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Myeloma Today

A Publication of the International Myeloma Foundation

Highlights

The Importance of Knowing the Potential Outcome: Role for the new International Prognostic Index (IPI)

By Brian G.M. Durie, M.D.

When myeloma is first suspected, knowledge of the projected survival is critical to both patient and physician. Is the diagnosis MGUS or active myeloma? If it is myeloma, will planned treatment work well and can there be long survival? These latter questions were the ones asked in 1975 when the Durie-Salmon staging system was developed. Stages I, II, and III reflect increasing amounts of myeloma plus the fractional likelihood of drug resistant clones evolving as the myeloma cells increase in number. The subscripts A and B indicate the presence or absence of abnormal renal function. Kidney function is the single "host" or patient factor which impairs bodily functioning and ability to do well or not with therapy.

"...now in 2002, additional factors can be used to precisely predict outcome."

This system of classifying patients into stages has worked well for decades. But now in 2002, additional factors can be used to precisely predict outcome. During the 1980s, serum β_2 microglobulin testing emerged as a powerful prognostic factor. Increasing levels indicate a larger and more aggressive myeloma tumor burden. Several other factors, some simple, such as age and serum albumin level, provide additional predictive power. More complex tests such as the labelling index (a measure of growth fraction), evaluation of the way myeloma cells look under the microscope (classified into immature/plasmablastic or not), and detailed chromosome analysis directly or by fluorescent techniques (FISH) can add further precision. The newest observation of chromosome 13 deletion or abnormality associated with poorer outcome is the most predictive.

So how can all this information be brought together *and* have international medical consensus? The latter point is the most important and the most difficult to achieve. This is the goal of Drs. San Miguel and Greipp and their colleagues developing the new International Prognostic Index (IPI). This project is supported by a grant from the International Myeloma Foundation (IMF). Data collection from over 20 centers from around the world is now proceeding to develop both a basic prognostic system using parameters (such as SβM, s. albumin, and age) available to everyone, and a more complex system integrating kinetic and genetic information which will allow correlation with current molecular and biologic research.

The goal is to have data analysis completed by the end of 2002. The presentation will be made at the International Myeloma Workshop in Salamanca in 2003. These new levels of precision will guide physicians to select the most appropriate treatment for each individual patient as well as allow patients and their families to know what to expect. The results of this project will interface well with another IMF-supported project: the Myeloma Guidelines Consensus report. These guidelines are being developed by a panel of IMF Scientific Advisors, who will meet for the second St. John's Retreat in May 2002. Specifics of treatment and testing guidelines are being summarized to relate both to the diagnostic and prognostic categories as well as to new planned clinical trials. Novel therapies must be integrated into current management in an organized way to maximize the advantages of the combination therapy approach. Each step forward improves both quality and length of survival for myeloma patients.

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

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2002 Calendar of Events

April 14, 2002	*Second Annual Myeloma March*	*Niantic, Connecticut*
April 18-21, 2002	*ONS Annual Meeting (Oncology Nursing Society)*	*Washington, D.C.*
April 24, 2002	*Cancer Care Teleconference: Understanding Anemia & Fatigue, Part IV*	**see below*
April 27-28, 2002	*IMF Patient & Family Seminar*	*Vienna, AUSTRIA*
April 30 - May 1, 2002	*Advocacy Days*	*Washington, D.C.*
May 11-15, 2002	*IMF Scientific Advisory Board Retreat*	*St. John, USVI*
May 18, 2002	*3rd Annual JC Invitational Golf Tournament*	*Clearwater, MN*
May 18-21, 2002	*ASCO Annual Meeting (American Society of Clinical Oncology)*	*Orlando, Florida*
June 3-4, 2002	*OVAC Advocacy Days (One Voice Against Cancer)*	*Washington, D.C.*
June 7-8, 2002	*IMF Patient & Family Seminar*	*Washington, D.C.*
June 24, 2002	*IMF Golf Challenge 2002*	*Stamford, CT*
August 2-3, 2002	*IMF Patient & Family Seminar*	*Chicago, Illinois*
August 10, 2002	*Challenging Cases*	*New York, New York*
August 26- September 1, 2002	*Myeloma Awareness Week*	*Nationwide*
September 13, 2002	*IMF Patient & Family Seminar*	*Sydney, AUSTRALIA*
October 5, 2002	*IMF Ribbon of Hope Annual Gala*	*Washington, D.C.*
October 10, 2002	*IMF Support Group Leaders Retreat*	*Durham, NC*
November 8-9, 2002	*IMF Patient & Family Seminar*	*Seattle, WA*
December 6-10, 2002	*ASH Annual Meeting (American Society of Hematology)*	*Philadelphia, PA*

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

**To register for a Cancer Care teleconference, please call (800) 813-4673 at least 2 weeks in advance or check the CancerCare website at www.cancercare.org.*

The registrations for the IMF Washington, D.C. Patient & Family Seminar are pouring in.
Only 250 IMFers will be able to attend this exciting event.

DON'T DELAY – REGISTER TODAY!

Update: Friday Welcome Dinner will feature Keynote Speaker Dr. Andrew von Eschenbach, Director of NCI.

ASK THE EXPERTS:
Genetic Testing to Determine the Cause and Outcome Of Myeloma

Gareth J. Morgan, PhD, FRCP, FRCPath
Professor of Haematology and
Director LRF Molecular Epidemiology Programme
University of Leeds, Leeds
W. Yorkshire, United Kingdom

By Gareth J. Morgan, PhD

A question of interest to both patients and doctors alike is why, if a group of people encounter a toxic exposure, only a limited number of them develop disease. "Is it just bad luck?" is a frequently asked question. While there is undoubtedly a contribution of chance, it is not the whole story. Doctors are just beginning to address this question using the information coming from our new understandings of human genome. It is clear to everyone that people differ in size, eye and skin colour and nobody would be surprised to be told that people with dark skin are less susceptible to developing sunburn if they lie on the beach in the summer. The same is true for all the systems of the body where a range of functional activity between people can be identified. These variations are governed by minor genetic changes and can affect the risk of developing a variety of different diseases including cancer and myeloma. The trouble has been that until now we have not been able to recognise these differences.

What has changed recently is that we can now recognise some of the changes in the genetic code, which makes up DNA that governs these differences. The commonest of these changes are known as SNPs (single nucleotide polymorphisms) and there could be as many as 60,000 of these which exert effects on disease. The changes alter either the amount of a protein or its function and, therefore, they can affect the chance of developing myeloma, its time of onset or its severity, and what is more, it is now being suggested that, these changes can affect the outcome of treatment. These changes can now be easily detected using modern diagnostic tests, which means for the first time their clinical significance can be fully explored. Over the next years, it is expected that we will be able to detect a complete genetic profile for an individual and so predict their likelihood of developing a disease and their outcome after treatment.

Now that we can detect these changes, we need to apply them in the clinical environment with the aim of solving issues important for myeloma patients. One common question that causes major concern is whether they have an inherited disease, which means their children are at increased risk of developing myeloma. Certain rare families with an apparent increased risk of myeloma have been identified, but in the overwhelming majority of cases it is not considered to be familial and does not pose any increased risk for the children or families of patient. So it can cause confusion if doctors say that inherited genetic variation can contribute to the risk of developing myeloma. It is, therefore, important to point out the major differences between a familial disease and a genetic predisposition. The most important differential features of these two distinct states is the number and type of genes involved. In a familial disease it is usually a single gene, which causes very obvious effects and inevitably gives rise to disease usually at a young age. For the genetic predisposition we describe here, it is not a single abnormality that is important but the combined effects of variation within a number of different body systems together with a significant impact from life style and environmental exposures. Consequently, in order to study this question, scientists need to combine expertise in genetics with exposure assessment and epidemiology rather than looking within families. The studies often have to be large, well designed, and combine an assessment of exposure with tests for genetic variation.

"...it is expected that we will be able to detect a complete genetic profile for an individual and so predict their likelihood of developing a disease and their outcome after treatment."

"A number of distinct body systems have been identified which can affect the damage occurring as a consequence of environmental exposures."

One of the important features of these genetic variants is that they can modify the effects of toxic exposures, which can cause myeloma encountered in everyday life. This type of effect is referred to as a "gene/environment interaction". This concept is well illustrated by considering the consequences of exposing a group of individuals to a large amount of a toxin known to cause myeloma. In this case the majority of exposed individuals would be expected to develop disease. However, in the normal environment, exposure levels are low and only susceptible individuals would be expected to develop disease. The susceptible individuals could be identified by their genetic make up but would be at no increased risk in the absence of the toxic exposure.

A number of distinct body systems have been identified which can affect the damage occurring as a consequence of environmental exposures. These include the Glutathione S Transferase (GST) family of proteins, which protect against a number of toxic environmental exposures, and the cytochrome P450 (CYP450) family of proteins, which can act to increase the damaging effects of a toxin before it is removed from the body. Underactivity at GST may therefore be a risk factor as may over-activity at CYP450. DNA damage is one of the key features of myeloma. Another important area being studied is how variation in the capacity of the body to repair such damage can affect the risk of developing myeloma. Genetic variation in the cytokine control of the immune system could also affect the risk of developing myeloma. IL6 is a key cytokine and a number of studies have looked at inherited variation within this gene. No associations have been found as yet but there has been a suggestion that variation affecting the pro-inflammatory cytokine TNFa has been suggested to affect the risk of developing myeloma.

"DNA damage is one of the key features of myeloma. Another important area being studied is how variation in the capacity of the body to repair such damage can affect the risk of developing myeloma."

Using these new tests in this fashion is designed to help us understand what exposures cause myeloma and also to identify individuals who are at increased risk. While this type of

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BENCH TO BEDSIDE: Is It a Myth?

Brian G.M. Durie, M.D.
Cedars Sinai Comprehensive Cancer Center
Los Angeles, California

By Brian G.M. Durie, M.D.

In evaluating the new innovations that have contributed to better survival and quality of life for myeloma patients, it is helpful to ask: Where did these new innovations come from? By way of illustration, several items have been selected and are summarized in the accompanying Table.

It is very clear that the origin of myeloma management advances derives from pharmaceutical and related corporations. However, the impetus to these corporations has frequently stemmed from academic research, but at a basic level of chemistry, physics, molecular and cellular biology, and the like. Fundamental research involves organisms as diverse as yeast, worms, flies, and mice, which share many essential molecular mechanisms with humans. The lowly fruit fly (*Drosophila Melanogaster*), whose genome has now been fully sequenced, has perhaps revealed the most about genes and disease.

The application to myeloma has come from clinical investigators – frequently keen young investigators looking for new ideas, who have introduced new diagnostics or therapies as part of clinical trials. The critical observations have been assessments of benefit in terms of better diagnosis, more frequent response to treatment, and/or longer or better quality of survival.

We do not yet have a cure for myeloma. But combination therapy can be curative for several cancers, including testicular cancer (see *Myeloma Today* Volume 3, Number 6), childhood acute leukemia, and lymphomas. Clinicians came up with the curative therapy through "investigator initiated" trials. It is likely that the cure for myeloma will emerge from similar "bedside research" involving physicians not working in a laboratory.

"Bench to Bedside" is therefore not exactly a myth , *but* the bench work usually substantially precedes the bedside research and is typically in a different city or country from the subsequent pivotal clinical observations.

Identifying promising strategies and expediting appropriate clinical trials are therefore the rate-limiting steps. The IMF is committed in its research program to support and accelerate clinical research development of the several new approaches currently under development.

INNOVATION EXAMPLE	ORIGIN *Corporations or other entities*	APPLICATION IN MYELOMA *Clinical Trials*
Diagnostics		
• Serum b2 microglobulin test	Pharmacia (Scandinavia)	Clinical trials in the U.S., U.K., France, Australia
• MRI	Single inventor/ developer: subsequently sold to corporations	Clinical trials in U.S. and Germany
Supportive Care		
• Recombinant erythropoietin (EPO)	Johnson/Johnson; Ortho Biotec; AMGEN	First clinical trial in Austria
• Bisphosphonates	Several corporations (e.g. Chiron, Novartis)	Pivotal trials in Finland, U.K., and U.S. (multi-national)
Myeloma Treatment		
• Alpha Interferon	Schering-Plough and Roche	Early trials with Finnish Red Cross; pivotal trial in Italy with recombinant product
• Standard Chemotherapy – Melphalan	Burroughs Welcome	Trials in U.K., U.S. and Canada
– Adriamycin	Adria Laboratories	Cooperative group studies plus VAD U.S. trial

After Any Diagnosis

Carol Svec

By Carol Svec

"Getting diagnosed with an illness is like hearing the starting pistol at the beginning of a race. Whether it's a sprint or a marathon, a grueling endurance run or a jog through the park, the race is yours alone. No one can run it for you."

Those are the beginning lines of my first book, *AFTER ANY DIAGNOSIS: How to Take Action Against Your Illness Using the Best and Most Current Medical Information Available*, and they ring as true to me today as they did in 1999 when I first wrote them. The book is my attempt to help people "run a better race." My goal in writing it was to help people find, understand, evaluate, and use medical information so they could become more active in their health care and better able to participate fully in making shared medical decisions.

I'm not a doctor, but my experiences have given me an up-close perspective of the issues that are important to patients. I was trained as a scientist, so I understand the processes of experimentation and the slow, inch-by-inch nature of medical advances. I received a master's degree from the University of Toronto, with a specialty in health psychology. I've been doing research, in laboratories or libraries, for more than 20 years, so I know how to find information quickly. For the past 5 years, I've been a freelance health writer, and I consider myself a patient advocate. Throughout this book, I strive to be objective in describing current medical practices, and empathetic to the needs of people who find themselves in the most frightening and sometimes grueling times of their lives.

Because of the nature of my work, I get calls from friends and relatives all the time asking what I can tell them about a particular disease they've just had diagnosed. I've had to inform and counsel my own family through my sister's recovery from a brain tumor, and translate complex medical records for my father-in-law, who recently succumbed to colon cancer. I felt privileged to help, and honored that they trusted me enough to ask me to help find information about some very personal problems. That's when I began thinking about writing the book, to offer people without a health researcher in the family a chance to gain access to the same medical information I had. The idea finally gelled after an interview I had with an oncologist at Johns Hopkins University. I asked him what was the first thing he told his newly diagnosed patients. Without hesitation, he said that the most important thing was to go out and gather as much information about their specific disease as possible. Then he paused, sighed, and said, "Unfortunately, nobody knows how to do that."

That's where this book comes in. As a health writer and researcher, I need to locate and digest information on a wide variety of medical topics quickly. The information has to be current and accurate, otherwise I'm out of a job. The stakes are even higher for those of you dealing with a serious illness. The goal of this book is to guide you through the process of becoming a more active patient and, it is hoped, a healthier person with a better quality of life.

"Research conducted over the past 25 years has shown that patients who are active in their health care are physically and emotionally better off than more passive patients. "

Who are active patients ?

They are people who are involved in understanding their disease, have a good partnership with a physician they trust, make monitoring their symptoms and managing their care a routine, and participate in making shared medical decisions. It isn't always easy, but the results are well worth the effort. Research conducted over the past 25 years has shown that patients who are active in their health care are physically and emotionally better off than more passive patients. Patients who participate have a better understanding of their illness, cope with their disease better, are less anxious before medical procedures, are hospitalized less frequently, and claim to have a better quality of life. Informed patients also tend to get better faster and maintain better health, perhaps because they seek out the best care. Some studies have shown that active patients with cancer experience fewer chemotherapy symptoms, are less depressed, and report lower levels of pain compared with more passive patients.

As frightening as it might be for patients to approach their doctor, most physicians are thrilled when their patients express an interest in becoming more active. Recently, I heard from a woman who had read this book after being diagnosed with breast cancer. Because she was too nervous to approach her doctor directly, she wrote him a letter explaining what she wanted, and would he mind if she considered him her health care partner. At her next office visit, he was enthusiastic about her plan, and their style of communicating immediately changed from passively exchanging information to having an active dialog.

Physicians have a reason for being enthusiastic. An informed patient allows doctors to focus on specific issues and treatment, instead of spending time explaining disease basics. In addition, patients are being called on to make decisions about their medical treatments — choices that can seem frightening in terms of their risks or side effects. Informed and active patients, working in close partnership with their doctors, learn to make the best decisions for themselves. When doctors and patients share in making medical decisions, they take into account not only the medical pros and cons, but also the patients' life priorities, experiences, desires, and hopes for the future.

The basics of becoming an active patient are simple, but putting them into action can be difficult. I've spoken with physicians who teach patients how to become more active who say that they themselves sometimes have difficulty putting plans into action. It is hard to break old habits, but the changes are worth it. Here are a few action items to guide you in the process of becoming an active patient:

- Seek out and understand information about your disease and treatment. Read as much as you can, ask questions, join support group… anything.
- Establish partnerships with your doctors. Some doctors do this routinely; others need to be asked. Make it clear that you don't want to "take over" for the doctor, but to participate in decisions and care issues.

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GALA 2002 HONOREE: Daniel E. Smith

Daniel E. Smith

The IMF is pleased to honor Daniel E. Smith at the *Ribbon of Hope-Making a World of Difference* 12th Anniversary Gala, to be held at The Ritz-Carlton in Washington, D.C. on October 5th, 2002.

Mr. Smith is the National Vice President of federal and state government relations for the American Cancer Society (ACS). He is responsible for coordinating the development and execution of strategic federal and state advocacy programs and practices on behalf of the ACS's two million volunteers and 28 million donors.

Prior to joining the ACS, Mr. Smith worked for 10 years in the U.S. Senate where he held several senior staff positions in the office of Senator Tom Harkin of Iowa, including four years as Chief of Staff. Mr. Smith also served as Minority Staff Director for the Senate Committee on Agriculture, Nutrition and Forestry. Mr. Smith was responsible for drafting major pieces of legislation and building a consensus around a variety of issues with other members of Congress, the White House, federal regulatory agencies, and constituents. He also has extensive experience in a number of Presidential, Senatorial, and Congressional campaigns including Gore 1988 and State Director for Clinton/Gore in 1992.

Based in Washington, D.C., Mr. Smith leads the ACS's advocacy team in the development and implementation of the Society's key legislative priorities:

1. *Increase Investments For Cancer Research and Application Programs.*
2. *Increase Access to Cancer Care, Prevention, and Awareness Programs.*
3. *Reduce Health Disparities Among Minorities and the Medically Underserved.*
4. *Reduce And Prevent Suffering from Tobacco-Related Illness.*

Mr. Smith is also the founder of One Voice Against Cancer (OVAC), a collaboration of over 40 cancer and public health organizations representing more than 15 million Americans. OVAC delivers a unified message to Congress and the White House on the need for increased cancer-related appropriations.

OVAC began in January 2000 as a working group of public interest organizations dedicated to ensuring that the federal government provides the necessary investments for cancer research and application programs. It has since grown into an effective lobby coalition on cancer funding that has enabled the cancer community to enhance policymakers' awareness of the need for substantial increases in essential cancer programs. Lawmakers and federal agencies are asked also to focus efforts on research and outreach into ethnic minority and other undeserved populations, many of which have a higher risk and mortality from various forms of cancer.

OVAC 's united front enhances each organization's ability to attain the funding levels necessary to win the war on cancer and to equip those facing cancer with the tools they need to fight this deadly disease. OVAC commits its participating organizations to cooperative efforts that increase understanding of the need for both cancer research and application programs. At the same time, OVAC empowers its volunteers and those touched by cancer to deliver this message creatively and powerfully to policymakers.

A native of Iowa, Mr. Smith graduated from the University of Iowa with highest distinction. He received his law degree from the Georgetown University Law Center in Washington, D.C.

GALA UPDATE

The IMF is pleased to announce that, for the third year in a row, the incomparable Robin Leach will serve as the Gala Master of Ceremonies and Guest Auctioneer.

Our wonderful Dinner Chairs, Carol and Benson Klein, are hard at work with the members of the Gala committees gathering auction items and packages. If you have any ideas or items you wish to contribute, contact Carol at (301) 469-7457 or *carol@kbk.org*.

If you wish to attend the Gala, please contact Suzanne Battaglia at (800) 452-2873 ext. 227 or *SBattaglia@myeloma.org*. For other ways of participating in the Gala event, please see the enclosed insert .

With your help, this is going to be the best event yet. We look forward to seeing you there!

FASHIONS4 A CURE

By Ashley S. Barit

My mother, Jerra S. Barit, was diagnosed with multiple myeloma in December of 1998, while I was still in high school. In her honor, I organized the first annual "Fashions 4 A Cure" fundraiser on May 8, 1999. With the help of friends and family, and the support of local businesses, that first event raised $5,000 to support myeloma research. Since then, three more events have been held, the most recent on March 16, 2002. The "Fashions 4 A Cure" program has now raised $45,000 for myeloma research.

Jerra and Ahley Barit (top row) with "Fashions 4 A Cure" models

Becoming involved with "Fashions 4 A Cure" has changed the lives of the Barit Family. It has bought us closer together. Also, it has helped us reconnect with friends and family. Our hope is that the funds we have raised will help my mom and the thousands of other myeloma patients.

Since my first contact with the IMF four years ago, I have become involved in many activities with the IMF. My family and I have attended the IMF Patient & Family Seminars, Senate hearings, and the IMF *Ribbon of Hope – Making a World of Difference* Gala. I would like to thank the staff of the IMF, especially Susie Novis, Romi Brozeit and Pam Jones for their continued support.

Adult models of the "Fashions 4 A Cure" event

OVAC AdvocacyDay

Greg Brozeit of the IMF shares a moment with former President George and First Lady Barbara Bush, co-chairs of the National Dialogue on Cancer, at one of last year's semi-annual meetings. The IMF is a Partner in the NDC, a 160-member coalition dedicated to shaping a national cancer agenda to prevent one million new cancer cases and 500,000 cancer deaths by 2010.

By Greg Brozeit

The 3rd annual One Voice Against Cancer (OVAC) Advocacy Day will be held on June 3-4, 2002 at the Hyatt Regency on Washington, DC's Capitol Hill. The IMF supports the OVAC funding agenda because it is the best hope for increased federal funding to benefit all cancer patients, especially those with an interest in myeloma and other under-funded orphan cancers. The IMF website has posted registration information.

Senator Tom Harkin (D-IA), chairman of the Senate Appropriations Subcommittee on Labor, Health and Human Services, and Education — which is responsible for funding most federal cancer research — has scheduled a hearing to highlight the OVAC agenda on the morning of June 4. The hearing is expected to focus attention on funding of orphan cancers, especially multiple myeloma and pancreatic cancer, and determining methods of accelerating research that will benefit today's cancer patients.

OVAC is a coalition of the spectrum of cancer advocacy organizations which is dedicated to increasing funding for diversified research and prevention programs at the National Institutes of Health (NIH), the National Cancer Institute (NCI), and cancer programs at Centers for Disease Control and Prevention (CDC). OVAC has been credited with maintaining recent funding increases for federal cancer research funding.

The New Paradigm

Why support the OVAC agenda and not just myeloma research? The funding figures and the state of the science help explain.

This year the NCI will spend almost $4.2 billion on cancer research. To compare, the American Cancer Society, the largest cancer research funding organization in the world, will invest more than $100 million over the same period. And one of the most visible advocacy organizations, the Susan G. Komen Foundation for breast cancer research, has raised more than $240 million since its inception in 1982.

These numbers demonstrate why political advocacy is as important a task for members of the myeloma community as other fundraising activities. While many organizations, including the IMF, annually raise cumulative millions for research, our federal government appropriates annual billions for cancer research agencies and institutes. But as we engage in community fundraisers for research, let us also commit at least as much time and effort to educate our members of Congress about the value of allocating our fair share of tax dollars to cancer research.

The IMF also believes that the OVAC agenda is the best mechanism to support newly appointed NCI Director Dr. Andrew von Eschenbach's emphasis on the New Paradigm of cancer research. This New Paradigm places less emphasis on research by body part or tumor type. This new approach will put more emphasis on the most promising, state-of-the-art research of genomics, drugs that treat cancer at the molecular level.

"Your view that promoting full funding for the NCI Director's Bypass Budget request will best serve your constituents is an enlightened one. A rising tide does indeed raise all ships."
NCI Director Dr. Andrew von Eschenbach in a March 15, 2002 letter to the IMF

The traditional way of thinking about cancer treatment has been "search and destroy," which is best exemplified by chemo-therapy. In plain English, these therapies try to kill cancers with toxic drugs with the hope that enough healthy cells survive the process to maintain the continued health of the patient. As too many of us know, some of these treatments are as bad or worse than the disease they are trying to eliminate.

The New Paradigm, which replaces the "search and destroy" mindset with "command and control," demonstrated with drugs like Gleevec® for chronic myelogenous leukemia, Iressa® for lung cancer, or Herceptin® for breast cancer, targets the molecular mechanisms that trigger growth of cancers without debilitating or destroying healthy cells, organs, or systems.

When we look at cancer at the molecular level, targets will not be conveniently categorized through body parts or tumor types. The key is to identify, through research, the targets that trigger the malignant growth of cancer cells. In the case of myeloma, there may be dozens, if not hundreds, of targets that must be identified. And some of the targets in myeloma, at the molecular level, may look more like other traditional cancer types — lung, colon, kidney, or pancreatic — than other hematological cancers.

Congress recognized this opportunity in last year's appropriations bill when it declared "that NIH should distribute funding on the basis of scientific opportunity" and "urge[d NIH] and the Administration to continue to resist pressures to earmark, set-aside and otherwise politicize" funding for medical research programs (House Report 107-229).

In other words, the appropriators, those who control the purse strings of the NIH and NCI, specifically granted the directors of the institutes the authority to ignore congressional attempts by other committees to authorize specific body part or tumor type programs in favor of "scientific opportunity." More precisely, they gave credence to NCI Director von Eschenbach's vision of the New Paradigm in cancer research.

Director von Eschenbach underscored this view in a March 15, 2002 letter to the IMF stating, "Your view that promoting full funding for the NCI Director's Bypass Budget request will best serve your constituents is an enlightened one. A rising tide does indeed raise all ships."

The OVAC agenda — which maintains support for the 5-year funding doubling pledge for NIH, fulfillment of the NCI Director's annual Bypass Budget proposal, and the applied research programs at CDC — is the most logical and constructive plan to achieve those goals in the foreseeable future.

The Bigger Picture

Indirectly, fulfillment of the OVAC agenda would also support the goals of the IMF's other primary legislative priority — enactment of the Access to Cancer Therapies Act (H.R. 1624 and S. 913). This legislation would provide Medicare coverage for all oral cancer drugs. In addition to the drugs mentioned above, this bill would include coverage for Thalidomid® and

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Did You Know?

The Neuropathy Support Group of Los Angeles meets monthly at the UCLA Medical Center. For more information, please call Cathy at (310) 286-7442.

Online registration for the June 3-4, 2002, third annual One Voice Against Cancer Lobby Days is available at *www.b-there.com/ersengine/ovac2002*.

To obtain a free copy of the *Pain Action Guide*, please call the American Pain Foundation at (888) 615-PAIN or send an email to *info@painfoundation.org*.

Cancer patients dealing with insurance, job discrimination, and debt crisis issues can appeal for assistance to the Patient Advocate Foundation at (800) 532-5274 or visit *www.patientadvocate.org*.

Patients who cannot afford to pay for medications may qualify for the drug manufacturers' Indigent Programs. Your physician must apply on your behalf.

Dendreon Corporation has received orphan drug status from the U.S. Food and Drug Administration (FDA) for the company's therapeutic vaccine for multiple myeloma, Mylovenge (™). Orphan drug designation by the FDA is designed to encourage research and development of new therapies for diseases that affect fewer than 200,000 people in the United States. In receiving orphan drug status, the company is eligible for tax credits for related clinical development costs and assistance from the FDA to facilitate the regulatory review and approval process.

A Patient's Perspective: A Diet to Control Pain

by Coralie W. Crafton

I am a wife and proud mother of two daughters. When I retired from teaching elementary general and vocal music, my husband and I decided to invest in a few more rental properties for me to manage. My husband and I sing in our church choir and I am active in the Lancaster Opera Company.

In November of 1998, back pain caused me to see my family doctor. A couple of months of chiropractic treatments did not relieve the pain. My family physician took a SED (sedimentation) rate and made the initial diagnosis of myeloma. I saw an oncologist and he confirmed the diagnosis. I was 53.

Our family was shocked and scared. At first I thought it was a definite death sentence. Everyone I had known who had cancer had died from it. Now I think of my disease more like a chronic illness. I can live with it and still have a full, enjoyable life.

In June of 1999, I received my first treatment of chemotherapy (alkeran and prednisone) and Aredia. I became so weak that I had to hold onto furniture to walk around the house. Because of that experience I chose to try several alternative treatments, but they did not stop my myeloma from progressing to Stage III.

In March of 2000, I decided to go back on chemotherapy, but this time without the steroid. I tolerated the alkeran and Aredia very well, and by October my condition had improved 75%! In February of 2001, my oncologist stopped the chemotherapy and started me on thalidomide. My test results continue to show improvement. In May of 2001, I celebrated my 56th birthday.

After my diagnosis, I spoke with a friend, retired homeopathic osteopath Dr. Luelle Hamilton, about the extreme back pain I was experiencing. She put me on a diet to turn the acidity of my body to alkalinity, because an alkaline body experiences less pain. Even when I was not using Aredia (June 1999 - March 2000), this diet helped me manage my back pain. I did not need to use pain pills.

These foods make the body acidic. I have eliminated them from my diet:

- Dairy products
- White potatoes
- Tomatoes
- Red meats
- White rice
- Pasta
- Oranges
- All dry legumes
- Mushrooms
- Pineapple
- Eggplant
- Plums
- Prunes
- Wheat
- Limes
- Carbonated beverages
- Black & Cayenne pepper
- Peanuts or peanut butter
- Berries (except blueberries)
- Red, Yellow or Green bell peppers
- Vinegar, Pickles & Sauerkraut
- Processed foods & chemical preservatives
- Sugar, Aspartame & Saccharin

These foods help my body be alkaline:

- Soft cooked eggs
- Juice of one lemon in 6-8 oz. of water
- Fresh fruit such as tart apples and tropicals such as papaya, mango, tangelos, tangerines, clementines, and grapefruit (but no oranges!). Pears, grapes, and stone fruits are bland and combine well with peaches, apricots, and cherries.
- Most vegetables are alkaline. Dark salad greens, raw spinach, and kale have more nutrients than iceberg lettuce.
- Nuts such as pecans, almonds, and cashews are good protein. Wash and blanche or roast them to remove mold.
- White chicken, white turkey, white fish.

Do not combine:

- Citrus and bananas
- Citrus and any cereal
- Starch and protein at the same meal

Make positive lifestyle choices:

- Do not allow your activities to tire you. Rest for 10 minutes for every hour of activity. An afternoon nap is a must to avoid fatigue. A fatigued body is more likely to become acidic and painful.

For two years, this program has helped me be pain free, vigorous, and cheerful. No two people are alike, but I wanted to share my experience with others looking for ways beyond pain medication to manage their suffering. The improvement in the quality of my life has definitely been worth the lifestyle change and effort. There is hope.

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

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Atlanta IMF Patient & Family Seminar Report

Leon Parker

By Leon Parker

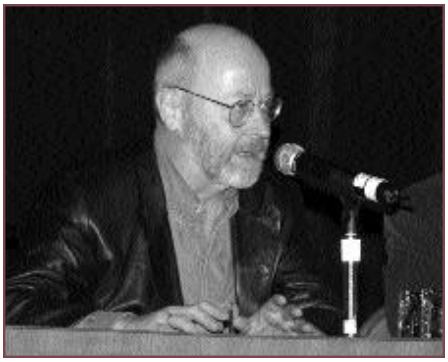
The IMF Atlanta Patient & Family Seminar was held on March 8-9, 2002. This seminar originally had been scheduled for September, 2001, but had to be postponed because of the events of 9/11.

IMFers Dr. and Mrs. Joseph Lerner with Dr. Robert A. Kyle

This seminar was my second chance to attend one of these very informative IMF learning and networking opportunities. I attended my first IMF seminar here in Atlanta about three years ago and found it to be extremely enlightening. The IMF staff was very friendly and very well organized. The registrants of the convention covered people across the entire treatment spectrum. There were people there who had been diagnosed as recently as a couple of months ago and people who were survivors of 15 years.

Susie Novis Dr. Alice Caldwell

The seminar was a fast-moving one with information being presented by an extremely capable and well recognized myeloma expert faculty that is unrivaled. Each session lasted about 20-30 minutes and there was always an opportunity to ask questions. I must admit that sometimes the questions got a little repetitive and off subject, but what can you expect when you've got 300-400 concerned and anxious people in



Dr. Bart Barlogie takes the podium

attendance – many of whom really need personal and subjective advice.

The first session was Myeloma 101 , a primer of all the basics that we need to know and tend to forget if we've not focused on it recently. It was very good for me because I am one who tends to move away from the "Myeloma World" and on to living my life for periods of time when I am really feeling well. When I was initially diagnosed back in May, 1996, I spent hours poring over materials

Dr. Vesole addresses participants of a break-out group

and data trying to learn something about this little-known and devastating disease. Since then, I have had a stem cell transplant and various regimens of chemotheraphy. I have been on thalidomide since August, 2000. It's been a lifesaver and has stabilized my counts, and I now enjoy a good quality of life.

The next session was Standard Therapy by Dr. Robert Kyle of the Mayo Clinic. Dr. Kyle covered the various treatment options that one has when diagnosed. I took

Susie Novis with IMF Gold Benefactors Jan and Charles Briscoe

note of his thoughtful comparisons of the various treatments that I had chosen and those that had been chosen for me since my diagnosis.

Dr. David Vesole addressed the topic Transplantation and covered it well. I found the talk interesting but doubt that transplantation is something that I would choose to do again. The remission after my

Cathy Lebkuecher accepts the Francesca Thompson Distinguished Service Award from Michael Katz as husband Andrew looks on

transplant lasted about eighteen months and I understand that the remissions get shorter with each transplant. Never say never, but it now seems to me that if you can maintain control of this disease by utilizing any of the other less invasive methods of treatment, then that certainly is the way to go.

There was also a session conducted by Dr. David Roodman covering Bone

Please see page 10

IMF Gold Benefactor Chuck Newman with Susie Novis

ASK THE EXPERTS – continued

observation will in time lead us to understand, and possibly prevent, exposure to factors which cause myeloma, there is another use to which this information can be put. In many ways, the current treatments used for myeloma can be considered as toxic exposure where the benefits of exposure far outweigh the toxic effects. However, in some individuals the risks of side effects may be greater, and where alternate treatment options are available it may be preferable to use these. Genetic testing is beginning to help in this area. The GST P1 subtype of glutathione S transferase is important in the metabolism of some of the most effective chemotherapy agents used for the treatment of myeloma (alkylating agents like melphalan and cyclophosphamide). It has a number of different genetic variants, which can decrease its activity. Individuals who have inherited the under-active variants seem to have an increased risk of side effects but seem to have a better outcome after treatment. This approach is not fully developed and could not be used to direct treatment at present, but if this sort of testing is integrated into future trials it will allow us to use our treatments better. Genetic testing can also be used to help in the development of new treatments. Many pharmaceutical companies discard active therapeutic agents because the rare individual develops side effects. These individuals often have a defined genetic make up, and if this can be recognised, the drug can be reserved for people who do not get side effects and will benefit from treatment. The study of this area is called pharmacogenomics. These tests have to be distinguished from tests on the myeloma tumour DNA. Tests on this material using the new genetic approaches are designed with the aim of predicting how the tumour cells will respond to treatment.

Access to genetic information is one of the key developments that has given doctors a new tool to develop more effective prevention and treatment strategies for myeloma. It is important to use this new approach in the correct clinical settings: clinical trials and case control studies. This means that patients will be asked to give their permission for their blood samples to be taken, stored, and tested. If we are going to make effective progress in eradicating the clinical consequences of myeloma, it is important that patients take part in these studies. These studies have to be large, and consequently doctors and scientists will have to come together in large groupings with the common goal of understanding and treating this disease.

AFTER ANY DIAGNOSIS– continued

- Be entirely open with your doctors… even about the embarrassing things, and even if you think it makes you look bad (such as not taking medication). There are solutions to many problems, but doctors are not mind-readers and cannot help if they don't know what's wrong.
- Don't leave the office without understanding what your doctor said. If the doctor is using words you don't understand, ask him or her to say it in a different way. If you run out of time, ask if a nurse or other professional could explain things more clearly. You shouldn't need a translator to decode medical buzzwords when you visit a doctor.
- Bring a friend to help you ask questions if you are nervous or shy.
- Prepare for office visits by bringing records of anything that has happened since your last visit, including symptoms, medication side effects, and the results of tests or medications prescribed by other doctors. If you have questions, write them down in advance so you don't forget.

Those are the basics, but you can become as involved as you want to be. *AFTER ANY DIAGNOSIS* can guide you through the process. I've heard doctors and patients say that in health matters, peace of mind comes knowing that you've done everything possible to take control of your health. That's the best any of us can do.

ADVOCACY– continued

all the future genomics-based drugs that will target tumor growth at the molecular level.

Currently, it is estimated that 5-10% of all cancer drugs are taken orally. In the coming decade, that figure is expected to rise to at least 25%. The logical outcome of the New Paradigm will be a dramatic acceleration in the discovery and approval of genomic drugs that may push those percentages even higher, and limit – and hopefully eliminate – the need for "search and destroy" chemotherapies.

Although this legislation is not a part of the OVAC agenda, which is appropriations-based, it completes the vision of the New Paradigm. The IMF recognizes that support of a comprehensive, OVAC-based funding mechanism will provide the comprehensive framework that links federal activity to the translational research needed to produce the drugs and therapies needed by all cancer patients.

And the future of the IMF advocacy agenda will not be dictated by trying to carve out turf for myeloma research. It will, instead, ensure that myeloma is represented in the new research. This search for new therapeutic targets will create a logical, visible path from incurable condition to chronic, manageable disease to, ultimately, a cure for myeloma.

SEMINAR – continued

Disease. Zometa®, recently approved to help myeloma patients with bone disease, is given in just 15 minutes versus the two hours that Aredia® takes. That's really convenient for a lot of people. However, having had a kidney issue in the past, I am going to play it safe and stick with Aredia®. If it ain't broke, don't fix it!

Dr. Alec Goldenberg talked about the new Goldenberg Snare Coil that has been developed to help make bone marrow biopsies a lot more bearable. Sounds good!

The highlights of the seminar, from my perspective, were the sessions that focused on Novel Therapies. Thankfully, there are many: PS-341, Genasense, Beta LT, Mylovenge, Neovastat, O-6-benzylguanine, Panzem®, Trisenox®, and others. All of the above mentioned are already in either Phase II or Phase III trials. The trial results with PS-341 (Millennium Pharmaceuticals) have been so good that they are widening the Phase III trials to include more medical facilities and more people across the country. The problem there for me is that you are not eligible for the trials if you suffer from neuropathy. I do have a neuropathy problem as a result of taking thalidomide.

Not to worry. With all of the new drugs in trial, and with more money than ever before going into myeloma research, I left the seminar feeling more optimistic than ever. It is inevitable that some drug will be discovered to control multiple myeloma the same way many chronic diseases are controlled. I left this seminar feeling very informed and very confident that there is more reason than ever before for real hope.

IMFers sign up for break-out sessions at the Altanta Seminar

Twelve Simple Truths to Soothe Stress

Susie Mantell

By Susie Mantell

You'd be hard-pressed to find an oncologist's waiting room not brimming with illness-related stress. People often arrive already deeply frustrated by previous attempts at diagnosis and care, presenting overtaxed systems ravaged by stress, sleeplessness, and pain. Paradigm-shifting work is underway examining the relationships between emotions and health, transmitters, peptides; suggesting that emotions reside not only in our heads, but in fact at a cellular level. Endorphins – morphine-like substances produced naturally in the body-mind – attach to receptor sites and relay "stop-pain" messages, sometimes easing anxiety, lifting depression, lightening mood as well.

"Feel-Good" activities, and finding humor in exasperating circumstances, are drug-free ways to reduce pain and stress, enhancing overall well-being. Life can be very difficult, and brings extraordinary challenges to many. But some stress is influenced by perspective. How we experience an event determines its "stress value" for us. A positive outlook, humor, gentle touch, and honest, supportive relationships all increase the "Feel-Good" factor.

I wish you all those things and above all, Hope. Hope is what sees us through our most challenging moments, and reminds us of the promise that just may be around the very next corner!

Note: Susie Mantell is an award-winning stress-relief facilitator and author of "Your Present: A Half-Hour of Peace" (CD/Cassette). To subscribe to Susie's free e-mail Stress-Tips, please visit *www.relaxintuit.com.*

1. Stress Happens. Every Day.
2. Life is always about choices… even when it doesn't feel that way.
3. Mind informs Body. Stress impacts our health, r elationships... and who we will become.
4. How we manage stress deter mines the quality of our lives.
5. Every action stems from one of two roots: Love… or Fear.
6. "The Golden Rule" is still a very good idea.
7. One smile can turn two people's entire day around.
8. Love Heals. So do Laughter and Forgiveness. Anger never will.
9. To love anything requires a leap of faith – in ourselves, others, and the power of Love itself.
10. We can spend a lifetime grieving what was, or what never was… or living for what is, or can be.
11. We're never too old to learn or change.
12. We grow toward the light... or wither on the vine.

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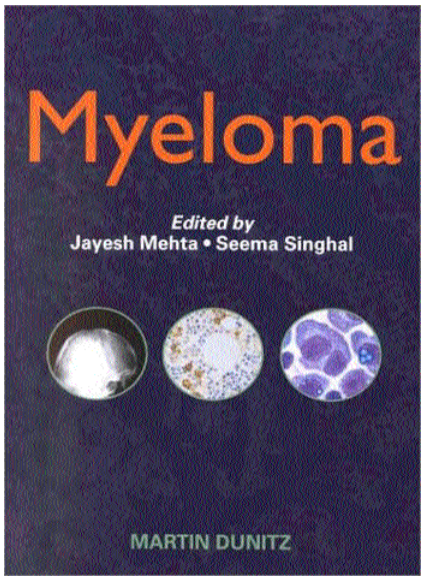
News & Notes

New Myeloma Textbook

IMF Scientific Advisors Drs. Seema Singhal and Jayesh Mehta have co-edited a textbook titled *Myeloma* – a comprehensive text on multiple myeloma and related diseases. The forward for the textbook was written by IMF Chairman of the Board and Scientific Advisor Dr. Brian G.M. Durie. Written for hematologists, oncologists, and researchers, the book covers all aspects of myeloma – the molecular and biological background, clinical aspects and investigations, and developments in therapy. The book is available through www.a*mazon.com* .



Bisphosphonates

Patients who receive infusions of Aredia® (pamidronate) should be aware that there are now alternative versions of this bisphosphonate on the market. One generic pamidronate is being distributed by Bedford Laboratories of Bedford, Ohio. Others may soon be on the market. The IMF encourages patients to be aware if you are receiving the brand-name Aredia® or a generic pamidronate.

In addition, as the IMF has previously reported, the FDA approved a new bisphosphonate, Zometa® (zoledronic acid), for the treatment of multiple myeloma. The drug was originally approved in August 2001 for the treatment of hypercalcemia of malignancy, a common metabolic complication associated with cancer. The safety and effectiveness of Zometa® was supported by three large international trials that included more than 3,000 subjects. Results demonstrated that Zometa® decreased skeletal complications of subjects with multiple myeloma or metastases from solid tumors.

IMF Scientific Advisors Drs. Robert Kyle and James Berenson concur that Zometa® provides a convenient alternative to pamidronate for the myeloma patient with skeletal disease. With an efficacy profile similar to that of Aredia®, Zometa®'s major advantage is its infusion time of 15 minutes rather than the 2 to 4 hours required for Aredia®. For more information on Zometa, please visit the product web site at *www.zometa.com*.

Nancy Baxter and Debbie Birns

IMF Hotline Service Expands

The IMF is pleased to announce the recent addition of two new staffers to our team. The IMF Hotline coverage has been expanded with the recruitment of cancer information specialists Debbie Birns and Nancy Baxter. Both Debbie and Nancy were trained as cancer information specialists by the National Cancer Institute-sponsored information line at UCLA's Jonsson Comprehensive Cancer Center. They are available Monday through Friday to answer your questions about multiple myeloma treatments and side effects, supportive care issues, clinical trials, and resources available to myeloma patients and their families. You are also welcome to continue to submit your questions and concerns via e-mail at *TheIMF@myeloma.org*.

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