



# Myeloma Matters

## MATTERS MYELOMA

The newsletter of **MYELOMA MATTERS**

info@myeloma.org.nz or 04 236 7564

**Vol 1 Issue 3 MAY 2006**

It is a bit late to say happy New Year but as the first newsletter of the year it is appropriate. I hope 2006 has been good to you. We have faced our share of complications but are still here.

News, lots has happened in the world of myeloma and the first item relates to an article in this weeks Sunday Star Times about two myeloma patients from New Zealand joining a case action against a drug company over ONJ. The paper referred to a recent Med Safe article that you will find in this newsletter. This basically repeats what Dr Rose Mary Jones told us when she came to talk about ONJ when it was still very, very new to all.

One of the Wellington patients who has a nasty case of ONJ was pretty blunt when we spoke this morning. His view was that there never were any guarantees with this disease, except that it would kill him sooner rather than later and even if the Pamidronate he took may be partly responsible for his still living a pretty good life – even with the nightmare of ONJ. He added “This is just one of things that we have to live with, you have a choice, you have the treatment that may cause problems but may also keep you alive or you don’t and you die, it is up to you”.

The Mayo Clinic is bringing the 4<sup>th</sup> State of the Art Symposium on Hematologic Malignancies to Wellington Jan 14<sup>th</sup> - 18<sup>th</sup> 2007. This is huge in all sorts of ways. This meeting will welcome all those involved in the treatment, care and research of blood cancers, offering them the to opportunity to hear world leaders in that field of hematology. It will focus the attention of perhaps 1000 haematologists and others from around the world on Wellington and showcase what we have and what we can do. A good number of Australian and New Zealand specialists will join the large group of Mayo experts presenting at this meeting. This happened because of the visit of Dr Philip Greipp to Wellington in August last year, he liked what he saw, was impressed by those he met, saw that he could help and he is doing just that.

There is an afternoon session that has a patient focus and you are welcome to attend. The program is in the final stages of completion and I am unable to tell you very much until it is fully approved in the next few days. However this afternoon session will look at how to manage some of the more distressing problems so many face, fatigue, neuropathy etc. I hope you will come along and participate in this unique event. Check it out <http://www.mayo.edu/cme/jan2007.html>

Mike Berridge, Group Leader, Malaghan Institute of Medical Research is a major part of the local team working with the Mayo Clinic on their upcoming visit and also working to create a long term relationship that will be mutually beneficial to the two organisations. Mike wrote this article for

Myeloma Matters and gave it to me in January, sorry it has taken so long to publish Mike – we will do better next time.

When the Mayo Planning Team were here in March we took them to meet the Titahi Bay Wellness Group, a group of seniors who gather every week for exercise and fellowship. They have a weekly speaker and play Housie at 10 cents per line after lunch. They have raised a considerable sum of money for the Malaghan Institute for Medical Research over the years they have been meeting and their annual donation to the Malaghan Institute is directed to helping research into Multiple Myeloma. These good folk gave our visitors a sumptuous morning tea and everyone enjoyed themselves so much the group will come together during the Christmas break specifically to welcome the Mayo folk back

Dr William Mayo, one of the founders of the Clinic said, "The best interest of the patient is the only interest to be considered". That is a guiding principle of the Mayo Clinic to this day. Patients in the USA face as many problems getting appropriate treatment and care as we do, here the Government decides what care will be available and provides it. In the USA it is the Insurance Plans that decide what can and cannot be done. I heard a report from the NBC last week where a Dr at a 300 bed hospital in Missouri said he spent more time trying to get funded care for his patients than he did doctoring them. One of our team said the same thing to us the following day. There are many similarities and few obvious solutions.

Sunday August 6<sup>th</sup> 2006 will see the first Myeloma Matters workshop of the year, details to follow but it will basically follow the format outlined in the last newsletter, an interactive day discussing how to live well with myeloma. Duxton Hotel 10am – 4pm with lunch provided.

This newsletter has been brought to you by one of myeloma patients who lives in a remote community, he has missed his monthly myeloma read, he has commented on that frequently as this is his only contact with others. I have finally accepted his offer to pay for the printing of this edition on the basis that if the Cancer Society release the funds I raised for this purpose, and many of you are of the opinion that they will, I will repay his kind advance.  
Cheers Judi

### **ONJ – Dr Rose Mary Jones's Advice**

Maintain the highest standard of dental hygiene at all times  
Ensure your teeth are in good condition before you start any treatment  
Avoid invasive treatment, if in doubt refer your dentist to the Dental Department at Wellington Hospital / your local hospital  
The Wellington Hospital Dental Department will give you advice and suggest products to help with dry mouth, dental hygiene etc. and offer treatment if required on referral.

### **The Med-Safe Article, May 2006.**

#### **Bisphosphonates and osteonecrosis of the jaw**

*Ian Reid, Professor of Medicine and Endocrinology, Faculty of Medical and Health Sciences, University of Auckland, Auckland*

This is a new entity for most doctors. It refers to the development of areas of exposed, necrotic bone in either the mandible or maxilla, which persist for a number of months. This problem is being recognised in oncology patients, many of whom have been treated with high-dose monthly bisphosphonates. This is most commonly seen in those with metastatic breast cancer or with multiple myeloma. The possible association with the use of bisphosphonates has raised the issue as to whether this is a problem in those who use bisphosphonates for benign indications, such as osteoporosis and Paget's disease. There have now been some case reports of this phenomenon, although they constitute less than five percent of the total number of cases recorded. For instance, there have been about one hundred cases reported worldwide with alendronate in the context of twenty million patient-years of use of this medicine. The lesions seem to develop following major dental procedures, such as extractions or dental implants, although they are sometimes associated with local trauma from dentures. Some dentists are recommending such procedures are entirely avoided in those with a history of bisphosphonate use. To many working in the field, this seems an over-reaction to what is, outside the context of oncological practice, a very rare event. While the pathogenesis and aetiology of this condition are being further explored, it does seem cautious to carry out any planned major dental procedures *before* individuals start on bisphosphonates. However, it must be borne in mind that substantial delays to the initiation of bisphosphonate therapy in those at a substantial risk of fracture will lead to the occurrence of preventable fractures.

\*\*\*\*\*

## **Myeloma Matters at the Malaghan - Cancer Stem Cells under attack**

**by Mike Berridge** January 2006

*Malaghan Institute of Medical Research, PO Box 7060, Wellington*

The Malaghan Institute is taking on the cancer stem cell. In a quirk of fate that began some 30 years ago with attempts to fingerprint a rare population of blood-forming stem cells in the bone marrow, researchers at the Malaghan Institute have this year developed a novel assay for cancer stem cells. What is remarkable and unique about this assay is that the cell target is a quiescent or slowly-dividing cancer cell with properties similar to those of stem cells. In contrast, most current anticancer drugs target rapidly-dividing tumour cells but not the cancer stem cell.

The cancer stem cell assay will be used to screen potential anticancer drugs that block a vital life support system used by these stem cells. Surprisingly, the target is in the outer lipid membrane of the cell in contrast to the vast majority of current anticancer drugs that act inside the cell to block cogs in the machinery of the cell division cycle. As a result, side effects that are the hallmark of many current cancer drugs should be greatly reduced. In joint research with synthetic organic chemist, Professor Robin Smith at Otago University, and with funding from the Genesis Oncology Trust, designer drugs will be built that position in the outer membrane of the cell, blocking a stress release pathway used by cancer stem cells as well as other cancer cells.

### **The cancer stem cell enigma**

Almost fifty years after their discovery, cancer stem cells remain an elusive target in our anticancer drug armoury. This is because they exist as rare subpopulations of tumour cells that divide infrequently in a protected environment and therefore resist cytotoxic drugs that kill dividing cells. Cancer stem cells, in common with other stem cell populations in the body, are

characterised by an ability to self-renew slowly without loss of proliferative potential. Alternatively, they can produce "committed" daughter cells that are unable to self-renew. These daughter cells divide rapidly but have a limited proliferative potential. With normal stem cells, these "committed" cells eventually generate the large numbers of functional cells that make up, for example, the blood and immune systems, and the linings of the body. With cancer, proliferating cells that cannot self-renew, predominate and maturation to generate non-dividing functional cells is often blocked or slowed down. In support of the stem cell model of cancer, cancer stem cells have recently been demonstrated to comprise only a few percent of tumour cells while the vast majority of dividing cells in the tumour are non-tumorigenic, that is, they are unable to self-renew and reproduce tumours when transplanted into suitable recipients. Cancer stem cells have now been demonstrated in a wide range of different cancers including breast, colon, neuroblastoma and haematological malignancies.

In May of last year, Professor Michael Clarke from the University of Michigan Medical School was an invited keynote speaker at the NZ Society for Oncology conference in Wellington where he talked about his pioneering research on breast cancer stem cells, including their isolation, assay and gene expression profiling.

The irony is that cancer can now be considered to be a disease of non-dividing cancer stem cells, rather than of rapidly-proliferating cells which form the bulk of the tumour but cannot sustain tumour growth indefinitely. If cancer cure is our ultimate goal, then we must find ways to seek out and eradicate the cancer stem cell.

The November 2005 issue of Myeloma Matters featured an article on Stem Cells by Scott LaFee, San Diego Union-Tribune writer. In that article, the potential of normal stem cell populations to repair and regenerate damaged tissues and organs was contrasted with their dark side when genetic change turns them into rogue cancer stem cells. The rogue cancer stem cells will then produce dividing tumour cells that form most of the tumour mass.

The focus of attention of most cancer research and pharmaceutical cancer drug development has been rapidly-dividing tumour cells, rather than quiescent cancer stem cells. As a consequence, while cancer growth may be contained and tumours may shrink, remissions are often transient, drug resistance a major problem, and drug withdrawal results in aggressive return of the cancer. This was shown in recent mathematical modelling of chronic myeloid leukaemia (CML) where treatment with the new wonder-drug, gleevec/imanitib, resulted in complete and sustained clinical remission, but drug withdrawal, even 3-4 years later, resulted in explosive return of Bcr/Abl-positive leukaemic cells, consistent with residual cancer stem cells surviving drug treatment. Multiple myeloma shares many of the treatment characteristics of CML and is therefore likely to be a stem cell disease.

### **Cancer cure inversely related the molecular targets available**

Cancer is a large family of several hundred genetic diseases. Fuelled by cancer genome projects, knowledge about genetic changes involved in cancer has exploded in recent years, to the point where the number of molecular targets defined by genetic change approximates the number of different types of cancer involved and includes oncogenes, tumour suppressor genes, DNA repair genes and epigenetic changes. Despite this new knowledge, progress in developing new drugs based on this information has been exceedingly slow over the past 10-15 years and there is no sign that the floodgates are about to open. Why are we making so little progress utilizing the

plethora of genetic information on cancer now available? The answer probably lies in the fact that many of the genetic changes identified in cancer reflect the properties of proliferating tumour cells rather than characteristics of quiescent cancer stem cells, which, although they harbour cancer genes, may not express these altered genes. Loss of ability to self-renew would then release the information contained in these silent yet aberrant genes, resulting in uncontrolled cell proliferation.

### **Back to the future**

What is desperately needed is more knowledge about the basic cell biology of the tumour-perpetuating cancer stem cell. New knowledge about this cancer stem cell will lead to the development of novel targeting strategies that are specific for this elusive cell. For half a century now, cancer has largely outsmarted us by masquerading as a disease of proliferating cells, whereas in fact the essence of the disease is a minor subpopulation of non-dividing stem cells. If our hypothesis is correct, then strategies that target non-dividing tumour cells that self-renew in a protected hypoxic environment and thus employ glycolytic metabolism for energy production purposes, may provide the ultimate answer to the dichotomy that exists between increased knowledge about cancer yet slower progress in identifying new and relevant cancer drug targets.

\*\*\*\*\*

A good friend sent this and I love it, hope you do too.

In April, Maya Angelou was interviewed by Oprah on her 70+ birthday. Oprah asked her what she thought of growing older. And, there on television, she said it was "exciting." Regarding body changes she said there were many, occurring every day...like her breasts. They seem to be in a race to see which will reach her waist, first. The audience laughed so hard they cried. She is such a simple and honest woman, with so much wisdom in her words! Maya Angelou said this:

"I've learned that no matter what happens, or how bad it seems today, life does go on, and it will be better tomorrow."

"I've learned that you can tell a lot about a person by the way he/she handles these three things: a rainy day, lost luggage, and tangled Christmas tree lights."

"I've learned that regardless of your relationship with your parents, you'll miss them when they're gone from your life."

"I've learned that making a "living" is not the same thing as "making a life"

"I've learned that life sometimes gives you a second chance."

"I've learned that you shouldn't go through life with a catcher's mitt on both hands; you need to be able to throw some things back."

"I've learned that whenever I decide something with an open heart, I usually make the right decision."

"I've learned that even when I have pains, I don't have to be one."

"I've learned that every day you should reach out and touch someone. People love a warm hug, or just a friendly pat on the back."

"I've learned that I still have a lot to learn."

"I've learned that people will forget what you said, people will forget what you did, but people will never forget how you made them feel."

\*\*\*\*\*

New Drugs, we are part of a long line of patients all wanting access to new and expensive medications. Some cancer groups can call on big money, massive commercial support, even more massive popular support and still their needs will be hard if not impossible to achieve. How do a small group of myeloma patients have their need for new, incredibly expensive drugs heard? The costs quoted are in \$US. I was recently told that Revlimid was costing \$70,000pa in the US, Velcade could cost as much or more. These drugs are said to work, what chance do we have of seeing them in use here? Herceptin has been approved for use in NZ after a loud campaign by breast cancer patients but seeing it funded is a different matter.

### **Cost of Survival: New cancer drugs can extend life, but come at a high price**

When you're being robbed at gunpoint, the question often asked is, "Your money or your life?" Increasingly, that is the choice cancer patients are being offered.

The cost for many new cancer drugs is almost unbelievable. Herceptin, a drug for breast-cancer patients, costs \$3,200 a month. Avastin, for colorectal cancer, can cost \$4,400 a month. Rituxan, for nonHodgkin's lymphoma, runs \$13,000 to \$25,000 for one cycle of treatment. Revlimid, a newly approved treatment for multiple myeloma, could cost up to \$60,000 a year. And Erbitux, for head and neck cancer or colorectal cancer, might exceed \$110,000 a year.

Even for people with insurance, these bills are traumatic. Some plans require patients to pay a steep co-payment or a percentage of the total cost. Even 10 percent of such big bills can add up to thousands of dollars.

And no matter how much they raise their premiums, it is hard for insurance companies to keep up with the skyrocketing increases in cancer-drug costs. That may be why they do their best to wiggle out of covering "experimental" therapies. A revolutionary medicine such as Avastin that is approved by the Food and Drug Administration for colon cancer may not yet have official approval against ovarian cancer, even though oncologists are prescribing it for this malignancy. Because this is considered an unapproved use, some insurance companies might try to get out of paying for this potentially life-extending therapy.

Anyone without insurance is out of luck. Although some people are poor enough to qualify for company-sponsored assistance, middle-class cancer patients often aren't eligible.

There are 45 million Americans without health insurance. And once you have a diagnosis of cancer, your chances of getting independent insurance drop dramatically. That means that millions are left with astronomical bills for medications they need to survive.

What's behind the enormous cost of cancer medicine? Twenty years ago, we spoke with a drug-company insider. This former executive related a top-level meeting in which the question was raised, "If you found a cure for cancer, what would you charge for it?" The executive who was being grilled admitted that they would almost have to give it away. At that time, pharmaceutical leaders feared they would be seen as unethical if they gouged patients for life-saving medicine.

Those restraints have disappeared. These days, cancer therapies have become the holy grail for profitability. Many new high-tech compounds don't cure people, but they do extend lives. The drugs are more effective and often better tolerated than old-fashioned chemotherapy. A patient who survives an extra 10 years could run up a bill of \$1 million.

Drug companies often justify high prices by pointing to the expense of conducting research. No one doubts that developing anti-cancer compounds is expensive. But when a year's treatment tops \$100,000 a patient, the industry risks pricing itself out of the market for lifesaving drugs. (from the Winston-Salem Journal medications Tuesday, April 4, 2006 KING FEATURES SYNDICATE)

## **Detailed Guide: Multiple Myeloma**

### **What Is Multiple Myeloma?**

Multiple myeloma is a type of cancer formed by malignant plasma cells. Normal plasma cells are an important part of the immune system. The immune system is composed of several types of cells that work together to fight infections and other diseases. Lymphocytes (lymph cells) are the main cell type of the immune system. There are 2 types of lymphocytes: T cells and B cells.

When B cells respond to an infection, they mature and change into plasma cells. Plasma cells live mainly in the bone marrow. Bone marrow is the soft, inner part of bones. The role of plasma cells is to produce and release proteins called antibodies (or immunoglobulins) to attack and help kill disease-causing germs such as bacteria and viruses. When plasma cells grow out of control, they can produce a tumor. These tumors generally develop in the bone marrow. If there is only one tumor, it is called a plasmacytoma. Usually, the plasma cell tumors are spread throughout the bone marrow and then they are referred to as myeloma or multiple myeloma.

The overgrowth of plasma cells can interfere with the normal blood-forming functions of the bone marrow. This can result in a shortage of red blood cells, a condition called anemia. Anemia causes fatigue. A shortage of blood platelets (cells that seal damaged blood vessels) can also occur. This can lead to excessive bleeding after cuts or scrapes. Another problem caused by an excess of plasma cells is leukopenia, a condition in which there is a shortage of normal infection-fighting white blood cells. A shortage of these cells causes decreased resistance to infections.

The myeloma also reacts with bone-dissolving cells. There are two major kinds of bone cells. Osteoblasts make bone and osteoclasts dissolve it. These work together to model each bone into its proper shape. Myeloma cells make a substance that stimulates osteoclasts and speeds up the dissolving of bone. Weakened and even fractured bones are a major problem in people with myeloma. The abnormal plasma cells do not protect the body from infections. As mentioned before, normal plasma cells produce antibodies that attack specific infectious agents. For example, if you developed pneumonia, normal plasma cells would produce antibodies that specifically attack and kill this type of bacteria. However, the antibodies produced by myeloma cells are not helpful in fighting infections.

Sometimes, before multiple myeloma develops, it is preceded by another condition of excessive plasma cell growth. This condition is called monoclonal gammopathy of undetermined significance.

### **Monoclonal Gammopathy of Undetermined Significance (MGUS)**

In monoclonal gammopathy of undetermined significance (MGUS), abnormal plasma cells produce excess amounts of antibody protein. However, these plasma cells do not form an actual tumor or mass and do not cause any symptoms. MGUS usually does not affect a person's health. In particular, it doesn't cause bone weakening. It is found because a routine blood test finds a

high level of protein in the blood and further testing shows the protein is immunoglobulin.

With time, many people with MGUS eventually develop multiple myeloma, lymphoma, or a disease called amyloidosis. The rate of this happening is about 1% per year. The risk of this happening is higher in people whose protein levels are particularly high. Patients with MGUS usually need frequent medical examinations and tests to detect possible progression to multiple myeloma, but they do not need immediate treatment.

Recently, scientists have studied the genes of the plasma cells in patients with MGUS. They found that the genetic make-up of these plasma cells more resembles myeloma plasma cells than normal plasma cells. This suggests that these cells are truly malignant, not just slow growing. Because, in general, people with MGUS are elderly, they may not live long enough for their MGUS to transform into myeloma.

### **Solitary Plasmacytomas**

This is another category of plasma cell growth. Rather than multiple tumors in different locations as in multiple myeloma, there is only 1 tumor, hence the name "solitary" plasmacytomas. Solitary plasmacytomas develop in bone marrow, or they may start in tissues other than bone marrow (such as the lungs or the lining of the sinuses, throat, or other organs). This is called extramedullary disease, meaning outside the bone marrow. These tumors are treated by radiation therapy and/or sometimes with surgery. Their outlook for recovery or survival is usually excellent if no other plasmacytomas are found later on. However, most people with solitary plasmacytoma will develop multiple myeloma, especially if the plasmacytoma were in bone, and therefore these people need frequent examinations and tests to detect this progression as early as possible. Early treatment may lead to an improved outcome.

### **And another definition:**

Multiple myeloma is a cancer of the blood which develops in the bone marrow of patients. Bisphosphonates are used to treat the bone lesions that result from the cancer -- these lesions give rise to a high risk of fractures and considerable bone pain. Approximately 50% of multiple myeloma patients experience kidney problems, making renal safety a key consideration for physicians.<sup>2</sup>

### **About Bone Disease in Cancer**

Metastatic bone disease occurs when the cancerous cells from the original tumour spread to the bone via the blood stream resulting in pain, fractures and other clinical consequences like compression of the spine and hypercalcaemia (high concentrations of calcium in the blood stream). It is most commonly associated with breast, prostate, lung, kidney and thyroid cancer. The most common sites for metastatic bone disease are the ribs, skull, pelvis, hips, vertebrae and the ends of long bones.

Multiple myeloma is a progressive bone marrow disease. In multiple myeloma, bone is the primary site of tumour and in the great majority of patients causes extensive lesions, with a high risk of fractures and high levels of bone pain. If left untreated, bone disease can have a tremendous impact on cancer patients' quality of life (e.g. limited mobility, disturbance in sleeping patterns, reduction in appetite).

\*\*\*\*\*

## **CANCER DEATH RATE KEEPS DECLINING**

WASHINGTON — The nation's overall cancer death rate continues to decline, including deaths from the four most common types — prostate, breast, lung and colorectal — the National Cancer Institute said Thursday.

Lung cancer death rates in women continue to rise, but not as rapidly as before.

The institute said there have been increases in the incidence of cancers of the breast in women and of prostate and testis in men, as well as leukemia, non-Hodgkin's lymphoma, myeloma, melanoma of skin, and cancers of the thyroid, kidney and esophagus.

Smoking by youths has been declining since 1997, the report said.

The Kansas City Star

### **'A VACCINE HELPED CURE MY CANCER'**

By Denise Villani for CNN

More than three and a half years ago, I was diagnosed with multiple myeloma, an incurable cancer of the plasma cells. I was 47 at the time.

Plasma cells usually make up less than five percent of cells in the body's bone marrow, but if you have multiple myeloma, a group of abnormal plasma cells (myeloma cells) multiply, raising the percentage of plasma cells to more than 10 percent of the cells in your bone marrow. The result can be erosion of the bones. The disease also interferes with the function of your bone marrow and immune system, which can lead to anemia and infection, and can cause problems with kidneys.

The standard treatment is three months of chemotherapy, followed by a bone marrow or stem cell transplant. The average life expectancy after this treatment is two to five years. I had no noticeable symptoms, apart from anemia, and although the cancer had not yet affected my bones, it was a devastating scenario. I was a single mom with two sons, aged 16 and 18.

My doctors were in touch with doctors at Johns Hopkins University Hospital in Baltimore and presented me with the option of participating in a clinical trial where they would take my cancer cells and develop a vaccine. I would still receive the standard treatment, followed by the vaccine. The doctors hoped the vaccine would create an immune response within my body to resist returning myeloma cells. I returned to hospital the week after my diagnosis, and received a four days of chemotherapy, around the clock. I did this once a month, for three months.

The aim of the chemo treatments was to lower the cancer cell count to make my body more receptive to a successful bone marrow transplant. After the third month, my body had developed a "rejection clone," which resisted the chemo. I was put on Thalidomide, an oral type of chemo that my body responded well to, and which is commonly used for chemo-resistant patients with myeloma. During these months of treatment, I was extremely fatigued. This was caused by the steroids that are often given in conjunction with certain chemo drugs. And yes, my hair fell out.

During these months, I was also visiting Johns Hopkins Hospital on a regular basis. There I had all types of tests, including bone marrow biopsies, and it was recommended I have a stem cell

transplant versus a bone marrow transplant. The death rate is quite high with a bone marrow transplant because of the risk of rejection disease, called graft versus host disease or GVH. Prior to the transplant, they took my blood and isolated, cleaned and froze the stem cells.

The week before the transplant I was given high doses of chemotherapy and whole body radiation to kill as many remaining cancer cells as possible. The transplant, similar to a transfusion, was successful and I was on the road to recovery.

I developed a pretty mean rash that was diagnosed as GVH, which should not have happened because the stem cells I'd received were my own. The doctors weren't sure how this happened, but one thought was that the vaccine (one dose was administered before stem cell collection, and pre-transplant) may have caused this when given the stem cells during transplantation. Regardless, my doctors felt this may be the cure for me on its own, because the only enemy left to reject in my body were returning myeloma cells. The rash cleared up and after three weeks in the hospital, I was sent home to recover.

The vaccine clinical trial continued with one round of vaccines given every three weeks for eight rounds. My body continued to show signs of recovery and immune response. Any remaining cells were dwindling. By July 2003, it was written in my record, "no evidence of disease." I could only thank God and the wonderful doctors and nurses.

I have been cancer-free for more than two years. There is no evidence in my body of this "incurable" disease. I continue to live my life to the fullest every day, as I have been able to get my sons in college and continue to work full time. There are wonderful researchers doing amazing things in the field of cancer. Hopefully within a few years these procedures will be approved for standard treatment. Never give up hope.

\*\*\*\*\*

## **With Cancer, Treatment Is Only Part of the Picture** **By JANE E. BRODY**

More than 10 million people in the United States are cancer survivors, and their numbers increase daily. Many are considered cured. Some are still in treatment and one day may - or may not - be counted among the cured. Others are living with advanced disease.

But nearly all have similar needs:

- A need to know about and cope with the physical and emotional consequences of cancer and its treatment, including current challenges to quality of life and delayed health effects.
- A need to know when to worry and when not to worry about symptoms that could signal a recurrence or a new cancer.
- A need for reliable information and assistance on matters like diet, exercise and smoking cessation that may improve survival chances.
- A need to deal with employment and insurance problems related to their medical histories.

Such needs inspired a panel of the National Academies this month to call for major improvements in follow-up care for cancer patients, who are too often left to struggle on their own with serious cancer-related matters.

### **Making a Plan**

"Successful cancer care doesn't end when patients walk out the door after completion of their initial treatments," said Dr. Sheldon Greenfield, director of the Center for Health Policy Research at the University of California, Irvine, who led the committee.

Patients need to have a "survivorship care plan" that provides information critical to proper long-term care, including the exact cancer diagnosis, a detailed list of treatments received and the potential consequences of those treatments. "Cancer can be considered a chronic disease, in part because of the serious consequences and persistent nature of some of cancer's late effects," the committee said. This suggests that cancer survivors, like other patients with chronic diseases, need a plan for optimal functioning.

The committee's findings are spelled out in a 500-page book, "From Cancer Patient to Cancer Survivor: Lost in Transition," produced by the Academies' Institute of Medicine and National Research Council. The recommendations were endorsed by the American Society of Clinical Oncology, which represents 20,000 cancer treatment specialists, but it could take years for doctors to carry out the measures nationwide.

For now, there are steps that cancer survivors can take on their own to enhance their knowledge and improve their medical, emotional and social well-being. If patients cannot do this for themselves, then someone who can serve as the patient's advocate - a family member or friend - should do it for them.

A friend who just had surgery for breast cancer asked me how she could improve her diet or exercise habits and what supplements she should take to ward off a recurrence. In advance of further treatments, she also wanted to know how her appearance and sex life would be affected, now and in the future, by the various choices of postsurgery drugs and radiation.

In the next 12 months, more than 211,000 women who learn they have breast cancer will face similar questions, but few will know how to get reliable answers. Many will go through life feeling as if the sword of Damocles hangs over their heads. I recognize the feeling. Although I have every reason to believe I was cured of breast cancer six years ago, I do worry whenever I get a new symptom that I can't explain, like a pain in my ribs, a suspicious bruise, soreness in my breast. Could it mean my disease has recurred or spread?

### **Waiting for Warnings**

I was never told what to look out for. Nor was I told that hardening and extreme sensitivity of breast tissue could be a lasting consequence of radiation therapy. How many breast cancer survivors now taking an aromatase inhibitor like Arimidex know that their risk of developing osteoporosis and fractures is increased as a result, and what they can do to reduce that risk?

When faced with a life-threatening illness, most patients readily accept their physicians' treatment recommendations no matter how dire the potential consequences. Only later do they wonder if something might have been done, say, to preserve their fertility or virility or to prevent

lymphedema, chronic swelling of a limb after lymph node removal.

Patients have a right to know beforehand if surgery planned for head and neck cancer is likely to affect their ability to speak, swallow or breathe, or, for patients with prostate cancer, what their chances are of experiencing incontinence or erectile dysfunction as a result of surgery or radiation therapy. It's not that knowing possible side effects is likely to prompt cancer patients to reject life-saving treatment. Rather, a prepared patient is better able to deal with such life-disrupting consequences. On the other hand, a patient who will gain only a short period of time from a debilitating therapy may choose not to be treated.

### **Writing It Down**

At the time of diagnosis, through the course of treatment and after treatment is completed, patients or their advocates should come equipped to ask questions and record answers when meeting with their physicians. They should leave with a written record that includes these items:

- The precise nature of the cancer, including its pathological type and stage, indicating its aggressiveness, scope and likelihood of spreading.
- The treatments received, including the type and extent of surgery or radiation treatments, and a complete list of chemotherapeutic drugs and medications to prevent relapse, along with their possible long-term effects.
- A monitoring program to check for the late effects of treatment, like heart damage, thyroid disorders or bone marrow disease.
- A follow-up plan to check for a recurrence or the appearance of a second cancer.
- A list of symptoms that might indicate recurrence or spread of the cancer.
- Advice about diet and exercise that can help improve stamina and immune defenses and counter post-treatment depression, and referral, if needed, to a smoking cessation program.
- A list of self-help groups for emotional and sometimes practical support, friendship and understanding of the problems of cancer survivors. The diagnosis of cancer often becomes a "teachable moment" - a chance to persuade people to change habits that might have contributed to their disease or that may impede their recovery.

Many cancer patients and survivors continue to smoke because they believe it is too late to quit, but cessation of smoking can reduce treatment complications, improve survival chances and reduce the risk of a second cancer, as well as the risk of developing heart and lung disease.

Likewise, survivors should be encouraged to be active. An increase in physical activity enhances their vigor and vitality, cardiopulmonary fitness and overall quality of life and counters post-treatment depression, anxiety and fatigue. For significantly overweight patients, better diets emphasizing fruits, vegetables, whole grains and lean protein can improve survival among those with breast and prostate cancer.

As for unconventional remedies, the new report cites potential benefits from massage, imagery,

relaxation training and participation in support groups, but notes that other measures, like phytoestrogens for breast cancer survivors on anti-estrogen, can be harmful.  
Copyright 2005 The New York Times Company

## **NOBODY'S PERFECT**

**Nobody's It turns out there is no norm for DNA, scientists say. Discoveries about the variability of the human genome help shed light on disease and evolution.**

It was a nice idea that we're all genetically 99.9 percent identical, but new research says it's not so simple. The old thinking held that coiled in our cells, we all carry the same instruction book with just a few alternative spellings. But upon closer scrutiny, it appears our DNA is full of long strings of genetic code that are copied sometimes hundreds of times, the number of copies varying wildly from person to person.

And each of us is apparently missing quite a few large chunks of DNA. Other large segments of genetic code are misplaced on their chromosomes or pasted in backward. Not that there's any one designated normal arrangement - we're all just different.

As this all was becoming clear over the last several years, scientists expressed some surprise that the human genetic code is such a disorganized mess. "This changes how we think about evolution and, in some respects, disease," says Evan Eichler, a researcher at the University of Washington, Seattle. "That's the part that's exciting."

This newfound variability may help explain not only differences that affect health, but how we and other living things have evolved. Scientists are coming across places in our chromosomes called genetic "hot spots," critical for evolution to continue reshaping the human race.

The first hints of large genetic differences surfaced as scientists completed the Human Genome Project - an endeavor that created a reference genetic code based on DNA samples from five individuals of various ethnic backgrounds.

We all carry a genetic code that's about three billion characters long, written in the four different chemical building blocks of DNA - adenine, thymine, cytosine and guanine, abbreviated A, T, C, and G. In the process of reading the code carried by their volunteers, scientists found some areas just couldn't be decoded in a linear way.

"The handwriting was on the wall that the genome was very dynamic," Eichler says. Several years ago, his lab decided to evaluate the accuracy of the genome project's results by comparing the genetic code of a single female volunteer with the "reference" sequence.

They found there were dozens of genes the woman appeared to be missing and others she carried in multiple copies. It's hard to explain how the scientists behind the genome project were able to keep creating this reference with so much inconsistency, says Michael Wigler, a researcher at Cold Spring Harbor Laboratory, on Long Island. It involved a certain amount of compromise, he says.

In 2004, Wigler and his colleagues compared the DNA for 20 healthy volunteers and found 500

genes that can appear in different numbers of copies - a stretch of DNA that codes for a single protein. "It did surprise us," he said. "The question is, what impact does this have?" Some variations are not necessarily going to result in a health problem, he said, but might have subtle influences on risk of heart disease, diabetes, cancer or immune deficiencies.

Last year, scientists found that your odds of getting infected with HIV after an unprotected sexual encounter with someone who has the virus depend partly on how many copies you carry of a gene called CCL3L1. That finding followed from an earlier discovery that a rare mutation in about 1 percent of Europeans creates profound resistance to HIV - "like a genetic condom," says Sunil Ahuja of the University of Texas Health Science Center in San Antonio.

Ahuja and colleague Matthew Dolan started looking for more common genetic variants that influence relative HIV resistance, starting with those that control production of a protein called a chemokine. Chemokines offer protection by blocking the portals through which HIV enters the cells it infects. The gene CCL3L1 orchestrated the production of a chemokine and showed up in varying numbers, some people carrying two copies, some 12 or more. In a group of more than 4,000 people of different HIV status, the scientists found those who carried an above-average number of copies of CCL3L1 were less likely to be infected.

At Cold Spring Harbor Laboratory, Jonathan Sebat is studying autistic children, looking for structural differences in their DNA. He suspects many autistic people carry new genetic changes that aren't carried by their parents, but spring up in the copying of DNA into egg or sperm cells.

Washington's Eichler is looking for similar factors underlying cases of mental retardation, many of which can't be connected to a known genetic or environmental cause. Eichler also is studying the effect of this larger-scale DNA diversity on evolution by comparing human genetic material with that of the chimpanzee, our closest relative.

In some cases, chimps and humans shared a gene, but humans carried about four copies, chimps 500, he said. In the end, he found so many larger-scale structural differences that he estimates humans and chimps are around 4 percent genetically different, not 1.2 percent, as previously thought. It turns out that big structural differences in DNA accumulate in certain zones - rough spots in the genetic code, he said. These so-called evolutionary hot spots may underlie some of the more obvious physical and behavioral differences between us and our primate cousins. Natural selection needs variety, it needs new traits, and to get these, DNA has to be changeable, dynamic.

Eichler calls these variable parts "crucibles of evolution." Since the rise of anatomically modern humanity around 100,000 years ago, we have continued to evolve, especially in our abilities to deal with variable and changing environments. Descendants of those from malaria-prone places often carry genetic resistance in the form of a sickle-cell gene, for example, while those who descend from Northern European dairy farmers acquired enzymes needed to digest milk.

Science is quickly dismantling the false premise behind eugenics - that there's one perfect human genetic code and that anything deviating from it represents a mistake or defect. "Part of the strategy of success in humans is our ability to diversify rapidly," Wigler says. Faced with variable food sources and an ever-changing array of disease threats, he said, "you don't want to be a

sitting target.

health&science By Faye Flam Inquirer Staff Writer © 2006 Philadelphia Inquirer

**Remimder: Myeloma Matters Monthly Lunch this Saturday 27<sup>th</sup> May  
La Bella Italia 10 Nevis St Petone RSVP Terry or Lesley phone 9727276**

This newsletter is compiled by:

Judi McBride-Wilson 17 Richard Street Titahi Bay New Zealand  
Phones 04 64 236 7564 025 420 694 e-mail: [info@myewell.org.nz](mailto:info@myewell.org.nz)