<i>SYMPTOM</i>	<i>TREATMENT</i>	<i>COMMENTS</i>
Fatigue and weakness due to anemia	<ul style="list-style-type: none"> • Blood transfusion (packed red blood cells: leukoreduced, virus screened) if anemia severe • Erythropoietin if anemia mild to moderate 	The treatments are simple, usually highly beneficial, and improve feelings of well being.
Bone Pain	<ul style="list-style-type: none"> • Bisphosphonate (e.g., Aredia® 90mg IV over 2-4 hrs monthly; Zometa® 4 mg IV over 15-45 minutes monthly) • Pain medication as needed (e.g., Tylenol®, oral morphine derivatives, Fentanyl® “Pain Patch”) 	Relief of bone pain is important in itself and improves physical activity, which in turn promotes bone strength and healing and improves emotional well-being. Potential damage to kidneys and jaws, though rare, can result from chronic bisphosphonate therapy. Awareness is the key to prevention.
Fever and/or evidence of infection	<ul style="list-style-type: none"> • Appropriate antibiotics • Neupogen® if necessary to boost low white blood cell count • Intravenous gamma globulin for severe infections • Tests as needed to diagnose the exact type of infection (except for dangerous biopsies/cultures) should be performed. 	Although antibiotics should be selected and used with care, it is extremely important that infections be brought under control promptly. Having an antibiotic on hand for emergency use (especially if traveling) is recommended.

Beyond the management of specific symptoms, a whole range of supportive measures is critically important:

- **Physical activity** – Patients should check with their physicians to clarify if full physical activity is feasible or if adjustments need to be made because of bone disease and particular areas of bone damage. Usually, some physical activity such as planned walking or swimming, flexibility and strengthening exercises, and/or a personalized yoga program, can be set up.
- **Diet** – No specific diet has been developed for myeloma patients. This is an area of ongoing research. In general, “healthy diet” recommendations from other disease settings such as cardiac disease and cancer in general (e.g., breast cancer) can be utilized. Caution should be used in two areas:
- **Vitamin C** – High doses (i.e., >1000 mg/day) may be counter-productive in myeloma and increase the risk of kidney damage.
- **Herbal and vitamin supplements** – Talk to your doctor about using supplements along with chemotherapy or other drug treatment. Drug interactions can create medical problems.
- **Mental health** – Your mental health is critical as you move forward with planned treatment. Make sure you are comfortable with the treatment planned. Schedule an appointment with a mental health professional if you believe that you might be depressed, or if others are concerned that you might be depressed.
- **Regular sleep** – This is very important for your immune system.
- **Make adjustments** – As much as possible, reduce or eliminate stress in job, family, or social situations. Management of the myeloma is the top priority until remission and/or a stable situation has been achieved.

IF FRONTLINE THERAPY IS NOT WORKING

There are numerous treatment options beyond the scope of this introductory handbook. Emerging new therapies are increasingly available and can provide major benefit.

Please visit the IMF website at www.myeloma.org for more information and regular updates or call the IMF at 800-452-CURE (2873).

QUESTIONS TO ASK YOUR DOCTOR

Treatment decisions are critically important to the survival and quality of life of the myeloma patient. To make an informed decision, the patient needs to have the facts. Some patients want to discuss all aspects of their situation, treatment, and prognosis. Others just want to know what to do next. Most doctors are sensitive to this and will vary their approach based on what they perceive to be the patient’s wishes.

We encourage patients to be explicit about how deeply they want to get into the details of the treatment decision. And, no matter how comfortable the patient feels with a doctor, it is generally good practice to get more than one opinion before proceeding.

1. Get a complete description of the treatment program:

- What exactly is the treatment?
- What are the objectives of the treatment?

- **Over what period will the treatment be given?**
- **What is involved?** How often must the patient visit a medical facility? Is hospitalization required or a probability? What is the likely impact on the patient's ability to function (i.e., work and play)? How do people feel before, during, and after treatment? How do they look? What are typical recovery time frames?
- **What follow-up or maintenance programs are required?**
- **What will the treatment program cost?** Will it be covered by health insurance?

2. How well has this treatment worked for others in similar situations?

Effectiveness is measured in many different ways:

- **How much experience is there with the treatment?** How many patients have received it? How long have those patients been followed after the treatment?
- **What are the odds of achieving a complete or partial remission?** Which factors suggest better or worse odds?
- **How long have the patients' remissions lasted?** Which factors correlate to long or to short remissions?
- **What would be the options in the event of a relapse?** (These options may change in the interim.)
- **What are reasonable expectations for relieving symptoms such as bone pain, pathological fractures, anemia, fatigue, hypercalcemia?** What are the factors that predict how well these treatments will work for symptoms?
- **How long have people who have received the treatment survived?** For newer treatments, how many of the original group of patients are still alive?

3. Like most cancer treatments, myeloma treatments generally use strong drugs and other measures aimed at destroying malignant cells and/or rebalancing body chemistry. **Typically, there are side effects.** Some manifest themselves

during treatment. Others may show up well after the treatment is completed.

- **What side effects have been observed in patients receiving the treatment?** When do they typically occur? In what percentage of patients do they occur? How serious are the side effects? Are they life threatening? Are they painful? Are they permanent? How long do they last?
 - **Are there treatments for the side effects?** Do the treatments for the side effects have side effects?
4. **There are always alternatives.** You need to ask all of these questions for each of the alternatives:
- What are the alternatives to the recommended treatment?
 - What are the relative pros and cons of the alternatives?
 - What are the pros and cons of the alternative treatments vs. no treatment?

Because the disease is rare, there are a limited number of practitioners and centers specializing in myeloma. It is very common for a myeloma patient to seek a second opinion from a specialist at a research center while continuing to rely on a local referring physician to administer and monitor treatment.

Making good decisions about treatment requires resourcefulness, careful questioning, serious thought, and courage. But, most of all, it requires that the patient and his/her support group take charge of the process.

Because there is no known cure, because there are no guarantees, because every individual is different, the ultimate decision depends on the preferences and priorities of the patient.

TERMS & DEFINITIONS

Accrual: The process of enrolling patients in a clinical research study (trial), or the number of patients already enrolled in a trial or anticipated to enroll in a trial.

Acute: A sudden onset of symptoms or disease.

Albumin: Simple water-soluble proteins that are found in blood serum and many other animal and plant tissues.

Alkylating Agent: A chemotherapeutic agent such as melphalan or cyclophosphamide. Alkylating refers to the way in which these agents cross-link the DNA of myeloma cells and block cell division.

Allogeneic: See “Transplantation.”

Amyloidosis: A condition in which myeloma light chains (Bence Jones proteins) are deposited in tissues and organs throughout the body. This occurs more commonly with lambda versus kappa Bence Jones proteins. In patients with amyloidosis, the light chain proteins bind to certain tissues such as heart, nerves and kidney rather than being excreted out of the body through the kidneys.

Analgesic: Any drug that relieves pain. Aspirin and acetaminophen are mild analgesics.

Analog: A chemical compound that is structurally similar to another but differs slightly in composition.

Anemia: A decrease in the normal number of red blood cells, usually below 10 g/dL with over 13-14 g/dL being normal. Myeloma in the bone marrow blocks red blood cell production, causing shortness of breath, weakness, and tiredness.

Anesthesia: Loss of feeling or awareness. Local anesthesia causes loss of feeling in a part of the body. General anesthesia puts the person to sleep.

Angiogenesis: Blood vessel formation, which usually accompanies the growth of malignant tissue, including myeloma.

Angiogenesis inhibitors: Compounds that attempt to cut off the blood supply to tumors.

Antibiotics: Drugs used to treat infection.

Antibody: A protein produced by certain white blood cells (plasma cells) to fight infection and disease in the form of antigens such as bacteria, viruses, toxins, or tumors. Each antibody can bind only to a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies disable antigens directly. Others make the antigen more vulnerable to destruction by other white blood cells.

Anti-emetic agent: A drug that prevents or controls nausea and vomiting.

Antifungal agent: A drug used to treat fungal infections.

Antigen: Any foreign substance (such as a bacteria, virus, toxin or tumor) that, when introduced into or arising in the body, causes the immune system to produce natural antibodies.

Antineoplastic agent: A drug that prevents, kills, or blocks the growth and spread of cancer cells.

Appendicular skeleton: The long bones (i.e., arms and legs), which are attached to spine, chest and pelvis.

Apoptosis: A normal cellular process involving a genetically programmed series of events leading to the death of a cell.

Aspiration: The process of removing fluid or tissue, or both, from a specific area.

Asymptomatic myeloma: Myeloma that presents no signs or symptoms of disease. Also called indolent, smoldering, or early myeloma.

Axial skeleton: The skull, spine, and pelvis region of the skeleton.

B cells: White blood cells that develop into plasma cells in the bone marrow and are the source of antibodies. Also known as B lymphocytes.

Basophil: A type of white blood cell. Basophils are granulocytes.

Bence Jones: A myeloma protein present in urine. The amount of Bence Jones protein is expressed in terms of grams per 24 hours. Normally a very small amount of protein (<0.1 g/24 h) can be present in the urine, but this is albumin rather than Bence Jones protein. The presence of any Bence Jones protein is abnormal.

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. MGUS is a benign condition.

Beta 2 microglobulin (β 2M): A small protein found in the blood. High levels occur in patients with active myeloma. Low or normal levels occur in patients with early myeloma and/or inactive disease. Approximately 10% of patients have myeloma that does not produce β 2M. For these patients, β 2M testing cannot be used to monitor the disease. At the time of relapse, β 2M can increase before there is any change in the myeloma protein level. Therefore, 90% of the time, β 2M is very useful for determining disease activity.

Biopsy: The removal of a sample of tissue for microscopic examination to aid in diagnosis.

Bisphosphonate: A type of drug that binds to the surface of bone where it is being resorbed (or destroyed) and protects against osteoclast activity.

Blood cells: Minute structures produced in the bone marrow; they include red blood cells, white blood cells, and platelets.

Blood count: The number of red blood cells, white blood cells, and platelets in a sample of blood.

Bone marrow: The soft, spongy tissue in the center of bones that produces white blood cells, red blood cells, and platelets.

Bone marrow aspiration: The removal, by a needle, of a sample of fluid and cells from the bone marrow for examination under a microscope.

Bone marrow biopsy: The removal, by a needle, of a sample of tissue from the bone. The cells are checked to see whether they are cancerous. If cancerous plasma cells are found, the pathologist estimates how much of the bone marrow is affected. Bone marrow biopsy is usually done at the same time as bone marrow aspiration.

Bone remodeling: The normal coordination (coupling) between osteoclast cells (which resorb or destroy bone) and osteoblast cells (which create new bone matrix) to maintain a balanced state of bone production and destruction.

BUN (Blood Urea Nitrogen): A measure of the urea level in the blood. Urea is cleared by the kidney. BUN is a laboratory blood test to assess how well the kidney is functioning. Diseases, such as myeloma, which compromise kidney function, frequently lead to increased levels of BUN.

Calcium: A mineral found mainly in the hard part of bone matrix or hydroxyapatite.

Cancer: A term for diseases in which malignant cells divide without control. Cancer cells can invade nearby tissues and spread through the bloodstream and lymphatic system to other parts of the body.

Carcinogen: Any substance or agent that produces or stimulates cancer growth.

CAT or CT [Computerized (Axial) Tomography scan]: A test using computerized X-rays to create three-dimensional images of organs and structures inside the body, used to detect small areas of bone damage or soft tissue involvement.

Catheter: A tube that is placed in a blood vessel to provide a pathway for drugs or nutrients. A Central Venous Catheter is a special tubing that is surgically inserted into a large vein near the heart and exits from the chest or abdomen. The catheter allows medications, fluids, or blood products to be given and blood samples to be taken.

Cell: The basic unit of any living organism.

Cell differentiation: The process during which young, immature (unspecialized) cells take on individual characteristics and reach their mature (specialized) form and function.

Cell proliferation: An increase in the number of cells as a result of cell growth and cell division.

Chemotherapy: The treatment of cancer with drugs that kill all rapidly-dividing cells.

- **Combination chemotherapy** – The use of more than one drug given in a chemotherapy regimen during cancer treatment.

Chromosome: A strand of DNA and proteins in the nucleus of a cell. Chromosomes carry genes and function in the transmission of genetic information. Normally, human cells contain 46 chromosomes.

Chronic: Persisting over a long period of time.

Clinical: Involving direct observation of a patient.

Clinical trial: A research study of new treatment that involves patients. Each study is designed to find better ways to prevent, detect, diagnose, or treat cancer and to answer scientific questions.

- **Control group** – The arm of a randomized clinical trial that gets the standard treatment.
- **End Point** – What a clinical trial is trying to measure or find out; the goal of the trial. Typical end points include measurements of toxicity, response rate, and survival.
- **Experimental group** – The arm of a randomized trial that gets the new treatment.
- **Randomized clinical trial** – A research study in which subjects are randomly assigned to receive a particular treatment.
- **Phase I trial** – A trial designed to determine the MTD (maximum tolerated dose) of a new drug or a new combination of drugs that has never been tried in humans. It is usually the first human testing of a new treatment, although in phase I trials of combination therapies, the individual elements may already have been well tested. Patients in phase I trials must have advanced cancer that is refractory to any standard treatment. In a typical phase I trial, successive groups (“cohorts”) of 3 to 6 patients are given the treatment. All patients in a cohort get the same dose. The first cohort typically gets a very low dose, and the dose is raised in each subsequent cohort until a set number of patients experience DLT (dose limiting toxicity). The dose level used for the previous cohort is then taken to be the Maximum Tolerated Dose. This dose is then used in a phase II trial.
- **Phase II trial** – A trial designed to determine the response rate of a new therapy that has already been tested in phase I trials. Typically, 14 to 50 patients with one type of cancer are treated to see how many have a response. Patients are usually required to have advanced cancer that is refractory to any standard treatment, and in addition, they must have measurable disease. If results from a phase II trial are promising enough, the treatment may then be tested in a phase III trial. If the results are obviously much better than the standard treatment, then it may not be necessary to do a phase III trial, and the treatment may become standard based on phase II trial results.
- **Phase III trial** – A trial designed to compare two or more treatments for a given type and stage of cancer. The end point of a phase III trial is usually survival or disease-free survival. Phase III trials are usually randomized, so patients don’t choose which treatment they receive. A typical phase III trial has 50 to thousands of patients. Some phase III trials compare a new treatment that has had good results in phase II trials with an older, well known, standard treatment. Other phase III trials compare treatments that are already in common use. Some treatments in phase III trials may be available outside the clinical trial setting.

Creatinine: A small chemical compound normally excreted by the kidneys. If the kidneys are damaged, the serum level of creatinine builds up, resulting in an elevated serum creatinine. The serum creatinine test is used to measure kidney function.

Cyst: An accumulation of fluid or semisolid material within a sac.

Cytokine: A substance secreted by cells of the immune system that stimulates growth/activity in a particular type of cell. Cytokines are produced locally (i.e., in the bone marrow) and circulate in the bloodstream.

DEXA (Dual Photon X-ray Absorptiometry) study: Measures the amount of bone loss; the best measure of bone density.

Dexamethasone: A powerful corticosteroid given alone or with other drugs.

Diagnosis: The process of identifying a disease by its signs and symptoms.

Dialysis: When a patient’s kidneys are unable to filter blood, the blood is cleaned by passing it through a dialysis machine.

Disease-free survival: The length of time the patient survives without any detectable cancer.

DLT (Dose Limiting Toxicity): Side-effects that are severe enough to prevent giving more of the treatment.

DNA: The substance of heredity; a large molecule that carries the genetic information that cells need to replicate and to produce proteins.

Drug resistance: The result of cells’ ability to resist the effects of a specific drug.

Edema: Swelling; an abnormal accumulation of fluid in part of the body.

Efficacy: The power to produce an effect; in cancer research ‘efficacy’ refers to whether the treatment is effective.

Electrophoresis: A laboratory test in which a patient’s serum (blood) or urine molecules are subjected to separation according to their size and electrical charge. For myeloma patients, electrophoresis of the blood or urine allows both the calculation of the amount of myeloma protein (M-protein) as well as the identification of the specific M-spike characteristic for each patient. Electrophoresis is used as a tool both for diagnosis and for monitoring.

Enzyme: A substance that affects the rate at which chemical changes take place in the body.

Erythrocytes: Red blood cells (RBCs). RBCs carry oxygen to body cells and carbon dioxide away from body cells.

Erythropoietin: A hormone produced by the kidneys. Myeloma patients with damaged kidneys don't produce enough erythropoietin and can become anemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency. Synthetic erythropoietin is being used prophylactically before chemotherapy and as a supportive therapy after chemotherapy to avoid anemia.

Free light chains: A portion of the monoclonal protein of light molecular weight that can be measured in a sensitive assay, the Freelite® test.

Gene: A specific sequence of DNA or RNA; the biological unit of heredity located in a specific place on a chromosome and found in all cells in the body. When genes are missing or damaged, cancer may occur.

Gene therapy: Treatment that alters genes. Using genes to stimulate the immune system. In studies of gene therapy for cancer, researchers are trying to improve the body's natural ability to fight the disease and to make the tumor more sensitive to other kinds of therapy. Treatment focuses on replacing damaged or missing genes with healthy copies.

Genetic: Inherited; having to do with information that is passed from parents to children through DNA in the genes.

Graft-versus-host disease (GVHD): A reaction of donated bone marrow against the recipient's own tissue.

Granulocyte: A type of white blood cell that kills bacteria. Neutrophils, eosinophils, and basophils are granulocytes.

Hematocrit (Hct): The percentage of red blood cells in the blood. A low hematocrit measurement indicates anemia.

Hematologic: Originating in the blood, or disseminated by the circulation or through the bloodstream.

Hematologist: A doctor who specializes in the problems of blood and bone marrow.

Herpes simplex: A common virus, it causes sores often seen around the mouth, commonly called cold sores.

Herpes zoster: A virus that settles around certain nerves in patients who have previously had a chicken pox (varicella) infection, causing blisters, swelling, and pain. This condition is also called shingles.

Hormones: Chemicals produced by various glands of the body that regulate the actions of certain cells or organs.

Human leukocyte antigen (HLA) test: A blood test used to match a blood or bone marrow donor to a recipient for transfusion or transplant.

Hypercalcemia: A higher-than-normal level of calcium in the blood. This condition can cause a number of symptoms, including loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness, and confusion. Common in myeloma patients and usually resulting from bone destruction with release of calcium into the blood stream. Often associated with reduced kidney function since calcium can be toxic to the kidneys. For this reason, hypercalcemia is usually treated on an emergency basis using IV fluids combined with drugs to reduce bone destruction along with direct treatment for the myeloma.

IgG, IgA: The two most common types of myeloma. The G and the A refer to the type of protein produced by the myeloma cells. The myeloma protein, which is an immunoglobulin, consists of two heavy chains, (for example of a G type) combined with two light chains, which are either kappa or lambda. Therefore, the two most common subtypes of myeloma have identical heavy chains (i.e. IgG kappa and IgG lambda). The terms heavy and light refer to the size or molecular weight of the protein, with the heavy chains being larger than the light chains. Since the light chains are smaller, they are more likely to leak out into the urine, resulting in urine Bence Jones protein.

IgD, IgE: Two types of myeloma that occur less frequently.

IgM: Usually associated with Waldenstrom's macroglobulemia. In rare cases can be a type of myeloma.

Immune system: The complex group of organs and cells that produces antibodies to defend the body against foreign substances such as bacteria, viruses, toxins, and cancers.

Immunodeficiency: A lowering of the body's ability to fight off infection and disease.

Immunofixation: An immunologic test of the serum or urine used to identify proteins in the blood. For myeloma patients, it enables the doctor to identify the M-protein type (IgG, IgA, kappa, or lambda). The most sensitive routine immunostaining technique, it identifies the exact heavy and light chain type of M-protein.

Immunoglobulin (Ig): A protein produced by plasma cells; an essential part of the body's immune system. Immunoglobulins attach to foreign substances (antigens) and assist in destroying them. The classes of immunoglobulins are IgA, IgG, IgM, IgD, and IgE.

Immunosuppression: Weakening of the immune system that causes a lowered ability to fight infection and disease. Immunosuppression may be deliberate, such as in preparation for bone marrow transplantation to prevent rejection by the host of the donor tissue, or incidental, such as often results from chemotherapy for the treatment of cancer.

Immunotherapy: Treatment that stimulates the body's natural defenses to fight cancer. Also called biological therapy.

Incidence: The number of new cases of a disease diagnosed each year.

Induction therapy: The initial treatment used in an effort to achieve remission in a newly diagnosed myeloma patient.

Informed consent: The process requiring a doctor to give a patient enough information about a proposed procedure for the patient to make an informed decision about whether or not to undergo it. The doctor must, in addition to explaining all procedures, address the issues of risks, benefits, alternatives, and potential costs.

Infusion: Delivering fluids or medications into the bloodstream over a period of time.

Infusion pump: A device that delivers measured amounts of fluids or medications into the bloodstream over a period of time.

Inhibit: To stop something, to hold in check.

Injection: Pushing a medication into the body with the use of a syringe and needle.

Interferon: A naturally produced hormone (cytokine) released by the body in response to infection or disease which stimulates the growth of certain disease-fighting blood cells in the immune system. Interferon can be artificially produced by genetic engineering techniques and used as a form of immunotherapy, primarily in the maintenance (plateau) phase to block any regrowth of myeloma and thus delay or prevent relapse.

Interleukin: A naturally produced chemical released by the body or a substance used in biological therapy. Interleukins stimulate the growth and activities of certain kinds of white blood cells. Interleukin-2 (IL-2) is a type of biological response modifier that stimulates the growth of certain blood cells in the immune system that can fight some types of cancer. Interleukin-6 (IL-6) is a cytokine which is a potent stimulus to osteoclast and plasma cell activities.

LDH: Lactate dehydrogenase, an enzyme that may be used to monitor myeloma activity.

Lesion: An area of abnormal tissue change. A lump or abscess that may be caused by injury or disease, such as cancer. In myeloma, "lesion" can refer to a plasmacytoma or a hole in the bone.

Leukocytes: Cells that help the body fight infections and other diseases. Also called white blood cells (WBCs).

Leukopenia: A low number of white blood cells.

Lymphocytes: White blood cells that fight infection and disease.

Lytic lesions: The damaged area of a bone that shows up as a dark spot on an X-ray when enough of the healthy bone in any one area is eaten away. Lytic lesions look like holes in the bone and are evidence that the bone is being weakened.

M proteins (M spike): Antibodies or parts of antibodies found in unusually large amounts in the blood or urine of multiple myeloma patients. M spike refers to the sharp pattern that occurs on protein electrophoresis when an M protein is present. Synonymous with monoclonal protein and myeloma protein. (see "monoclonal" below)

Maintenance therapy: Drugs given to patients in remission to delay or prevent a relapse.

Malignant: Cancerous; capable of invading nearby tissue and spreading to other parts of the body.

MDR (Multi Drug Resistance): A resistance to standard treatment, typically associated with resistance to Adriamycin and vincristine, both chemotherapy drugs. The resistance is caused by a buildup of the p-glycoprotein in the outer cell membrane of the myeloma cells. This results in drugs being kicked back out of the myeloma cell instead of building up and eventually killing that cell.

Melanoma: A cancer of the pigment-forming cells of the skin or the retina of the eye. Not associated with myeloma despite the similar-sounding name.

Metastasize: To spread from one part of the body to another. When cancer cells metastasize and form secondary tumors, the cells in the metastatic tumor are like those in the original (primary) tumor. This term is commonly used to describe a disease process in solid tumors (e.g., breast, prostate) and not in myeloma, which is a blood-related cancer.

MGUS (Monoclonal Gammopathy of Undetermined Significance): A benign condition in which the M protein is present but there is no underlying disease.

Molecule: The smallest particle of a substance that retains all the properties of the substance and is composed of one or more atoms.

Monoclonal: A clone or duplicate of a single cell. Myeloma develops from a single malignant plasma cell (monoclonal). The type of myeloma protein produced is also monoclonal; a single form rather than many forms (polyclonal). The important practical aspect of a monoclonal protein is that it shows up as a sharp spike (M spike) in the serum electrophoresis test.

Monoclonal antibodies: Artificially manufactured antibodies specifically designed to find and bind to cancer cells for diagnostic or treatment purposes. They can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to tumor cells.

Monocyte: A type of white blood cell.

MRI (Magnetic Resonance Imaging): A diagnostic test that uses magnetic energy, rather than X-ray energy, to produce detailed two- or three-dimensional images of organs and structures inside the body. Gives very fine resolution of soft tissues, especially encroachments on the spinal cord, but is less accurate for bone lesions.

MTD (Maximum Tolerated Dose): The highest dose of a treatment that most people can safely withstand.

Myelodysplastic syndrome: A condition in which the bone marrow does not function normally and does not produce enough blood cells. This condition may progress and become acute leukemia.

Myeloid: Referring to myelocytes, a type of white blood cell. Also called myelogenous. Multiple myeloma is a non-myeloid cancer.

Myelosuppression: A decrease in the production of red blood cells, platelets, and some white blood cells by the bone marrow.

Neoplasia: Abnormal new growth of cells.

Neoplasm: A new growth of tissue or cells; a tumor that can be referred to as benign or malignant.

Neutropenia: A reduced level of neutrophils. Cytotoxic chemotherapy has a tendency to induce neutropenia. In contrast, lymphocytes which are more important in viral infections, tend not to be affected by cytotoxic treatment. Neutropenia can be prevented or reduced using a synthetic hormone called G-CSF (e.g. Neupogen).

Neutrophil: A type of white blood cell necessary to combat bacterial infection.

Oncogene: A gene or DNA sequence that normally directs cell growth, but which can also promote or allow the uncontrolled growth of cancer if damaged (mutated) by an environmental exposure to carcinogens, or if damaged or missing because of an inherited defect. A gene that has the potential to cause a normal cell to become cancerous.

Oncologist: A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment.

Osteoblast: The cell that produces osteoid, which becomes mineralized with calcium to form new hard bone.

Osteoclast: A cell found in the bone marrow at the junction between the bone marrow and the bone that resorbs or breaks down old bone. In myeloma, the osteoclasts are over-stimulated while osteoblast activity is blocked. The combination of accelerated bone resorption and blocked new bone formation results in lytic lesions.

Osteoid: The protein product which becomes mineralized with calcium to form hard bones.

Osteonecrosis of the jaw: A previously rare jaw problem now being observed in a small percentage of patients taking bisphosphonates. The condition produces pain, swelling, and bone damage around the tooth sockets in the jaws. There is bone necrosis or loss of bone which can lead to loose teeth, sharp edges of exposed bone, bone spurs, and the breaking loose of small bone spicules or dead bone. A case definition is ≥ 3 months with non-healing exposed bone. Symptoms may not be obvious at first, or may include pain, swelling, numbness or a “heavy jaw” feeling, or loosening of a tooth.

Osteoporosis: Reduction in bone density typically associated with old age. Diffuse involvement of bones with myeloma produces what looks like osteoporosis on X-ray and bone density measurement.

Palliative treatment: Aimed to improve the quality of life by relieving pain and symptoms of disease but not intended to alter its course.

Pathological fracture: A break in a bone usually caused by cancer or some disease condition. Occurs in myeloma-weakened bones, which can't bear normal weight or stress.

Pathology: The study of disease by the examination of tissues and body fluids under the microscope. A doctor who specializes in pathology is called a pathologist.

PET (Positron Emission Tomography) scan: A diagnostic test that uses a sophisticated camera and computer to produce images of the body. PET scans show the difference between healthy and abnormally functioning tissues.

Placebo: An inert (inactive) substance often used in clinical trials for comparison with an experimental drug.

Plasma: The liquid part of the blood in which red blood cells, white blood cells, and platelets are suspended.

Plasma cells: Special white blood cells that produce antibodies. The malignant cell in myeloma. Normal plasma cells produce antibodies to fight infection. In myeloma, malignant plasma cells produce large amounts of abnormal antibodies that lack the capability to fight infection. The abnormal antibodies are the monoclonal protein, or M protein. Plasma cells also produce other chemicals that can cause organ and tissue damage (i.e. anemia, kidney damage, and nerve damage).

Plasmacytoma: A collection of plasma cells found in a single location rather than diffusely throughout the bone marrow, soft tissue, or bone.

Plasmapheresis: The process of removing certain proteins from the blood. Plasmapheresis can be used to remove excess antibodies from the blood of multiple myeloma patients.

Platelet: One of the three major blood elements, others being the red blood cells and white blood cells. Platelets plug up breaks in the blood vessel walls and release substances that stimulate blood clot formation. Platelets are the major defense against bleeding. Also called thrombocytes.

Port - Implanted: A catheter connected to a quarter-sized disc that is surgically placed just below the skin in the chest or abdomen. The catheter is inserted into a large vein or artery directly into the bloodstream. Fluids, drugs, or blood products can be infused, and blood can be drawn through a needle that is stuck into the disc.

Prognosis: The projected outcome or course of a disease; the chance of recovery; the life expectancy.

Progression-free survival: The time period during which the patient survives and the cancer does not become worse. The improved survival of a patient that can be directly attributed to the treatment given for the myeloma. This term identifies myeloma patients who are in complete remission versus those who have had an episode of relapse or progression.

Progressive disease: Disease that is becoming worse, as documented by tests.

Protocol: A detailed plan of treatment including the dose and schedule of any drugs used.

Precancerous: A term used to describe a condition that may, or is likely to become, cancer.

Radiation therapy: Treatment with x-rays, gamma rays, or electrons to damage or kill malignant cells. The radiation may come from outside the body (external radiation) or from radioactive materials placed directly in the tumor (implant radiation).

Radiologist: A doctor who specializes in creating and interpreting images of areas inside the body. The images are produced with x-rays, sound waves, magnetic fields, or other types of energy.

Recurrence: The reappearance of a disease after a period of remission.

Red blood cells (erythrocytes): Cells in the blood that contain hemoglobin and deliver oxygen to and take carbon dioxide from all parts of the body. Red cell production is stimulated by a hormone (erythropoietin) produced by the kidneys. Myeloma patients with damaged kidneys don't produce enough erythropoietin and can become anemic. Injections with synthetic erythropoietin can be helpful. Blood transfusion is another alternative, especially in an emergency. Synthetic erythropoietin is being used prophylactically before chemotherapy and as supportive therapy after chemotherapy to avoid anemia.

Refractory: Disease that is unresponsive to standard treatments.

Regression: The shrinkage of cancer growth.

Relapse: The reappearance of signs and symptoms of a disease after a period of improvement.

Remission or response: Complete or partial disappearance of the signs and symptoms of cancer. Remission and response are used interchangeably.

- **Complete Remission (CR)** – CR is the absence of myeloma protein from the serum and/or urine by standard testing; absence of myeloma cells from the bone marrow and/or other areas of myeloma involvement; clinical remission and improvement of other laboratory parameters to normal. CR is not the same thing as a cure.
- **Partial Remission (PR)** – PR is a level of response less than CR. In SWOG studies, it has meant >50% and <75% response. In other studies it has meant >50% response.

RNA (ribonucleic acid): Any of various nucleic acids that are associated with the control of cellular chemical activities. RNA is one of the two nucleic acids found in all cells – the other is DNA (deoxyribonucleic acid). RNA transfers genetic information from DNA to proteins produced by the cell.

Serum osteocalcin: A protein produced and secreted by osteoblasts when they are making osteoid. A low level reflects active myeloma. A higher than normal level reflects more stable myeloma.

Shingles: See “Herpes zoster.”

Side effects: Problems that occur due to drugs used for disease treatment. Common side effects of cancer chemotherapy are fatigue, nausea, vomiting, decreased blood cell counts, hair loss, and mouth sores.

Skeletal survey (metastatic survey): A series of plain X-rays of the skull, spine, ribs, pelvis, and long bones to look for lytic lesions and/or osteoporosis.

Stable disease: This describes patients who have some response to treatment but <50% reduction in myeloma protein levels. Stable disease is not necessarily bad or sub-optimal (as compared with CR or PR) provided the myeloma has stabilized and is not progressing. With slow-moving myeloma, stabilization can last for many years.

Stage: The extent of a cancer in the body.

Staging: Doing exams and tests to learn the extent of the cancer in the body.

Stem cells: The immature cells from which all blood cells develop. Normal stem cells give rise to normal blood components, including red cells, white cells, and platelets. Stem cells are normally located in the bone marrow and can be harvested for transplant.

Steroid: A type of hormone. Steroids are often given to patients along with one or more anticancer drugs and appear to help to control the effects of the disease on the body.

Supportive care: Treatment given to prevent, control, or relieve complications and side effects and to improve the patient’s comfort and quality of life.

Systemic therapy: Treatment using substances that travel through the bloodstream, reaching and affecting cancer cells all over the body.

Thrombocytes: See “Platelets.”

Thrombocytopenia: A low number of platelets in the blood. The normal level is 150,000-250,000. If the platelet count is less than 50,000, bleeding problems could occur. Major bleeding is usually associated with a reduction to less than 10,000.

TNF (Tumor Necrosis Factor): A type of biological response modifier that can improve the body’s natural response to disease.

Toxins: Poisons produced by certain animals, plants, or bacteria.

Transfusion: The transfer of blood or blood products.

Transplantation: Stem cells are used to rescue a patient’s blood-forming potential following high-dose chemotherapy and/or radiation treatment. Transplant is not a treatment, but a method of support to make high-dose treatment possible.

- **Bone marrow transplantation** – This term refers to the process of collecting stem cells from the bone marrow and infusing them into a patient. This term is used less frequently today in myeloma as stem cells are now collected from the peripheral or circulating blood.
- **Peripheral blood stem cell transplantation** – Doctors remove healthy stem cells from a patient’s circulating blood system (not from the bone marrow) and store them before the patient receives high-dose chemotherapy to destroy the cancer cells. The stem cells are then returned to the patient, where they can produce new blood cells to replace cells destroyed by the treatment.
- **Allogeneic** – The infusion of bone marrow or stem cells from one individual (donor) to another (recipient). A patient receives bone marrow or stem cells from a compatible, though not genetically identical, donor.
- **Autologous** – A procedure in which stem cells are removed from a patient’s blood and then are given back to the patient following intensive treatment.

- **Matched unrelated donor transplants (MUDs)** – Refers to stem cell transplantation procedures in which the patient and the stem cells are genetically matched but are not from family members. This procedure is not recommended for myeloma patients because it carries an unacceptably high mortality rate.
- **Syngeneic** – The infusion of bone marrow or stem cells from one identical twin into another.

Tumor: An abnormal mass of tissue that results from excessive cell division. Tumors perform no useful body function. They may either be benign or malignant.

Tumor marker: A substance in blood or other body fluids that may suggest that a person has cancer.

Vaccine: A preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms that is administered to produce or artificially increase immunity to a particular disease.

Virus: A small living particle that can infect cells and change how the cells function. Infection with a virus can cause a person to develop symptoms. The disease and symptoms that are caused depend on the type of virus and the type of cells that are infected.

Waldenstrom's macroglobulemia: A rare type of indolent lymphoma that affects plasma cells. Excessive amounts of IgM protein are produced. Not a type of myeloma.

White blood cells (WBC): General term for a variety of cells responsible for fighting invading germs, infection, and allergy-causing agents. These cells begin their development in the bone marrow and then travel to other parts of the body. Specific white blood cells include neutrophils, granulocytes, lymphocytes, and monocytes.

X-ray: High-energy electromagnetic radiation used in low doses to diagnose diseases and in high doses to treat cancer.