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MYELOMA TODAY

A PUBLICATION OF THE INTERNATIONAL MYELOMA FOUNDATION

HIGHLIGHTS

Dear Readers,

On October 3rd, at the Lymphoma & Myeloma 2002 clinical conference in New York City, Dr. Rubin Niesvizky presented me with an award in recognition of the work that I have done on behalf of myeloma patients and their families. I was particularly gratified to receive an award named for Dr. Joseph Michaeli, a very talented and dedicated man who made helping myeloma patients his life's work.

My co-recipient was Kathy Giusti of the MMRF whose efforts have greatly increased the level of myeloma research being performed. I met Kathy in June 1996 when she and her family, like so many others in need of information, attended an IMF Patient & Family Seminar. After meeting her I thought, "This woman is a dynamo!" and I guess I was right.

Unlike the clinicians in attendance at this conference, who set out to spend their lives working in myeloma, this terrible disease just happened to find its way into my life when my fiancé Brian Novis was diagnosed in 1988. Brian received his diagnosis over the phone. His doctor called him at work and said, "You have multiple myeloma." Brian said, "What's that?" The doctor replied "It's a cancer of the bone marrow, you have 3 to 5 years to live, stop by my office on your way home."

Like everyone who hears the words multiple myeloma for the first time, we were in shock and, worst of all, we felt completely alone. Fourteen years ago, there was no place for myeloma patients and their families

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IMF SUPPORT GROUP LEADERS' RETREAT

By Nancy Baxter

Duke University's beautiful R. David Thomas Executive Conference Center was the site of the IMF's third annual Support Group Leaders' Retreat, held the weekend of October 12th. Leaders from Alaska, Arizona, Delaware, Florida, Massachusetts, North Carolina, Pennsylvania, Wisconsin, Nova Scotia, and Japan attended, proving that the reach of the IMF is truly international. The hours were long, but the rewards were great for all who participated.

Friday night's reception and dinner gave participants a chance to meet and greet over a delicious meal. The guest speaker was Betsy Patterson, an experienced oncology nurse practitioner and herself a 17-year survivor of lymphoma. Her topic, "Planting the Seeds of Survivorship," was a perfect way to kick off the weekend and provided good, practical tips to myeloma patients and caregivers.

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The IMF is dedicated to improving the quality of life of myeloma patients while working toward prevention and a cure.

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Friends We Never Hoped to Meet

By Greg Brozeit

I've spent much of this year traveling around the country visiting with support groups to give some civics lessons for cancer advocates. But those visits, along with some of the events I have been lucky enough to represent the IMF, have taught me some things about the myeloma community. Here's a top ten list of thoughts that struck me during the year:

1. Through your myeloma experience, you end up meeting the best friends you wish you had never met. That's just one of the many poignant, bittersweet, and just plain bitter experiences that comes with the understanding of myeloma.

2. Your connection to a myeloma diagnosis makes you a part of a new community. Some of you find this out through your support group meetings, deeper relationships with the people who matter in your lives, and connections with others through the IMF-hosted myeloma list serve.

3. Myeloma is by no means rare. It may be uncommon, as board member Mike Scott often reminds me, but that does not mean it is rare. Myeloma's share of the 1% of all new cancer diagnoses in the U.S. adds up to about 15,000 people annually. Myeloma is everywhere.

4. Knowledge does make a difference. In my experience, the more patients and their support network know and understand their myeloma, the healthier they seem to be. After visiting this year with more than a dozen myeloma support groups, I have concluded that knowledge and support shared through support groups help myeloma patients by providing information leading to the best possible quality of life.

5. More support groups are better. Today, the IMF lists more than 85 myeloma support groups worldwide. Before Brian Novis and Brian Durie got together more than 12 years ago to found the IMF, there were none. The more I see, the more I am convinced that support groups are one of the best changes the myeloma community has experienced since the IMF's founding.

6. Reaching out can be therapeutic. It doesn't matter if your group has 5 or 50 attendees. The important thing is to get together, share, and advise. I was so impressed with the level of support, regardless of the size of the group, at every meeting I attended.

7. Support group leaders need support too. Support group leaders vary, but their burdens can become great. I would recommend attending the annual IMF Support Group Leaders Retreat to every myeloma support group leader. If the leader is unable to attend, it is important to send a representative from your group.

8. The science is changing; genomics may have the maps we need. As was outlined in the June 2002 issue of *Myeloma Today*, the future of cancer treatment will be targeted and at the molecular level. The key, rather than use chemotherapies, is to identify the pathways and targets that cause our cancers, regardless of where they may be.

9. Patient advocacy and public advocacy matter. Patients need advocates – sometimes themselves – to make their needs known and understood. In much the same way, we, as groups of myeloma and cancer communities, need to be just as forceful in making our needs and hopes known to policy makers. If we all spend only 20 minutes to 2 hours per year on educating our public officials about the issues that affect us, we can make a great difference.

10. Coalitions achieve more. Myeloma patients need to work together with each other to be effective. But they also need to see *public* advocacy as important a task as *patient* advocacy. Therefore, if we are serious about more research funding for myeloma, we need to support the One Voice Against Cancer agenda. If we are serious about getting oral cancer drugs reimbursed through Medicare, we need to work with the largest groups that support our goals.

Note: For information about myeloma support groups, visit *http://supportgroups.myeloma.org*. If you are interested in getting advocacy alerts, please contact Greg Brozeit at *greg.brozeit @worldnet.att.net*.

If you or someone you know has a story that might be of interest to our readers, please contact:

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Ask the Expert: Dr. Steve Schey Answers Your Questions

Steve Schey, M.D.
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What is a bone marrow aspirate and why is it so painful ?

Blood cells are manufactured in the bone marrow space and examination of these cells in myeloma is performed to identify an increase in the number of plasma cells which is one of the cardinal features used to confirm the diagnosis. In order to obtain these cells for examination the clinician needs to perform a bone marrow aspirate. The thin "skin" that coats the bone surface and carries the small nerves responsible for carrying sensation and pain, is anaesthetised using local anaesthetic. A special needle is then inserted into the bone. Marrow is withdrawn with a syringe attached to the needle, like a blood test.

When we are born, most of our bones contain marrow, but as we get older the marrow in our limbs is replaced by fat and the majority of the marrow resides in the spinal vertebrae, ribs, pelvis and breast bone. Samples are normally taken from the pelvis or breastbone and only very rarely from the spine. Although aspiration is uncomfortable, the pain that people may experience is due to the pressure that is exerted when the doctor draws back on the syringe attached to the special needle. This should only be a transient pain that is relieved as soon as the pressure is released after 3-4 seconds. Often the doctor may take an additional small sample of bone (a trephine) inside the needle to give extra information about the state of the marrow. The maneuvering of the needle in the bone to break off the sample inside the needle may cause an unusual sensation but normally this only lasts a few extra seconds. Once the anaesthetic has worn off there may be an ache at the site of the aspirate, best treated using paracetamol, and it should have resolved after about 24 hours.

What are the most recent developments in thalidomide ?

Thalidomide was first used in patients with myeloma about 3 years ago for patients with relapsed or refractory disease that was not responding to chemotherapy. Since the first report in the literature in 1999 there have been a number of studies which have confirmed the excellent results seen in the first study. More recently there has been a report of the use of thalidomide for patients who have not been previously treated with any chemotherapy with encouraging results. Thalidomide is a very important drug because it is not a chemotherapy drug and works in a different way. It has been known for 10 years that thalidomide interfered with new blood vessel formation and that this is an important mechanism for the survival and spread of solid tumours. It was only more recently however, that it became clear how important new blood vessel formation is in myeloma and other blood tumours. Although this may be an important mechanism in the anti-tumour activity of thalidomide, the effects of treatment are seen after only a few weeks of treatment, strongly suggesting that other mechanisms may be as, or more, important. It is now clear, however, that thalidomide also affects the secretion of factors that affect the survival and proliferation of myeloma cells by an effect directly on the myeloma cell itself, and indirectly via cells which have an immunological effect in controlling cell growth.

The main side effects of thalidomide are nerve damage, constipation, skin rashes, and somnolence. Most of these side-effects are manageable with simple medications, but in an attempt to reduce the side effects and improve the responses to this type of drug, the company that manufactures thalidomide have modified the structure of thalidomide and produced 2 new compounds. One of these agents, CC5013 (Revimid), has been used in patients in the United States and the other, CC4047 (Actimid), has been used in early clinical studies by ourselves at Guys & St Thomas' Hospital, London. Early results are very encouraging and it is hoped that further studies will be undertaken in this country later in the year with both CC4047 and CC5013.

Further studies are needed to ascertain the optimum dose of thalidomide and when best to use it in the course of the disease. A number of studies are also being undertaken by the UK Myeloma Forum (UKMF) and Medical Research Council (MRC) looking at the use of thalidomide in combination with other chemotherapy agents in an attempt to optimise its benefits.

What is the difference between X-ray, MRI and CT, and how often should you have them ?

X-rays use radiation to produce an image on a piece of X-ray film like the negatives you get when you develop your holiday photographs.

A CT uses the same kind of radiation as a plain X-ray but the information is fed into a computer to produce a cross-sectional image.

MRI does not use radiation but instead employs magnetic fields and radio waves to produce a cross-sectional image similar to that of a CT.

Each of these techniques has their own limitations and the most appropriate investigation will depend upon what the doctor is looking to define. Hence CT scans are useful for identifying soft tissue 'lumps' or masses of myeloma and can be very helpful to define myeloma in the chest particularly if it is arising from the spine or ribs. MRI is better for identifying disease in the bone itself and may be positive when the plain X-ray skeletal survey is negative, which is helpful to know when making decisions on when to initiate treatment.

On other occasions, radiological investigations are performed in an attempt to identify a complication of the disease such as an infection. These may commonly involve the chest, and plain X-rays and CT scans are excellent for identifying infection in this site.

MRI scans on the other hand are not useful in this site but may be more helpful for investigating the liver or spleen. The choice of investigation therefore depends upon the clinical situation and should be tailored to the individual patient's needs.

LEGAL ASSISTANCE FOR THE CANCER PATIENT

Barbara Ullman Schwerin, Esq.
Director, Cancer Legal Resource Center
and Adjunct Professor of Law at Loyola Law School
Los Angeles, California

By Barbara Ullman Schwerin, Esq.

The Cancer Legal Resource Center (CLRC), a joint program of Loyola Law School and the Western Law Center for Disability Rights, was founded in 1997 and provides information and education on all types of cancer-related legal issues for persons with cancer, their family and friends, caregivers and others impacted by the disease. The CLRC's founders recognized that, while there was medical and psycho-social support for people with cancer, there was no place for them to go with questions about employment, insurance, government benefits, estate planning issues and other legal issues that needed to be addressed.

The CLRC has assisted more than 17,000 people since its inception. Many callers are helped through the CLRC's telephone assistance line, staffed primarily by Loyola Law School students under the supervision of CLRC's legal staff. Additionally, the CLRC conducts 70-80 workshops annually in the cancer community, including cancer support groups, in service training for health care professionals, conferences, health fairs and other activities in the cancer community. The CLRC also has a volunteer panel of attorneys and other professionals who provide more in-depth counsel when needed. The CLRC is primarily California based. However, a significant percentage of its calls come from outside of California, with the CLRC finding local resources for these callers. The CLRC's services are free.

While the CLRC receives calls in many areas, the following will be a brief overview of the employment laws affecting persons with cancer.

THE AMERICANS WITH DISABILITIES ACT

In 1990, Congress passed the Americans with Disabilities Act (ADA). The ADA is a wide-ranging law, prohibiting discrimination in all areas of the employment process. It was designed to level the playing field in the employment arena – so that people would not be denied jobs, or the benefits of jobs, simply because they had disabilities.

The ADA applies to private employers with 15 or more employees. It also applies to employment agencies, labor organizations, and local and state governments. The ADA provides protection to a "qualified individual with a disability." An individual must be both disabled and qualified.

An individual with a disability under the ADA is an individual with a physical or mental impairment that substantially limits a major life activity. The major life activity can be, among other things, caring for oneself, walking, talking, seeing, breathing, or working. A person may also have a disability if she has a record of an impairment or is regarded as having an impairment. The impairment that substantially impacts a major life function must be severe, not temporary, and must produce a permanent or long-term impact.

In determining whether an impairment is substantially limiting, the impairment must be looked at in its corrected, or mitigated, state. Therefore, one must look at the employee's present condition, including whether the employee has already had surgery and where the employee is in his/her treatment program. One must look at the medications that may control the person's impairment, and also look at the side effects of the treatment, including the side effects of radiation and chemotherapy.

If the person's cancer is completely or substantially controlled through surgery, radiation and chemotherapy, the person may not have a qualifying disability under the ADA because they cannot show a substantial impact on a major life function. However, the person may be protected under one of the other two prongs of the ADA; namely, that they have a history of an impairment or are treated as having an impairment.

To be entitled to protection, the employee must also be a "qualified individual." This means the employee must be able to perform the essential functions of the job with or without a reasonable accommodation. Some examples of reasonable accommodations include a flexible schedule, reassignment

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Step-by-Step Nutrition Action Plans

Excerpt from Challenge Cancer and Win! Step-by-step nutrition action plans for your specific cancer

Kim Dalzell, Ph.D., R.D., L.D.

By Kim Dalzell, Ph.D., R.D., L.D.

The statistics are quite sobering: Over 40 percent of cancer patients die from causes related to malnutrition, not from cancer itself.[1] If you aren't adequately nourished or are depleted of protein or other nutrients, you may be suffering from malnutrition.

Why is malnutrition such a threat? Cancer causes changes that can alter the level of nutrients your body requires for optimal functioning. Side effects associated with chemotherapy, radiation, and surgery can complicate your ability to eat, absorb, or utilize foods. The final insult comes when a malnourished body can't support treatment goals. When you are poorly nourished, your current treatment may not be as effective, or you might not be able to tolerate further treatments.

Over time, inadequate or improper dietary habits can wreak havoc on the healthiest individuals, even "healthy" cancer patients. If you don't address dietary deficiencies, cachexia ensues. Think of cachexia as a downward spiral. Every cell in your body requires many nutrients to work effectively. Without the proper fuel, cells can't do their jobs, and debilitation begins. Without an opportunity for rebuilding, the chances of recovery are greatly reduced.

Before you dismiss malnutrition as a condition for the weak and debilitated, understand that even minor degrees of undernutrition are associated with a marked increased risk of hospital admissions and death.[2] Between 40 and 80 percent of all cancer patients develop some degree of clinical malnutrition.[3]

You can take several steps to make sure your nutritional status is up to par:

1. Address the weakening effects of poor nutrition before they become an issue.

Why choose to ignore your nutritional needs? Be prepared to address them right from the start. Communicate with your doctor. Discuss your risk for malnutrition with your healthcare providers and let them know you are concerned about your nutritional status. A clinical dietitian should be following your progress throughout your treatment and should be available to discuss your dietary needs or concerns. If you haven't met with a dietitian — ask! A dietitian or nutritionist can help you identify risk factors and devise solutions to any special needs related to your diet.

2. Ignore advice to "eat whatever you want."

Have you been told to eat whatever you want in order to keep your weight up? Instead, consider how nourishing your food is or whether your diet is detrimental to the immune system. Although it is better to eat something rather than nothing, what you eat can make a difference in your cancer outcome. If you eat rich, thick ice cream milkshakes and cream soups in an attempt to maintain your weight, you are not providing your body what it needs to rid itself of cancer. With a little planning and some knowledge, you can make better meals that are quick to prepare, taste good, are easy to digest, and support normal cell division and immune function.

3. Maintain your weight.

Weight loss is frequently used to evaluate early malnutrition and impacts the survival time of newly diagnosed cancer patients even more than their chemotherapy regimen.[4] If you lose as little as five percent of your current body weight, your health and cancer recovery can be compromised. Unintentional weight loss can occur at any stage of a cancer diagnosis or treatment plan. While a few pounds here or there probably aren't critical and most likely reflect a shifting fluid balance, it is important to be aware of weight change trends. Don't think that you can "starve" the cancer. Rapid or progressive weight loss usually signals lost muscle mass, impaired immunity, and free radical generation, and presents the greatest risk for complications that reduce the survival and quality of life for many cancer patients. The percentage of weight loss and the rate of loss are both critical for determining whether negative health consequences may arise. The following diagram shows that as weight loss continues, the risk of health complications and death increases:[5] If you think your weight loss may be affecting your health, ask your dietitian to assess your weight changes.

4. Lose weight safely if you are overweight.

Obesity, as well as undernutrition, can play a role in the disease process. Excess weight has been linked to a higher risk of many kinds of cancer (endometrial, kidney, postmenopausal breast, and possibly colon) and other degenerative diseases. If weight reduction is a health goal, limit your weight loss to no more than one to two pounds per week. When you have cancer, it is essential that you consult with a nutritionist who will help you determine realistic and safe goals for gradual weight loss.

5. Learn what your needs are.

I'm always shocked to hear that most patients do not know what their calorie and protein requirements are. Knowing what your body requires makes it easier to define your dietary goals. If you would like to know specifically what your energy and protein needs are, I suggest you contact the hospital dietitian or nutritionist. Nutritional professionals routinely calculate these requirements for every patient, so don't hesitate to ask.

6. Monitor your progress.

Anyone who undergoes cancer treatment has had their blood drawn at one point or another. Laboratory tests convey a general cell response trend that helps the doctor determine when changes in your treatment plan are necessary. If you become familiar with a few of the laboratory results, you will be able to get more involved in your treatment. Looking at the numbers on a

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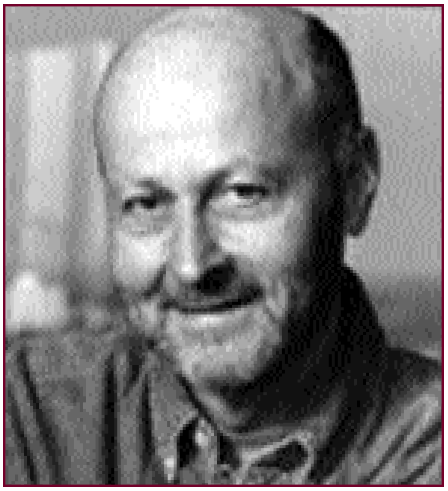
Percent Weight Loss and the Risk for Increased Morbidity and Mortality

0%	None	20%	Significant	40%	Life threatening
10%	Limited	30%	Serious	>40%	Lethal

MYELOMA CENTER SPOTLIGHT:

The Myeloma Institute for Research and Therapy, evolving from the breakthrough adv
for multiple myeloma and related disease entities through innovativ

COMPREHENSIVE MOLECULAR MANAGEMENT OF MULTIPLE MYELOMA



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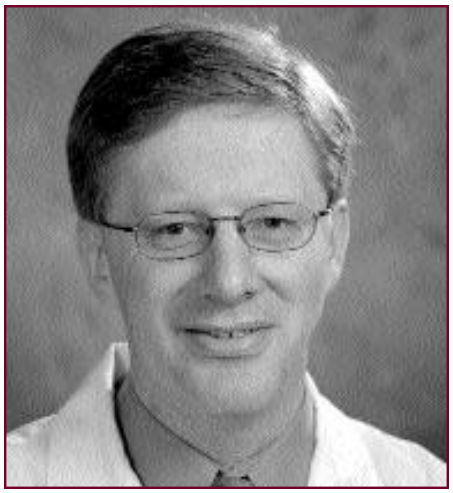

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The Arkansas Myeloma Program, launched in 1989 at the Arkansas Cancer Research Center on the campus of the University of Arkansas for Medical Sciences, owes its origins to the developmental therapeutics work headed by Emil J Freireich, M.D. at the University of Texas MD Anderson Cancer Center in Houston. Dr. Freireich's work led to curative therapies for malignancies such as leukemia, lymphoma, and testicular cancer, and the proven feasibility of autologous transplant. This work and his mentorship motivated Dr. Bart Barlogie and colleagues Dr. Sundar Jagannath and Dr. Joshua Epstein to develop a research and treatment program focused on understanding the biology and advancing the treatment of a single disease, namely multiple myeloma. It is this close interplay between basic science research and clinical practice, known as translational research, that is the unique hallmark of the Myeloma Institute for Research and Therapy. The Institute is the direct result of thirteen years of the Arkansas Myeloma Program, a program that has never strayed from these roots of the 'bench-to-bedside' approach to solving the myeloma puzzle.

In 1983, Dr. Tim McElwain, and colleagues, had demonstrated that increasing doses of melphalan by a factor of 6 to 10 resulted in a much higher percentage of myeloma patients obtaining a complete remission, when compared to standard therapy. This was subsequently confirmed by other investigators. This new treatment was promising but it resulted in very long periods of decreased white blood cell and platelet counts, which resulted in treatment-related mortality of 15% to 20%. To decrease this treatment-related mortality, Dr. Barlogie introduced the concept of bone marrow support after high dose melphalan. With this concept the dose of melphalan could be doubled. Although it appeared unlikely that such an intervention would cure end stage patients, because the bone marrow contained residual myeloma cells, it was hoped that the normal bone marrow cells would grow much faster than the myeloma cells and that survival could be significantly prolonged. Early investigations pursued the hypothesis that survival could be markedly improved by increasing the incidence of true complete remission.

Once benefit had been demonstrated in end-stage patients with a low treatment-related mortality, this approach was offered to newly diagnosed or relatively minimally-treated myeloma patients. Most autologous transplants at that time were administered to younger patients and incorporated very intensive chemotherapy schedules; it was thought that older myeloma patients would not be able to tolerate such high doses of therapy. Therefore, it was decided to give less intensive chemotherapy with melphalan alone, but to repeat this treatment 3 to 6 months later, when patients had completely recovered from the toxicities of the first transplant. It was hoped that the two transplants with less intensive high dose chemotherapy would be equally effective as one transplant with very intensive chemotherapy, and that the mortality associated with transplantation would be considerably lower. Thus, the concept of tandem transplants was born.

Based on the principals of St. Jude investigators led by Dr. Donald Pinkel, the Arkansas investigators developed "Total Therapy I" for newly diagnosed myeloma patients. This was based on the observation that high dose chemotherapy requiring hematopoietic stem cell support resulted in higher complete response rates and extended disease control, when compared to standard therapy. Total Therapy I incorporated induction therapy, double (tandem) autotransplant, and maintenance therapy, using a combination of agents likely in doses high enough to be effective while still preserving positive recovery.

Moving forward from Total Therapy I to its successor trial, Total Therapy II, certain phase II regimens such as DCEP and DT PACE were developed. Remission induction was intensified by treatment principles that were successful with therapies applied to post-transplant relapse. In this way, the dexamethasone-resistant tumor subpopulation, presumed to be critical to disease recurrence, could be targeted. To target

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'ances of the UAMS Myeloma program, is committed to accelerating curative therapies 'e clinical and basic science research and outstanding patient care.

REFLECTIONS ON MYELOMA – Past and Future Progress

By Bart Barlogie, M.D., Ph.D.

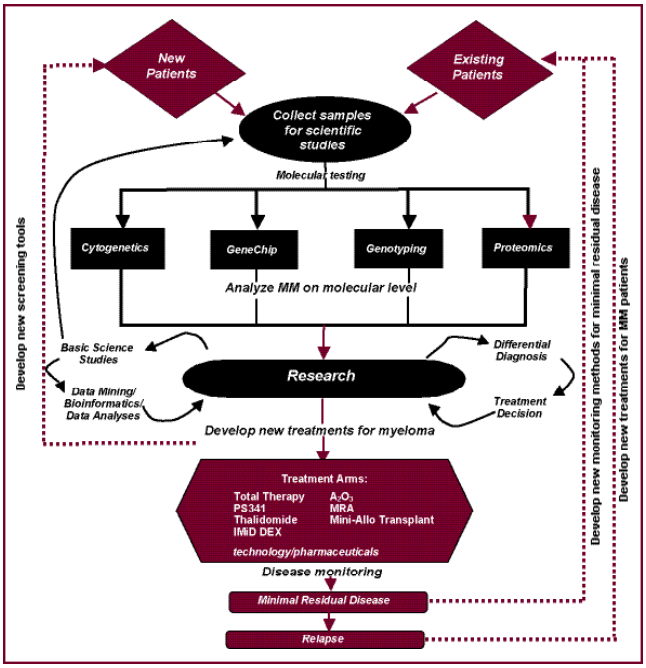
I am convinced that curing myeloma requires the full dedication of a bright and hard-charging team of creative investigators. Foremost, we have to embrace a well-founded optimism that the goal of cure or lifelong palliation is achievable.

During the first few decades of myeloma investigation, through the mid-1980s, a series of mildly cytotoxic regimens were employed so as to not further compromise patients' immune status and hematopoietic function, and thus potentially increase treatment-related mortality. Stem cell support and hematopoietic growth factors had not yet become available.

Inspiration was sparked by the remarkable activity of high does of dexamethasone, alone or administered as part of the VAD regimen, which was non-myelosuppressive and which effected bone marrow remissions regularly. Coincident with the findings of the late Tim McElwain that the increased dose intensity of melphalan did increase complete remission rates markedly, but was associated with toxic death due to prolonged neutropenia, we developed the autologous hematopoietic stem cell support strategy using bone marrow even when infiltrated by up to 30% tumor cells. The hypothesis was that these were mainly terminally differentiated cells with little self-renewal capacity. In fact, the first patient ever to receive an autologous bone marrow transplant had 30% marrow plasmacytosis. Yet, the bone marrow was effectively used to support chemoradiotherapy with melphalan and total body irradiation, resulting in a 6-year subsequent survival.

A major breakthrough was the discovery by Gianni and colleagues that cyclophosphamide-mobilized peripheral blood stem cells, unlike those obtained from the steady-state bone marrow environment, could markedly accelerate both granulocyte and platelet recovery. This indeed reduced morbidity and mortality, especially among older patients, and has made it possible for most procedures to be done today in the outpatient setting with a high level of safety.

Emphasis should be placed on addressing the long-standing controversy among myeloma investigators about standard vs. single vs. double transplants. Our justification for the tandem transplants comes from the arithmetic: tumor burden at the time of clinically defined complete remission is reduced from a trillion to perhaps 1 to 5 billion remaining tumor cells. With the availability of peripheral blood stem cells affording rapid hematopoietic recovery, it became feasible to introduce treatment regimens that produce marked reduction of disease burden. Abandoning total body irradiation, we believed that a more radical intervention with tandem transplants was more likely to produce positive clinical outcome in the majority of patients. The French Myeloma Intergroup has been able to confirm in two carefully conducted randomized trials that single high dose therapy was superior to standard treatment, and, just recently, that two such cycles are superior to a single cycle.



In light of exciting new drug developments, a certain level of hype is infiltrating the myeloma medical and patient communities. Some are quick to abandon the impressive results obtained with tandem transplants. In pursuit of our strategy that the risk of treatment intervention should match the risk of the disease, we believe that exciting new agents whose long-term efficacy and toxicity is not yet known, should be tested in high-risk disease, e.g. myeloma with chromosome 13 deletion or high LDH. Given that 80% of such patients will likely progress or relapse within 2 years, the new approaches seem justified, as long as patients have the opportunity early on of autologous stem cell collection. Sufficient stem cell collection ensures that standard melphalan-based autologous transplant remains an option in the event of unanticipated marrow damage from new agents.

Other discussions have focused on the issue of early vs. late salvage transplantation. The mission of attaining durable disease control and cure, mandates that that best treatment options be applied up-front to battle the already enormously complex genomic instability that probably accounts for much of the standard dose drug resistance.

Finally, it is distressing to observe that the treatment discussion, even among hematologists and oncologists, is often about transplant vs. standard therapy. An autologous "transplant" is simply a transfusion of autologous cells. The critical component of the "transplant" is the drug administered at the proper dose and schedule. Toxicities and mortality from a melphalan transplant are strictly dependent on the total dose administered. Thus, if there is increased risk of morbidity, as in the case of associated amyloidosis involving the heart, a reduced melphalan dose in a safe range of 50-70 mg/m2 should be considered. In the case of "malignant myeloma," we have begun to advocate other agent combinations, such as DT PACE, which do not target hematopoietic stem cells and are rather devoid of significant extramedullary toxicity, so that cycles can be administered as needed, within 2 to 3 weeks. This approach is critical for preventing rapid re-growth in a setting where single agent melphalan, even at high doses, fails to achieve a marked tumor reduction.

We anticipate that the comprehensive fundamental research into the molecular and biological disease features, as part of an organized clinical trial program, will make tremendous strides in the near future.

Note: For more information about the Myeloma Institute for Research and Therapy at UAMS, please call (501) 526-2873.

Cover Story – continued

Saturday's session was quite full and very productive. Wisconsin leader Chuck Koval gave a presentation on "How to Get Your Group Going." This was followed by two experienced facilitators from Duke's Cancer Patient Support Program, Rachel Schannberg and Tracy Berger, who gave concrete and practical tips on the art of group facilitation and how to "Manage the Dynamics." A question and answer session allowed more exchange of information between all participants. Next we heard from Carol Svec, who gave a comprehensive

Curt and LouAnn Brooks, with Betsy Patterson

talk on "The Art of Gathering Information." This well-received talk provided leaders with good methods of helping their members find reliable information and then sift through that information.

After a lunch break (and the food at the center was good and abundant!), we reconvened to hear Dr. Brian Durie discuss "Clinical Trials – Access and Options." Using one of the current Velcade trials as a "case study," Dr. Durie de-mystified the clinical trials process and solicited feedback from the group on what type of clinical trial information their members needed and how they would like to receive it. The IMF will use the results of this discussion to continue to

IMF Advocacy Consultant Greg Brozeit with Debbie Exner of the Philadelphia Multiple Myeloma Networking Group

Midori Horinouchi and Ikumi Okubo of the IMF (Japan)

improve how we share information about clinical trials with our patients.

The remainder of Saturday afternoon was led by Greg Pacini, who was back by popular demand. Greg's focus was on the "psychosocial" aspects of leading a group and the dynamics that dealing with a difficult disease like myeloma can create within the group. The topics of anxiety and grief were explored through song, discussion and action plans. It was both emotional and healing for the participants.

Saturday night's dinner was again delicious and everyone enjoyed a chance to chat informally and relax. We also got a

Cindy and Bob Feltzin

chance to hear from Dr. Durie about IMF research initiatives, including Bank on a Cure. Greg Brozeit updated everyone on IMF advocacy efforts and gave a brief civics lesson on the legislative process and how to use that process to increase spending on myeloma research.

Sunday morning's "Open Forum" gave the group a chance to discuss any unfinished business and to brainstorm specific problems with which leaders needed help. It was agreed that we should move next year's meeting back to the summer, if possible, and that Duke's facility was extraordinary. The retreat was a memorable and rewarding experience for all participants.

Nutrition – continued

laboratory test can help you create a picture in your mind of what is going on inside of you. This visualization can be very powerful for proactive healing.

7. Consider advanced nutrition support.

If high-calorie shakes, appetite stimulants, and other dietary modifications don't help you maintain your weight, you may need advanced nutritional support. Advanced nutritional support used as a adjuvant therapy to basic cancer treatment can decrease the risk of further deterioration, improve some nutritional and immunological parameters, avoid health complications associated with malnutrition, and enhance quality of life.[6] Nutritional support techniques used in cancer patients have reduced complication rates of surgery by 33 percent![7] Additionally, survival rates improved, without affecting tumor growth.[8]

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Note: *Challenge Cancer and Win! Step-by-step nutrition action plans for your specific cancer*, NutriQuest Press 2002, is available through *amazon.com* and BookMasters.

CLRC – continued

to a vacant position, a light duty position, or possibly an extended period of leave time. Each situation is intended to be assessed on an individualized basis, including whether the reasonable accommodation would be an undue hardship for the employer.

The ADA does not specifically provide a list of reasonable accommodations – it is meant to be a dialogue between the employee and employer and based upon the specific type of job and company involved. Additionally, accommodations are only required for the known disabilities of the individual – the employer must first be aware that an employee is seeking a reasonable accommodation under the ADA. It is also generally up to the individual needing the accommodation to make suggestions to the employer about the type of reasonable accommodations the employee is requesting.

The ADA can also provide protection for a person looking for a new job. If a prospective employee is applying for a new job, she does not need to disclose her medical condition unless she needs a reasonable accommodation for the application or interview process. An applicant need not reveal her disability when she applies even if she believes she will need an accommodation on the job. If the person has a visible impairment, the prospective employer can ask the potential employee how they would perform the job function, and ask them to demonstrate.

If a person receives a conditional job offer based upon undergoing a medical examination, such an examination must be required of all employees in the same job category. The offer cannot be rescinded unless the medical examination indicates that the person cannot perform the essential functions of the job with or without a reasonable accommodation or that the person would pose a direct threat to himself or others. Finally, any requests for reasonable accommodations under the ADA are to be kept confidential. They should be kept in a separate, locked file that is kept separate and apart from a person's personnel file.

What Other Laws May Apply in the Workplace?

There are other laws that may provide protections to employees in the workplace. The ADA can work hand in hand with another law, the Family and Medical Leave Act (FMLA). The FMLA provides for a person to take up to 12 weeks of unpaid medical leave to care for a seriously ill spouse, parent, or child. It also allows for up to 12 weeks of unpaid leave for the serious medical condition of the employee. Although unpaid, this is job-protected leave, which means the employee returns to the same or an equivalent position. This law also requires the employer to keep an employee's benefits intact.

The FMLA applies to employers with 50 or more employees. Covered employees must have been employed at least a year and have worked a minimum of 1,250 hours in that year. Sometimes, a person will need more than the 12 weeks of unpaid leave provided by the FMLA. In that case, a person may be able to take an extended period of leave time as a reasonable accommodation under the ADA after exhausting the 12 weeks of FMLA leave. Additionally, there may be state laws that provide protections equal to or greater than the ADA or FMLA.

Note: For assistance, please contact the CLRC

Cancer Legal Resource Center
919 S. Albany Street
Los Angeles, CA 90015
Tel: (213) 736-1455
Fax: (213) 736-1428
TDD: (213) 736-8310 [TDD]
clrc@majordomo.lls.edu
www.wlcdr.org

Dear Reader – continued

to turn to for help. Brian was determined to change that and in 1989 during a visit to England to see Dr. Brian Durie, the idea for the IMF was born. In 1990, we opened the door to a foundation that would forever change the lives of myeloma patients and their families.

From the very beginning, the IMF was a grassroots organization. We are about people helping people. Over the years, the IMF family has grown to over 100,000 members in 64 countries as patients and caregivers have stepped forward to look beyond their own battle with myeloma to help others. Special people like June Brazil, Lee Grayson, Sharon Rudolf, Leta Garvet, Elliot Bernstein, Michael Katz, Gary Takata, Cathy Lebkeucher, Peter Tischler, Michael Touhy, the list goes on and on.

From the very beginning, the IMF's goals have been education, support, and research but our focus is always on the patient. For the past 12 years, we've had one mission in mind — to improve the lives of myeloma patients today, because no-one knows what tomorrow brings.

Knowledge is power — the IMF has sent out over 150,000 free information packages and has developed programs to ensure that patients are empowered by the information they need to make intelligent decisions about what's right for them. As evidenced at this conference, there are a lot of treatment options. Education is the cornerstone of the IMF — many of the programs we've developed have become models both inside and outside of the myeloma community and thousands of patients and family members have attended the more than 50 IMF Patient & Family Seminars held around the world. Since many of the myeloma experts who have participated at IMF seminars presented at this clinical conference, I took the opportunity to thank them for donating their time and talent to help the IMF help others.

I also thanked the researchers for working so hard to try to put an end to cancer and the pain and suffering it causes. I thanked the clinicians for doing their very best to help the patients, knowing that they don't have that magic bullet to cure them, but using all they have in their toolbox to give them quality of life and the precious gift of time.

I've worked hard — it's a labor of love — but what I do is easy compared to the people who really deserve this award: the patients. So I accepted it on their behalf, in recognition of the courage, grace, dignity, and humor they display in their fight against this terrible disease, and on behalf of the thousands of friends that I've made and lost, who enriched my life and made me believe Brian Novis was right when he said, "One person can make a difference, two can make a miracle."

IMF Calendar

November 8-9, 2002
IMF Patient & Family Seminar
Seattle, WA

December 6-10, 2002
ASH (American Society of Hematology)
Annual Meeting
Philadelphia, PA

January 24-25, 2003
IMF Patient & Family Seminar
Los Angeles, CA

For more information, please check the IMF website at www.myeloma.org or contact the IMF at (800) 452-CURE.

UAMS – continued

angiogenesis (growth of blood vessels that feed tumors)the Arkansas program pioneered the use of thalidomide, which, among other effects, also curtails angiogenesis activity. After establishing its activity in refractory myeloma, thalidomide is now being tested up-front in Total Therapy II. Discovery of thalidomide for use in myeloma was a major milestone in that it represented an independently active agent in addition to melphalan and glucocorticoids, e.g. dexamethasone, prednisone, for the management of myeloma.

Major grant support from the National Cancer Institute has enabled the Arkansas program to continue with its extensive translational research. Research and diagnostic techniques applied to all new patients with myeloma include baseline FISH, traditional cytogenetics, gene expression profiling, analysis of telomere length and telomerase activity of myeloma cells and bone marrow cells, serum and bone marrow banking for future research, and, very important to the mix, magnetic resonance imaging (MRI). Even within the boundaries of stringently defined complete remission, focal lesions can be detected on MRI. When these lesions are subjected to CT-guided fine needle aspiration, active tumor cells, often with abnormal cytogenetics, are frequently revealed. Part of the current research at Arkansas includes determination as to whether patients whose MRIs confirm complete remission have superior event-free and overall survival.

Analysis of the first 231 patients enrolled in the Total Therapy II protocol indicates that complete and near complete remission rate has increased to >60%, that despite the more intensive therapies the treatment-related mortality is not higher than with the predecessor Total Therapy I protocol. This is especially true in the older population. In addition, event-free and overall survival curves are superior to those of Total Therapy I. Despite the use of intensive cytotoxic therapy during induction and following tandem transplants, careful scrutiny for secondary myelodysplasia, cytogenetically and by other means, has not yet revealed any case of myelodysplasia-associated karyotype (chromosomal) abnormalities.

It should be noted that the success of phase II efforts leading up to the Total Therapy II protocol was instrumental in convincing the Health Care Financing Administration (HCFA) that age, *per se*, was not an adverse feature for autologous transplant, neither from a safety or a disease point of view. This led to HCFA approval for autologous transplantation for Medicare patients (one autologous transplant is covered by Medicare; a second transplant, which the Arkansas clinicians considers critical for long-term disease control, is not covered by Medicare). This was a major milestone, similar to earlier efforts to demonstrate that high dose chemotherapy followed by autologous stem cell transplant was safe also in patients with renal failure.

Major Findings Drive Research

- **Bone Marrow Microenvironment**

It is clear that the bone marrow microenvironment affects the ability of myeloma cells to thrive, to survive and to become resistant to chemotherapy, especially if delivered at standard doses. Using a unique mouse model, Dr. Epstein and colleague Dr. Shmuel Yaccoby have been able to unravel the characteristics of the bone marrow microenvironment, such that therapies to make the microenvironment inhospitable to myeloma cells can be developed. A current study compares the gene expression in cells of the bone marrow environment that has been infiltrated with myeloma cells to the gene expression in cells of normal, healthy bone marrow. It is expected that this study will yield information as to whether gene chip analysis (to determine gene expression) will aid in 1) defining clinical disease manifestation; 2) predicting response and long-term prognosis; and 3) deciphering the molecular mechanisms of agents active in myeloma.

- **Molecular Genetics Research**

Dr. John Shaughnessy heads up the Lambert Laboratory for Molecular Genetics at Arkansas. His work is dedicated to identifying the critical molecular mechanisms and characteristics that affect patient prognosis. Through collaborative communication between basic scientists and clinical researchers, Dr. Shaughnessy's lab has performed gene chip analysis on almost 600 patients with various stages of myeloma, individuals with plasma cell dyscrasias such as Waldenström Macroglobulinemia and other B cell tumors including Chronic Lymphocytic Leukemia and non-Hodgkin's Lymphoma, as well as normal donors. Comparative gene expression profiling using sophisticated computer models has clearly distinguished normal from malignant plasma cells and plasma cells from patients with MGUS versus those with active myeloma.

With the clinical course of myeloma differing greatly, with some patients living a few months and others more than 10 years, DNA microarray technology gives a global profile of gene expression. Applying this technology to myeloma permit examination of genes that are pertinent to tumor growth and drug resistance; it will so help identify new molecular targets for new drugs. Dr. Shaughnessy has found that within the myeloma samples of 100 patients, differences in gene expression existed and , based on this, patient samples could be grouped into poor-, intermediate-, and high-risk groups. We will further these investigations into the genetic nature of myeloma by using microarray analysis to predict the disease course of myeloma, identify mechanisms of disease progression, and discover molecular targets that lend themselves to therapeutic intervention. This information could elucidate the mechanisms of plasma cell transformation, revolutionize diagnostic classification, and provide important directions for development of new therapeutics for myeloma patients.

- **Cytogenetics**

Dr. Jeffery Sawyer, Director of the Cytogenetics Laboratory, has demonstrated that cytogenetic abnormalities in multiple myeloma are enormously complex and important, with an average of 7 to 8 different chromosomes involved in only a few distinct recurring simple translocations. This genomic chaos, similar to abnormalities seen in solid tumors, is perhaps reflective of a strong environmental exposure over time, although even some very young patients exhibit these abnormalities. More than any other laboratory feature, the knowledge of a patient's karyotype has become the single most important staging tool in the Institute's clinical practice.

In "knowing the enemy" it is important to recognize markers that are powerful, such as chromosome 13 deletion and high LDH, which are critical features associated with high risk of relapse.

- **Immunotherapy, Vaccine Trials, and Other New Treatment Strategies**

Under the leadership of Dr. Guido Tricot, Dr. Frits van Rhee and Dr. Qing Yi are actively pursuing research investigating the hypothesis that developing a cure for myeloma requires multi-agent therapy directed at both tumor cells and accessory elements that support myeloma cell growth. New therapies under development for previously treated patients include cytotoxics, immunotherapy (idiotype or dendritic cell vaccination and donor lymphocyte infusions), antiangiogenic therapy (thalidomide), and anti-stromal cell treatments (bisphosphonates).

Further evidence that translational research is most successful when applied to large patient populations, Dr. Tricot and colleagues are addressing the potential consequence of therapy (Myelodysplastic Syndrome) using CD34 Gene Expression Profiling, FISH, telomere and *in vitro* stromal co-cultures along with SNP analysis to identify genetic predisposition. This research has obvious implications for understanding primary MDS as well. Vaccination research takes advantage of Cancer Testis Antigen expression (present in 30-50% of MM cells) to determine immune response and clinical efficacy. Continuing research over several areas will help close important gaps in understanding myelomagenesis, treatment mechanisms and paradigms, and the development of secondary malignancies. This continued research can translate into therapeutic prevention and intervention strategies that can work toward cure for myeloma in the 21st century.

THE WAMP SWIM

Elizabeth, Christopher, Julianne, and Courtney Stafford

By Elizabeth M. Stafford

On July 20, 2002 my siblings and I sponsored the Second Annual Wamp Swim. The event was hosted by Wampanoag Country Club in West Hartford, Connecticut where we are members and where I coach the swim team. Equipped with caps, goggles and a desire to raise money swimmers ranging in age from four to fifty took to the lanes and raised almost $13,000.00.

In February of 2001 my father Jeffrey was diagnosed with multiple myeloma. My siblings; Julianne (17), Christopher (14), Courtney (12), and myself (20), were driven to try and make our situation better. Armed with ambition and not a lot of know-how we were able to combine business with pleasure and raise money to help change the fate of people like our dad. This year armed with even more ambition and a little more know-how I was able to bring in twelve sponsors to donate money as well as goods to make our event a success.

The support of the Wampanoag community, the swim team, the parents, and the employees truly made this event a success. However, more importantly, without the support of the IMF my father might not be as healthy as he is today. We owe a great deal of health and happiness to the IMF and for this we are forever grateful. I have had an amazing experience as a member of the IMF family and know that that will only continue. From my family to yours, Thank you.

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