Breast Cancer in the Prime of Life

by Karen Stuyck

Breast cancer isn’t a disease you expect to see in young women, but when it strikes, it can be aggressive.

Usually associated with women over 45 years old, the appearance of breast cancer is unexpected in young women and often overlooked by patients and their doctors. Since screening mammography is usually not recommended until age 40 and nonmalignant breast problems such as fibroadenomas and cysts are quite common in younger women, “it takes a while for people to believe this could be cancer,” said Karin Hahn, M.D., an assistant professor in the Department of Breast Medical Oncology at The University of Texas M. D. Anderson Cancer Center.

Women might think they have a cyst related to their menstrual cycle rather than breast cancer, and the physician might suggest follow-up rather than diagnostic testing. As a result of this delay, couples with the frequent aggressiveness of the disease in young women, when a diagnosis of breast cancer is finally made, it is often a later-stage breast cancer, Dr. Hahn said. In these cases, the cancer is more likely to have spread to the lymph nodes and to be a larger mass when diagnosed.

“Younger women and their physicians should be aware that about 13% of women diagnosed with invasive breast cancer are under the age of 45.”

- Dr. Karin Hahn

(Continued on next page)
Breast Cancer in the Prime of Life
(Continued from page 1)

said Dr. Hahn. A breast mass that persists more than 6 weeks should be investigated radiographically by mammography and/or ultrasonography and biopsied if imaging does not show an apparently benign lesion, Dr. Hahn said. Each year, more than 28,000 women in the United States under the age of 45 are diagnosed with breast cancer, including many who do not have a family history of the disease. Approximately 150 of them receive care at M. D. Anderson each year.

Different challenges
Breast tumors in younger women are often a higher nuclear or histologic grade than tumors in postmenopausal women, according to Dr. Hahn. “These tumors look much more aggressive under the microscope and are more likely to be estrogen insensitive when compared with the tumors of postmenopausal women, which means antiestrogen treatments such as tamoxifen probably won’t be helpful,” she said. Women with estrogen-insensitive tumors are left with systemic treatment options such as chemotherapy, plus a biological agent such as Herceptin if they have a HER2/neu-positive tumor. “We know that even in premenopausal women, the antiestrogen therapies do decrease the risk of recurrence, but if the tumor isn’t estrogen-sensitive, the patient loses that opportunity.”

Younger women with breast cancer also often experience different side effects of treatment than their older counterparts. “Young women with breast cancer face different challenges than postmenopausal patients, such as infertility, increased bone loss, premature menopause, and a higher rate of fatigue,” said Dr. Hahn, who directs M. D. Anderson’s Breast Survivorship Clinic and oversees the Young Breast Cancer Survivors Program.

Treatment for breast cancer may cause young women to undergo premature menopause, experiencing attendant hot flashes, psychological discomfort, sleep disturbances, and loss of bone mass. More than 50% of breast cancer patients under age 40 will recover ovarian function after treatment, but after age 40, their chances decrease, Dr. Hahn said.

Bone loss is a big problem for young women with breast cancer. Dr. Hahn cited a recent study in the Journal of Clinical Oncology reporting that premenopausal women taking tamoxifen for estrogen-sensitive breast cancer can actually lose bone mass. Therefore, it is important for these women to receive bone density testing. Breast cancer survivors who experience premature menopause after treatment also should be monitored for bone loss because they are at a much increased risk of developing osteoporosis, said Dr. Hahn.

Any woman under the age of 40 who is diagnosed with breast cancer should be offered genetic counseling and testing for mutation of the BRCA1 and BRCA2 genes, which increases the risk of recurrent breast cancer. Mutation of the BRCA1 gene could also indicate an increased risk of ovarian cancer. “This information can help a woman consider such questions as whether or not she should have a bilateral mastectomy and whether she might choose to have a prophylactic oophorectomy,” said Dr. Hahn.

Psychological needs
Younger women with breast cancer often have different psychological needs than older women with the disease, according to Anita Broxson, a research nurse in M. D. Anderson’s Department of Breast Medical Oncology and the program director for the Young Breast Cancer Survivors Program. These young women feel very...
Young women with breast cancer may be eligible for these clinical trials. For more information and a more complete listing of available trials, visit www.mdanderson.org or call the M. D. Anderson Information Line at (800) 392-1611 or (713) 792-3245.

For premenopausal women
- Phase III trial of LHRH analog administration during chemotherapy to reduce ovarian failure following standard adjuvant chemotherapy in early-stage, hormone-receptor-negative breast cancer (SWOGS0230). Physician: Ana Maria Gonzalez-Angulo, M.D.
- Phase III trial evaluating the role of ovarian function suppression and the role of exemestane as adjuvant therapies for premenopausal women with endocrine-responsive breast cancer (SWOG) (2004-0453). Physician: Marjorie C. Green, M.D.

For pregnant women

Other
- Mini-allogenic peripheral blood progenitor cell transplantation for recurrent or metastatic breast cancer (DM97-268). Physician: Naoto Ueno, M.D., Ph.D.
- A randomized phase III study of conventional breast irradiation vs. partial breast irradiation for women with stage 0, I, or II breast cancer (RTOG0413). Physician: Eric Strom, M.D.

Further information about support for young breast cancer survivors is available through the Houston chapter of the Young Survival Coalition (www.youngsurvivor.org) and the Web site for the Young Breast Cancer Survivors Program (www.mdanderson.org/departments/youngbreastsrv).
Early Nutritional Intervention Recommended for Cancer Patients

by Manny Gonzales

The relationship between nutrition and cancer is not yet fully understood, but researchers do know that well-nourished patients have a better prognosis. For many patients with cancer, however, the onset of cachexia will ultimately make it difficult to avoid weight loss. Therefore, early intervention may be the key to effective nutritional support.

Traditionally, nutritional support has been recommended after a patient has lost at least 10% of his or her body weight, but experts now recommend intervening much sooner. Egidio Del Fabbro, M.D., assistant professor in the Department of Palliative Care and Rehabilitation Medicine at The University of Texas M. D. Anderson Cancer Center, pointed out that studies have shown that patients with a 5% or more loss in body weight have decreased survival rates and an inability to tolerate chemotherapy. “From a dietician’s perspective, it’s great if you can get them really early in the diagnosis, because they’re very open to making changes to their diet that might be beneficial,” said Ms. Lowenstein.

Registered dieticians at M. D. Anderson meet with patients and encourage them to maintain their weight in a healthy manner. “Now, we’re looking at the issue as more of a balance—what they can eat, what they will eat, and what they should eat,” Ms. Lowenstein said. “There are still some clinicians who will say, ‘Eat whatever you want because you’re going to have a difficult time eating,’ but the general consensus among nutrition professionals is to try to steer patients in the direction of things that will support their body’s immune system and their body’s good health to give them the best physical edge possible in fighting the disease.”

Because the nutritional needs of people with cancer differ from those of the general population, dieticians educate their patients on the specifics of their changing nutritional needs and how best to introduce changes to their diets. “Some patients are diagnosed and become very proactive, going into warrior mode. They arm themselves with all that they can, and diet is one of those things. And we encourage patients to take every advantage they can that’s not detrimental,” said Ms. Lowenstein.

Changes in diet should be made gradually to allow the body time to adjust, and patients should avoid radical changes in diet altogether. A dietician can work with patients who want to introduce certain changes and help them evaluate the alternatives. “It’s not unusual for a patient to get diagnosed and decide that this is the time in his or her life to become vegetarian, and that’s not always the best idea, because obviously, when you exclude a big food group, like meat, you’re excluding one of the best sources of protein,” said Ms. Lowenstein.

The use of appetite stimulants or meal replacement drinks, such as Boost or Ensure, should also be considered to help patients achieve adequate nutritional intake. Doctors should raise the issue of nutritional supplements with their patients as well because many patients may already be taking them at the time of diagnosis.
In Brief

Immune Response May Prevent Brain Tumor Development

Does immune system surveillance play a role in preventing the development of brain tumors? Researchers at M.D. Anderson Cancer Center think so, on the basis of their recent epidemiological study showing that allergies and asthma may have a protective effect against brain tumors. The researchers theorize that hay fever may produce enough inflammation in the brain to keep immune cells active and that this surveillance works to eliminate early signs of malignancy.

In the study, researchers compared the medical histories of 830 brain tumor patients with those of a control group of 831 individuals. They found that a history of allergies and asthma was significantly protective for the three different kinds of brain tumors examined in the study. Individuals with a history of allergies and asthma had a 35% reduced risk of developing glioblastoma, a 51% reduced risk of anaplastic astrocytoma, and a 36% reduced risk of low-grade gliomas.

Researchers also found, however, that use of antihistamines to counter inflammation in allergies eliminates the protective effect of allergies and asthma and increases the risk of developing brain tumors. Participants who used antihistamines had three times the risk of developing an anaplastic astrocytoma tumor and two times the risk of developing low-grade gliomas, compared with those who did not use antihistamines. The risk of developing a glioblastoma was also increased by 26%, but that was not statistically significant, the researchers said.

But researchers stress that no one should give up antihistamines because of this study. "Brain tumors are exceedingly rare, and many, many people use antihistamines, so we certainly are not suggesting a direct connection between the two," said the study's lead author, Melissa Bondy, Ph.D., a professor in the Department of Epidemiology.

"Our study suggests that those who have allergies and don’t do anything about it may be protected to some degree against brain tumors," Dr. Bondy said. "But those who use antihistamines could decrease that protection and increase their risk. The real question is if there are particular gene variants that would make a person susceptible."

"Our long-term goal is to look at genes that may be increasing or reducing the risk of developing these tumors, and then to assess whether some individuals might be genetically susceptible," said Michael E. Scheurer, Ph.D., a postdoctoral fellow in the Department of Epidemiology and the study’s first author.

Targeted Molecular Imaging of Cancer

Researchers at M.D. Anderson Cancer Center have created a new class of a hybrid virus and demonstrated its ability to find, highlight, and deliver genes to tumors in mice.

Researchers say the advance, reported in the journal Cell, is potentially an important step in making human cancer both more visible and accessible to treatment; it may also allow prediction and monitoring of how specific anticancer agents are actually working.

"In tumor-bearing mice, we show that this hybrid virus can target tumors systemically to deliver an imaging or therapeutic gene," said one co-leader of the study, Renata Pasqualini, Ph.D., professor of Medicine and Cancer Biology at M.D. Anderson. "The signal is specific only to tumors, so one can monitor drug effectiveness at the molecular level."

The research team created and characterized the hybrid viruses by combining genetic elements and biological attributes of an animal virus (adeno-associated virus, or AAV) with those of a bacterial virus (phage). Unlike animal viruses that infect mammalian cells, bacterial viruses have evolved to infect only bacterial hosts. The research shows how particles of the hybrid virus, called AAV (Continued on page 6)
(Continued from page 5)

phage or AAVP, can serve as a vehicle for targeted delivery of genes to experimental tumors in mice and to the tumors’ blood vessel supply, providing a strategy for finding tumors and genetically marking them for imaging on a clinic-ready body scanner.

“We could see by using positron emission tomography that the reporter and therapeutic genes were being expressed throughout the tumors in the animals,” said Juri Gelovani, M.D., Ph.D., chair of the Department of Experimental Diagnostic Imaging. “This is an example of the so-called ‘theragnostic’ approach, a combination of the words therapeutic and diagnostic.”

The AAVP hybrid combines the ability of the bacterial virus to target specific tissues with the capability of the mammalian virus to actually deliver genes to cells. The vectors in the AAVP hybrid retained the properties of their parental viruses, which the researchers called a surprising outcome.

“This is only a proof of concept, and although we have yet to translate these hybrid viruses for use in humans, we hope that this new system will have important clinical applications in the future,” said Wadhia Arap, M.D., the other co-leader of the study and professor of Medicine and Cancer Biology. “In addition to the obvious biological interest, when the vector is refined for patient use, it could perhaps help us diagnose, monitor, and treat human tumors more accurately.”

Avoiding Complications from Preoperative Chemotherapy

Physicians should exercise caution when selecting a preoperative chemotherapy drug to treat colorectal cancer that has spread to the liver, say researchers at M. D. Anderson Cancer Center, carefully matching the right drug with the patient.

Use of chemotherapy before surgery offers several important benefits, including reducing the size of tumors so that they are more easily removed, potentially doubling the survival rate. However, preoperative chemotherapy also has the potential to damage the liver.

New insight into the problem of chemotherapy-related hepatotoxicity emerged from a recent study conducted at M. D. Anderson and a hospital in Torino, Italy, and presented in the May 1 issue of the Journal of Clinical Oncology. The investigators found, in a cohort of 406 patients, that different drugs cause different types of liver injury. One drug, irinotecan, produced steatohepatitis, an inflamed “fatty” liver, in 20% of patients, while another drug called oxaliplatin caused sinusoidal dilatation, leading to the pooling of red blood cells in the liver in 19% of patients.

Steatohepatitis was the sole injury associated with an increased risk of postoperative mortality after liver surgery. Its presence in patients undergoing extensive liver surgery may result in failure to regenerate new liver tissue, leading to liver failure,” said lead author Jean-Nicolas Vauthy, M.D., professor in the Department of Surgical Oncology at M. D. Anderson.

Although steatohepatitis may affect people who have not undergone preoperative chemotherapy but who are overweight or who already have steatosis, researchers noted that irinotecan was associated with an increased risk of steatohepatitis with a more pronounced effect in patients with a higher body mass index (BMI).

“Most patients who are given preoperative chemotherapy when their colorectal cancer metastasizes to the liver do fine,” Dr. Vauthy said. “But this study shows us that we need to select the patients and use the drug that is right for them.”

Given these findings, researchers recommend that patients be screened in advance for high BMI and for preexisting steatosis, which can predispose patients to chemotherapy-induced steatohepatitis. Overall, these individuals are not the best candidates for irinotecan as a first-line treatment.

Vaccine Curbs Brain Tumor Growth

A novel vaccine has significantly increased life expectancy in patients with glioblastoma multiforme (GBM), the most dangerous type of brain tumor, a researcher from M. D. Anderson Cancer Center is reporting at the annual meeting of the American Association of Neurological Surgeons.

Median survival for the 23 patients who received the vaccine at M. D. Anderson and at Duke University Medical Center has been at least 19 months, and only four patients have died from the cancer, said Amy Heimberger, M.D., an assistant professor of Neurosurgery at M. D. Anderson.

This figure surpasses the median survival of 14 months for patients with GBM who are treated with the most current chemotherapy and radiation and the 4-month median survival for untreated patients, she said.

“We can’t say this vaccine is better than chemotherapy because we haven’t tested the two treatments head-to-head yet,” she said. “However, so far, results have exceeded the expectations we had for this vaccine.”

Given the statistically significant findings, a pharmaceutical company has acquired the rights to the drug and a larger, multi-institutional, randomized study is being planned, Dr. Heimberger said.

She describes the vaccine as an easy-to-use treatment that can potentially help up to 50% of all GBM patients keep their cancer at bay for a period of time. Interim results of a phase II clinical trial show that the vaccine significantly delays progression of tumors until the cancer finds a new growth pathway.

“This is a proof of concept, and optimal use of the vaccine may be in conjunction with chemotherapy to further retard progression,” said Dr. Heimberger. “Still, this is exciting to us because people have been trying to use immunotherapy against gliomas for a long time.”
How to Deal with Pain

One of the most distressing symptoms of any disease is pain. However, many people do not report their pain or seek treatment for it.

The pain may be short-lived or long-lasting, mild or severe, and have a variety of different causes. Each patient’s pain is unique. Therefore, patients must have a treatment plan that addresses their individual needs depending on their type of pain.

The more you know about your pain, the more you can help your caregivers plan the best treatment for you.

Step 1:
Talk about your pain
Telling your care team in detail about your pain is the best thing that you can do to assist them. Patients may not want to complain, they may fear becoming addicted to pain medications, they may fear the side effects of pain medicine more than the pain itself, or they may want to save their pain treatment options until they really need them. Each of these attitudes will hinder pain treatment.

Describing your pain
Answering the questions below will help you communicate with your healthcare provider about your pain.

Where is the pain? You may have pain in more than one place. Be sure to list all of the painful areas.

What does the pain feel like, specifically? Does it ache, throb, burn, or tingle? You may wish to use other words to describe your pain.

How bad is the pain? You can use a number scale to rate your pain from 0 to 10, where 0 means no pain and 10 means the worst pain you can imagine. Or, you can describe your pain with words such as “none,” “mild,” “moderate,” “severe,” or “worst possible pain.”

What makes the pain better or worse? You may have already found ways to make your pain feel better (for example, using heat or cold, or taking certain medicines). You may have also found that sitting or lying in certain positions or doing some activities affects the pain.

If you are being treated for pain now, how well is the treatment working? You may want to describe how well the treatment is working by saying how much of the pain is relieved.

Has the pain changed? You may notice that your pain changes over time. It may get better or worse, or it can feel different. For example, the pain may have been a dull ache at first and has changed to a tingle. Describe how the pain was before and how it is now.

Step 2:
Create a plan with your doctor or nurse
In a pain control plan, you and your doctor or nurse plan your pain control activities, including when to take your medicine, how and when to take extra medicine, and other things you can do to ease and prevent your pain. Your doctor or nurse may also list medicines and other treatments that will help with side effects or other aches and pains, such as headaches.

It may be helpful to keep a record of how the medicine is working. Sharing that record with your doctor or nurse will help them make your treatment more effective.

When to take your pain medicine
Take your medicine exactly as your doctor tells you. This will help to keep pain under control. Do not skip a dose of medicine or wait for the pain to get worse before taking your medicine. When taking “as needed” pain medicine, do not wait too long to take the medicine as it is more difficult to “catch up” with the pain than it is to keep it to a tolerable level.

Your doctor may give you pain medicine for “breakthrough pain” (a pain that occurs between regular doses of your pain medicine). If some activities make your pain worse (for example, riding in a car), your doctor may advise you to take more pain medicine before these activities. Ask your doctor or nurse how and when to take extra medicine.

If you continue to have bothersome pain, your medical team may wish to consult a specialist to assist in managing your pain.

For more information on pain management, visit the following Web sites:

- American Chronic Pain Association: www.theacpa.org
- American Pain Foundation: www.painfoundation.org
- M. D. Anderson Cancer Center: www.mdanderson.org/topics/paincontrol

For more information, talk to your physician, or:
- call the M. D. Anderson Cancer Center Information Line at (800) 392-1611 (Option 3) within the United States.
- visit www.mdanderson.org.

June 2006
©2006 The University of Texas M. D. Anderson Cancer Center
New Clinical Trials Enrolling

To follow is just a sample of recently opened clinical trials at M. D. Anderson Cancer Center. For more information and a broader listing of available trials, visit www.mdanderson.org or call the M. D. Anderson Information Line at (800) 392-1611 or (713) 792-3245.


- Phase II concurrent proton and chemotherapy in locally advanced stage IIIa/b non-small cell lung cancer (2004-0976). Physician: Joe Y. Chang, M.D.

- Phase II study of erlotinib with or without SU011248 in metastatic non-small cell lung cancer (2005-0796). Physician: George R. Blumenschein, Jr., M.D.

- Phase III trial of weekly cisplatin and radiation vs. cisplatin and irinotecan in cervical carcinoma limited to the pelvis (GOG 0219). Physician: Robert Coleman, M.D.

- Phase II trial of concurrent accelerated radiation and cisplatin vs. concurrent accelerated radiation, cisplatin, and cetuximab (C225) [followed by surgery for selected patients] for stage III and IV head and neck carcinomas (RTOG0522). Physician: David Rosenthal, M.D.

- Phase III trial of preoperative chemotherapy vs. preoperative concurrent chemotherapy and radiotherapy followed by surgical resection and consolidation chemotherapy in favorable-prognosis patients with stage IIIa (N2) non-small cell lung cancer (RTOG 0412). Physician: Ara Vapnoriyan, M.D.

- Phase III protocol of androgen suppression and 3DCRT/IMRT vs. androgen suppression and 3DCRT/IMRT followed by chemotherapy with docetaxel and prednisone for localized, high-risk prostate cancer (RTOG 0521). Physician: Deborah A. Kuban, M.D.


- Phase II evaluation of EMD121974 (NSC 707544, cilengitide) in asymptomatic patients with metastatic androgen-independent prostate cancer (2005-0871). Physician: Paul Mathew, M.D.

- Phase I study of BAT43-9006 (sorafenib) in combination with carboplatin, paclitaxel, and bevacizumab in previously untreated patients with stage IIIb or stage IV non-small cell lung cancer (2005-0818). Physician: George R. Blumenschein, Jr., M.D.

- Phase II study of goserelin plus anastrozole in male patients with hormone-receptor-positive metastatic or recurrent breast cancer (SWOGS0511). Physician: Sharon Hermes Giordano, M.D.

- Phase II study of carboplatin plus taxotere in patients with anaplastic prostate carcinoma (2006-0097). Physician: Christopher J. Logothethis, M.D.