

**REPORT TO  
PHYSICIANS**

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**MD ANDERSON  
CANCER CENTER**  
*Making Cancer History™*

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# MD Anderson Oncology

## Early Detection of Melanoma Spread May Increase Survival Benefits of Adjuvant Therapy

by Kerry L. Wright

**C**ancer of the skin is the most common form of cancer, and although only 4% of skin cancers are melanoma, the disease accounts for nearly 80% of skin cancer deaths—7,700 this year alone, according to the American Cancer Society.

If detected early, melanoma is highly curable, but the presence of lymphatic disease has long been known to indicate a much poorer prognosis. Improvements in sentinel node mapping over the last few years, however, are allowing earlier detection and prediction of the spread of melanoma and improving patients' chances to benefit from an increasing number of available adjuvant therapy protocols.

"The presence or absence of spread of melanoma to the sentinel lymph node is the single most important predictor of outcome for the patient," said Jeffrey Lee, M.D., an associate professor in the Department of Surgical Oncology and medical director of the Melanoma and Skin Center at The University of Texas M. D. Anderson Cancer Center.

Sentinel node mapping was first  
*(Continued on next page)*



Professor of Surgical Oncology **Merrick Ross, M.D.**, (right) and Senior Research Nurse **Marcia Emerson, R.N.**, examine patient **Gloria Ann Buller**. Allogeneic vaccines, autologous vaccines, and biochemotherapy are among the agents being examined as adjuvant therapy for patients such as Buller with melanoma.



## Benefits of Adjuvant Therapy for Patients with Melanoma

(Continued from page 1)

developed at the John Wayne Cancer Institute in Santa Monica, California, but was later adopted and evaluated at M. D. Anderson by Professor Merrick Ross, M.D., and Assistant Professor Jeffrey Gershenwald, M.D., in the Department of Surgical Oncology. During mapping, a blue indicator dye and a radiolabeled marker are injected into the skin at the site of a patient's tumor. The markers travel through the lymphatic system along the pathway the cancer is most likely to follow, and the first node the markers reach is designated the sentinel lymph node. Once properly identified, the sentinel node can be surgically removed and then submitted for histologic examination to look for metastatic disease.

The consistent use of both vital blue dye and radiolabeled markers allows surgeons to correctly identify at least one sentinel node more than 99% of the time, according to Dr. Gershenwald. Specialized pathologic techniques such as serial sectioning and immunohistochemical staining have improved the ability of pathologists to identify microscopic metastatic disease in the dissected nodes. If the sentinel node is free of disease, it indicates that the cancer has not yet spread, so more lymph nodes need not be removed; if it contains disease, further surgery is performed to remove other lymph nodes in the nodal basin to best control any additional regional metastatic disease and to optimize nodal staging.

"In general, for patients with sentinel node-negative disease, we have been recommending close observation without additional therapy," said Dr. Gershenwald. "For patients with node-positive disease, we have been offering adjuvant therapy or participation in adjuvant therapy trials." Even after the lymph nodes are removed, microscopic amounts of the tumor might be present elsewhere, and adjuvant therapy can be used as secondary prevention to decrease the likelihood of tumor recurrence.

Interferon is the only drug ap-

## Biochemotherapy Means Hope for Patients with Advanced Melanoma

by Kerry L. Wright

For patients with stage IV melanoma, treatment with the sequential biochemotherapy regimen at The University of Texas M. D. Anderson Cancer Center means three to four months of intense therapy. But the severe side effects sometimes caused by the treatment can be well worth it when biochemotherapy, one of the most promising treatments for advanced melanoma, is effective.

"It is an intensive and toxic treatment, but most patients come through it without serious complications," said Cynthia Hodges, M.S.N., an oncology nurse specialist in the Department of Melanoma/Sarcoma Medical Oncology. "Within three months it is sometimes difficult to tell we ever treated them."

Hodges has worked with patients who receive biochemotherapy since the treatment was first used at M. D. Anderson in 1989. She remembers when the chemotherapy and

biotherapy courses were given separately, and she has watched the evolution of the concurrent and sequential regimens as they are used today.

At M. D. Anderson, each course of sequential and concurrent biochemotherapy includes the chemotherapy agents cisplatin, vinblastine, and dacarbazine and the biologic agents interferon and interleukin-2.

While both treatments show activity against melanoma, concurrent biochemotherapy has less severe toxic effects because patients have more time to recover between treatments. Side effects can include flu-like symptoms, hypotension, and capillary leak syndrome, which make biochemotherapy an inpatient rather than an outpatient treatment.

There is no standard treatment for patients with advanced melanoma, said Jeffrey Lee, M.D., an associate professor in the Department of Surgical Oncology, but biochemotherapy "is the most effective therapy that we have for patients with distant spread of disease." At M. D. Anderson, patients with stage IV disease may also be treated with chemotherapy, chemoradiation, or novel molecular biotherapeutic agents. Agents featured in upcoming clinical trials

proved by the Food and Drug Administration for adjuvant therapy in patients with melanoma. Although phase III trials have shown that interferon may modify disease course and delay progression, the drug's survival benefits have not been confirmed.

"Interferon remains an appropriate choice for many patients with stage III melanoma as adjuvant therapy, but for many patients the best option is still to consider investigational treatments," said Dr. Lee. Biochemotherapy has been shown to be the most effective treatment for stage IV disease, and it is now under investigation to determine if it is superior to interferon as adjuvant therapy for regional disease.

Agop Bedikian, M.D., a professor in the Department of Melanoma/Sarcoma Medical Oncology, is currently leading a multicenter,

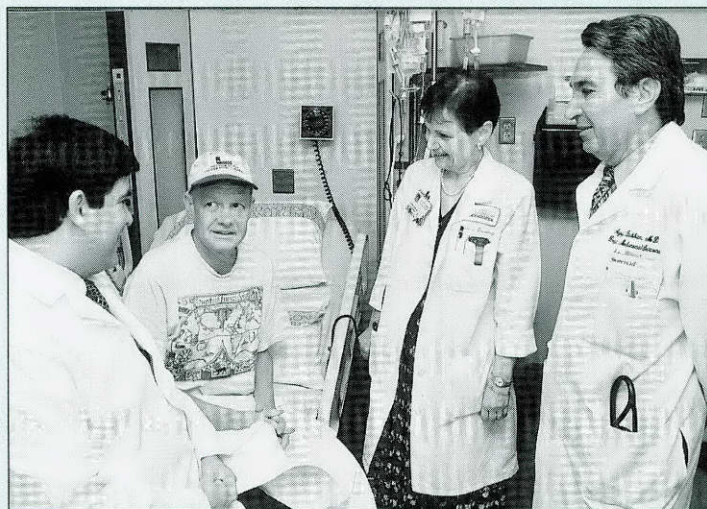
randomized phase III trial comparing high-dose interferon to concurrent biochemotherapy. Though both treatments involve some toxicity, one major difference is that the interferon is given over the course of a year, whereas the biochemotherapy is given in four, five-day courses over three months. The biochemotherapy regimen used was developed at M. D. Anderson and includes the chemotherapeutic drugs cisplatin, vinblastine, and dacarbazine in combination with the biologic agents interferon and interleukin-2.

The idea of using biochemotherapy as adjuvant treatment is catching on, and as preliminary data are being accumulated in Dr. Bedikian's study, the Eastern Cooperative Oncology Group and the Southwest Oncology Group are planning for a larger multicenter



include dacarbazine with a *bcl-2* antisense oligonucleotide and paclitaxel in combination with a matrix metalloprotease inhibitor.

Biochemotherapy's impact on patients with stage IV melanoma has recently been demonstrated in a large, randomized phase III clinical trial comparing sequential biochemotherapy to standard chemotherapy. Results of the M. D. Anderson trial, which accrued 190 patients over five years, were presented at the American Society of Clinical Oncology meeting in New Orleans in May by principal investigator Omar Eton, M.D., a medical oncologist in the Department of Melanoma/Sarcoma Medical Oncology. "In this randomized trial of patients with poor prognostic variables, the response rate for sequential biochemotherapy was 48%, which was almost twice that for chemotherapy alone," said Dr. Eton. Although the complete response rate for biochemotherapy was less than 15%, it was three times higher than the complete response rate for chemotherapy alone. Biochemotherapy also resulted in modest but significant improvement in time to progression and overall survival rate when compared to standard chemotherapy. Dr. Eton is now



*Medical Oncologist Omar Eton, M.D., Oncology Nurse Specialist Cynthia Hodges, M.S.N., and Professor Agop Bedikian, M.D., (left to right) from the Department of Melanoma/Sarcoma Medical Oncology meet with patient Tom Broyles to discuss his treatment.*

pursuing a dose intensification trial of biochemotherapy in an effort to augment complete response rates and control side effects.

"The one direction we are going now is to enhance the overall efficiency of biochemotherapy, specifically aimed at higher complete remission rates," said Agop Bedikian, M.D., a professor in the Department of Melanoma/Sarcoma Medical Oncology. Dr. Bedikian is investigating the efficacy of second-generation taxanes such as BMS-184476, which will be examined in a phase II clinical trial beginning in August. He plans to determine whether new taxanes will be even more powerful and less toxic than existing

ones, and he hopes that they will eventually be used to create new biochemotherapy programs.

As physicians prescribe and develop treatments, Hodges stays beside the patients, managing their symptoms and offering encouragement. She knows, as do most of them, that advanced-stage melanoma is often a deadly disease, but she also knows that biochemotherapy may be their best option.

"All the patients have such a desire to live and to be there for their families in the future," Hodges said. "Even when patients know they have a terminal illness and they could die any time, it is always tomorrow, never today, for most patients." ●

trial with a similar protocol comparing interferon and biochemotherapy.

While trials evaluate the effectiveness of biochemotherapy, a vaccine approach to adjuvant therapy is also being investigated at M. D. Anderson. A multicenter, randomized phase III trial sponsored by the John Wayne Cancer Institute is comparing an allogeneic, whole-cell vaccine called CancerVax with BCG, a nonspecific immune stimulator that is also a component of the vaccine.

The vaccine is prepared from tumor cells that are grown in culture, killed with radiation therapy, and mixed with BCG before being injected into patients. Because it is made from whole cells, the vaccine contains a variety of antigens that should be similar to antigens on a patient's own melanoma cells.

"In theory, when the body sees

those same antigens on its own melanoma cells, it may be encouraged to view them as being foreign and kill them," said Dr. Ross, who is the principal investigator of the M. D. Anderson portion of the allogeneic vaccine trial.

Autologous tumor-derived vaccines are also being investigated as adjuvant therapy for stage III and stage IV disease in a phase I study led by Omar Eton, M.D., a medical oncologist in the Department of Melanoma/Sarcoma Medical Oncology.

Each autologous vaccine is made by surgically removing a patient's tumor and extracting from the tumor cells heat shock protein gp96, an evolutionarily conserved glycoprotein that binds and shuttles peptides to important immune-signaling molecules. The investigators exploit

this molecular chaperone by using it to extract the patient's own tumor-specific peptides and then as a non-specific immune primer for professional antigen-presenting cells. When the peptides are displayed on the surface of a patient's antigen-presenting cells, a specific T-cell immune response can be generated against the tumor without having to identify individual peptides or select patients based on immunological phenotypes. Researchers hope to show that using gp96 and other chaperones together with peptides is more effective than using peptides alone.

"Patients enrolled in the adjuvant setting had advanced melanoma with disease that was resected as part of their routine management. Several of these patients have remained alive with no other treatment for more

*(Continued on page 4)*



## Melanoma Clinical Trials

Clinical trials in progress at The University of Texas M. D. Anderson Cancer Center include the following for patients with melanoma.

- A phase III randomized, double-blind trial of BCG plus a polyvalent melanoma vaccine, CancerVax, versus BCG plus a placebo as a postsurgical treatment for stage III melanoma (ID99-051).

*Physician: Merrick I. Ross, M.D.*

Participants must have been diagnosed with stage III disease (melanoma in one or more lymph nodes) and must have had a complete lymph node dissection with no evidence of residual disease.

- Phase III trial of hyperthermic isolated limb perfusion and melphalan with or without tumor necrosis factor in the patient with localized, advanced, extremity melanoma (ID99-143).

*Physician: Merrick I. Ross, M.D.*

This study is designed for patients with measurable melanoma of an extremity. Patients may have received chemotherapy, biotherapy, or radiotherapy if it was completed at least one month prior to enrollment.

- Preoperative lymphoscintigraphy and intraoperative lymphatic mapping for invasive cutaneous melanoma of the head and neck (ID97-068). *Physician: Susan A. Eicher, M.D.*

Participants must have histologically confirmed, invasive cutaneous melanoma (1-4 mm thick or <1 mm thick for ulcerated lesions).

- Trial of interferon alfa-2b versus biochemotherapy using cisplatin, vinblastine, dacarbazine (DTIC), and interferon plus interleukin-2 as adjuvant therapy for patients with melanoma and regional lymph node metastases (ID95-196). *Physician: Agop Y. Bedikian, M.D.*

This phase III study is for patients aged 10 to 66 years (up to 70 years if they are in excellent health) who have undergone a complete lymph node dissection and have no residual disease.

- A phase III randomized, double-blind trial of immunotherapy with a polyvalent melanoma vaccine (CancerVax) plus BCG versus a placebo plus BCG as a postsurgical treatment for patients with stage IV melanoma (ID98-193).

*Physician: Jeffrey E. Lee, M.D.*

Participants must have been diagnosed with stage IV disease no more than six months prior to study entry and must have no evidence of disease following a complete surgical resection.

- A multicenter trial of adjuvant interferon alfa-2b for patients with melanoma and early lymph node metastasis detected by lymphatic mapping and sentinel lymph node biopsy (ID97-241). *Physician: Merrick I. Ross, M.D.*

*Physician: Merrick I. Ross, M.D.*

Patients 18 to 70 years old who have been diagnosed with primary cutaneous melanoma with a Breslow thickness  $\geq$  1.0 mm are eligible.

- Phase II study of paclitaxel (Taxol), dacarbazine (DTIC), and cisplatin in metastatic melanoma (DM99-353). *Physician: Agop Y. Bedikian, M.D.*

Patients with advanced melanoma and a life expectancy of at least eight weeks are eligible. Patients must not have had prior chemotherapy with paclitaxel, dacarbazine, or cisplatin but can have had prior radiotherapy if unirradiated sites are available for evaluation.

- Phase I evaluation of weekly paclitaxel and concurrent whole-brain radiation therapy for patients with melanoma and multiple, unresectable brain metastases (ID98-301). *Physician: Nicholas E. J. Papadopoulos, M.D.*

Participants will receive whole-brain radiation therapy administered in 2 Gy fractions to a total dose of 36 Gy. Paclitaxel will be given as a weekly three-hour infusion for six consecutive weeks.

- A pilot study of high-dose concurrent biochemotherapy consisting of cisplatin, vinblastine, dacarbazine, interleukin-2, and interferon alfa-2b for advanced metastatic melanoma (DMP99-216). *Physician: Omar Eton, M.D.*

Participants must be between 16 and 65 years old with a histologically documented diagnosis of melanoma and metastases that can be evaluated clinically. ●

**FOR MORE INFORMATION** about these clinical trials, physicians or patients may call the M. D. Anderson Information Line. Those within the United States should call (800) 392-1611; those in Houston or outside the United States should call (713) 792-6161. Visit the M. D. Anderson Cancer Center clinical trials Web site at <http://www.clinicaltrials.org> for a broader listing of treatment research protocols.

(Continued from page 3)

than 18 months and with no evidence of disease progression," said Dr. Eton, who presented his preliminary results at the American Association of Cancer Research meeting in San Francisco in April.

Using a sensitive ELISPOT assay, Cherylyn Savary, Ph.D., an assistant professor in the departments of Surgical Oncology and Molecular and Cellular Oncology, has already shown that after treatment with gp96,

some patients had an increase in the number of white blood cells that could produce interferon- $\gamma$  after activation with their own tumors. Further studies of gp96 are planned with the goals of augmenting the clinical usefulness of gp96, learning more about how patients respond to vaccines made from their own tumors, and evaluating the usefulness of the ELISPOT assay as a marker for antitumor immune response.

The future may tell us which

adjuvant therapy is most useful for the general population. For now, researchers say all are promising in some respects, so all must be carefully evaluated by physicians and patients before decisions are made as to which type of therapy is most appropriate in individual cases. ●

**FOR MORE INFORMATION**, contact Dr. Lee at (713) 792-7218, Dr. Ross at (713) 792-7217, Dr. Gershenwald at (713) 792-6936, Dr. Bedikian at (713) 794-4458, or Dr. Eton at (713) 794-4633.





## Looking for Trouble: How to Spot Signs of Melanoma

**H**ave you taken a look at your moles lately? It seems like an odd question, but knowing the difference between a normal mole and an abnormal growth could save your life.

Each year, almost one million Americans will be diagnosed with skin cancer. Of these, about 5% (44,000) will have melanoma, the most serious—and potentially deadly—form of skin cancer. (The other 95% will be diagnosed with squamous cell or basal cell carcinomas, which appear as new growths or scaly places on the skin).

With careful inspection of the skin, most melanomas can be caught early and successfully treated. So it's vital for all of us to learn how to identify the cancer's early warning signs.

### What is melanoma?

Melanoma occurs when melanocytes, the cells that produce skin color, become abnormal and start dividing without control and invading nearby normal tissue. Melanoma can begin in an existing mole or as a new growth on the skin. Certain moles, however, are more likely than others to develop into melanoma. These unusual moles are called dysplastic nevi.

### What is normal and what isn't?

A normal mole is an evenly tan, brown, or black spot, either round or oval, with a distinct edge that separates the mole from the rest of the skin. It can be flat or raised and is usually less than a quarter inch in diameter—no bigger than a pencil eraser. Most people have between 10 and 40 normal moles.

Dysplastic nevi, on the other hand, are often a mixture of tan, brown, and red or pink with irregular or notched edges that sometimes

fade into the skin around them. They are frequently much bigger than normal moles, sometimes larger than half an inch wide. One of every 10 people has at least one of these atypical moles.

People who have several dysplastic nevi or a family history of dysplastic nevi or malignant melanoma should be examined by a dermatologist once a year.

### How can I conduct a full-scale search?

It is important to know the location, size, and color of the moles on your body so that you will be able to recognize any changes that occur in them. Look for changes in color, especially to grey or black, changes in shape, as in the case of a flat mole that becomes raised, and changes in outline, such as borders that become irregular. Moles that are asymmetrical (one side does not match the other) or that itch or sting could also be indications of melanoma.

Check your skin once a month after a bath or shower. Stand in front of a full-length mirror, using a hand-held mirror to inspect hard-to-see areas. Check any moles, blemishes, or birthmarks from the top of your head to your toes, noting anything new or unusual, such as a sore that does not heal. Be sure to check the front, back, and sides of your arms and legs, your groin, palms, fingernails, soles of your feet, areas between your toes, and even your scalp.

### What should I do if I find something?

Any unusual moles or moles that have changed in color, outline, or size should be inspected by a doctor or nurse. If your physician suspects melanoma or another skin cancer, the mole will be removed. This is usually a simple surgical procedure done under local anesthesia in the doctor's office. The mole will then

### The ABCs of Melanoma Detection

Signs of melanoma can include:

**A**symmetry

**B**order irregularity

**C**olor variation

**D**iameter greater than a quarter inch

**E**nlargement

be examined under a microscope to determine if it is cancerous.

### How can I protect myself?

Keeping your sun exposure to a minimum and using sunscreen rated SPF 15 or higher are excellent ways to prevent melanoma. It is also important to wear protective clothing, sunglasses, and a hat. Protecting children from the sun is especially important. Melanoma develops more often in people who have had many sunburns. Fair-skinned people who burn easily or those who have a tendency to develop many or atypical moles are at increased risk for melanoma and should make a special effort to avoid prolonged exposure to the sun.

By being cautious about the sun, regularly inspecting your skin, and reporting any suspicious changes to your doctor, you can help reduce your risk of melanoma. ●

For more information, contact your physician or contact the M. D. Anderson Information Line:

(800) 392-1611 within the United States, or

(713) 792-6161 in Houston and outside the United States.

May 2000

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# No Easy Answers: Women at Increased Risk for Breast Cancer Face Difficult Choices

by Stephanie Deming

**T**he spring of 1998 brought good news for women at increased risk for breast cancer: dramatic results from the Breast Cancer Prevention Trial showed that tamoxifen significantly lowered the risk of breast cancer in women at increased risk of the disease. The National Cancer Institute announced that tamoxifen was now an option for women at increased risk, and a flurry of articles in the medical and lay press spoke of “preventing cancer with a pill.”

Despite the good news about tamoxifen, however, women at increased risk for breast cancer still face difficult decisions because several prevention options are available, and all have both benefits and drawbacks.

According to Therese Bevers, M.D., an assistant professor in the Department of Clinical Cancer Prevention and medical director of the Cancer Prevention Center at The University of Texas M. D. Anderson Cancer Center, the first step for a woman concerned about her risk of breast cancer is to quantify that risk.

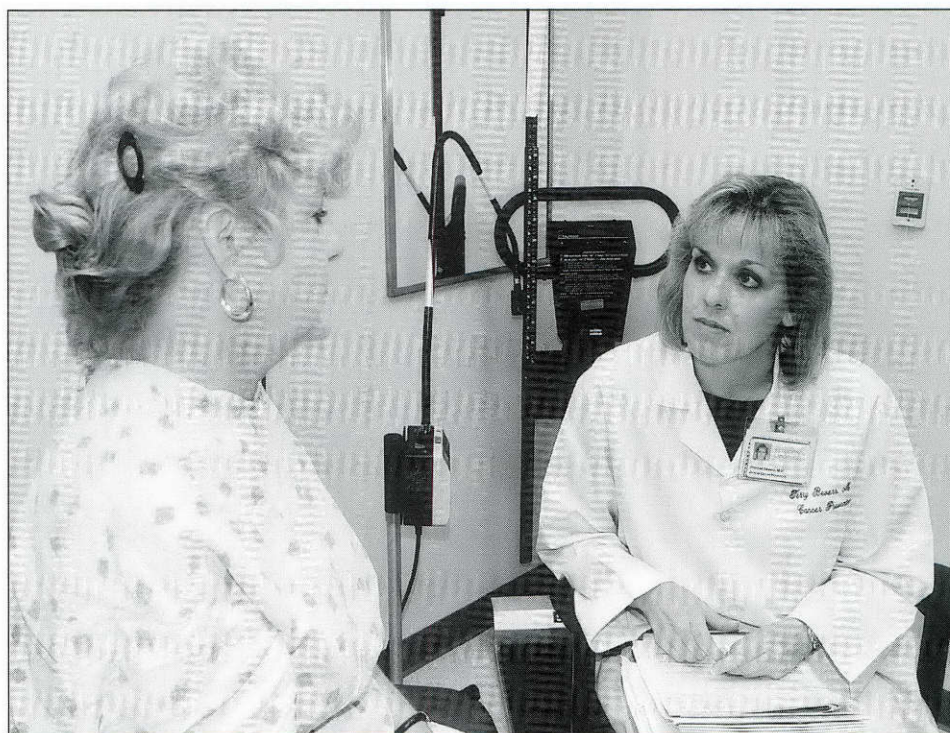
For women who most likely do not have a genetic predisposition for breast cancer, risk is estimated using a validated risk-assessment tool called the Gail model. The model, which has been refined several times since it was originally published in the mid-1980s, currently takes into account seven factors: age, age at menarche, age at first birth, number

of first-degree relatives with breast cancer, number of breast biopsies, number of biopsies showing hyperplasia, and race. The calculations required to arrive at a risk estimate are complicated, but the National Cancer Institute recently made available a computerized version of the Gail model that greatly simplifies the process. The health-care provider simply inputs data on the seven parameters, and the software produces a detailed one-page printout describing the woman's five-year and lifetime risks of breast cancer. A five-year risk higher than 1.7% is considered to be increased.

“Having something quantitative is very nice,” Dr. Bevers said. “You can actually sit down in the office with your patient and—recognizing the limitations of the model [for instance, it does not take into account

cancer in second-degree relatives or age at diagnosis in first-degree relatives]—say, ‘this is an estimate, and we can go from here.’”

For women in whom evidence of a genetic predisposition is strong, the Cancer Prevention Center's initial approach is different. These women complete an extensive family history questionnaire before their first clinic visit, and specialists in the center use this information to calculate the risk of a genetic mutation. When the woman comes in for her risk counseling session, said Dr. Bevers, her probability for having a genetic mutation is carefully explained to her, as are the ramifications of testing positive for a mutation, which include employment and insurance issues. According to Dr. Bevers, women who are concerned about a genetic predisposition should receive



The Cancer Prevention Center counsels women about their breast cancer prevention options. Here, **Dr. Therese Bevers**, an assistant professor in the Department of Clinical Cancer Prevention, talks to Sue Willits.



## **"I think that we have to look at the whole person first. A woman may be at increased risk for breast cancer, but we can't ignore her menopausal symptoms."**

**—Therese Bevers, M.D.**

Medical Director, Cancer Prevention Center

counseling at a center with expertise in genetic counseling.

"These women really need to go to a tertiary care center where genetic testing is done on a regular basis and where people are able to provide the latest in recommendations and advice," she said.

Whether or not the increased risk is a result of a genetic predisposition, women found to be at increased risk should be counseled about screening and prevention strategies.

Screening recommendations differ depending on the level of risk, but all women are encouraged to have regular mammograms and clinical breast examinations and to do monthly breast self-examination.

At the Cancer Prevention Center, the prevention discussion begins with some basic principles that apply to everyone: not smoking, limiting alcohol to one drink a day, eating a diet low in fat, maintaining an ideal body weight, and exercising.

"Whether there is a definitive reduction in breast cancer risk from following a healthy lifestyle, for that we'll just have to wait and see," Dr. Bevers said, "but certainly overall, following that healthy lifestyle is probably beneficial not just for breast cancer but for other diseases."

In addition, women who are at increased risk are counseled about the pros and cons of tamoxifen, which lowers breast cancer risk but increases the risk of endometrial cancer and vascular events. "And often," Dr. Bevers added, "because many of these women will already be on hormones, the discussion will involve the risks and benefits of hormone replacement therapy."

In the Cancer Prevention Center, the approach to prevention options is tailored to the individual woman's personal concerns. "What I basically

tell the woman is, 'you tell me where your biggest area of concern is, and then your secondary areas of concern, and then let's see how we can best approach them,'" said Dr. Bevers.

In some cases, decision-making is relatively easy. For a woman older than 50 who has had a hysterectomy, has increased breast cancer risk, and is already taking estrogen, said Dr. Bevers, "changing her to tamoxifen gives her no greater risk than what she already has right now because the risk for vascular events from tamoxifen is the same as that from estrogen replacement therapy." Additionally, tamoxifen appears to reduce the risk of bone fractures to a degree similar to estrogen. The risk for cardiovascular disease associated with tamoxifen remains uncertain, but it also appears to be similar to the risk associated with estrogen.

A more difficult scenario is the young woman who wants to have children and has a genetic predisposition for breast cancer. "That's a tough situation," said Dr. Bevers, "but there isn't a huge rush to start taking tamoxifen. We can start tamoxifen in five years. It's still going to be around. In fact, there may be better strategies by then." Another consideration is that the effectiveness of tamoxifen in women with a genetic predisposition is uncertain.

For women with an extremely high risk of breast cancer—a lifetime risk as high as 50% to 80% because of a known genetic mutation or a familial component determined by a genetic counselor—prophylactic mastectomy may be discussed.

"More and more people in breast cancer prevention," said Dr. Bevers, "are moving toward the idea that the reasonable population to consider for prophylactic mastectomy is

individuals who have the genetic mutation."

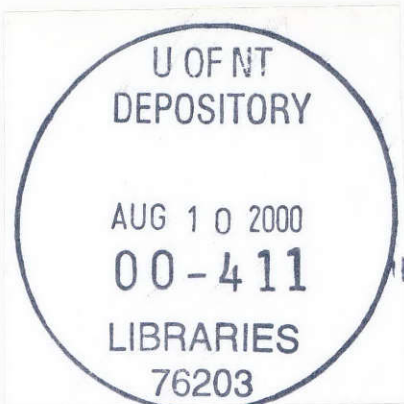
According to Dr. Bevers, prophylactic mastectomy also used to be considered for women with lobular carcinoma in situ, but increasingly, tamoxifen is recommended instead for these women because their risk is fairly comparable to that of a breast cancer survivor.

In helping women make decisions, Dr. Bevers said, "I think that we have to look at the whole person first. A woman may be at increased risk for breast cancer, but we can't ignore her menopausal symptoms, which may increase on tamoxifen, and that really helps to dictate some of the different strategies that we may consider."

The future holds the promise of more chemoprevention options, including raloxifene, a drug currently being studied in the Study of Tamoxifen and Raloxifene (STAR). "The STAR study is designed to hone prevention options—to find an agent that maybe prevents more cases of breast cancer with fewer side effects," said Dr. Bevers. In addition, she said, new drugs similar to tamoxifen and raloxifene may become available, and some preliminary evidence suggests that retinoids may have a role in prevention. "We're seeing prevention as a hot area now," said Dr. Bevers. "There's the big rush to find that magic little pill you can take every day to prevent cancer. Now it's going to be a matter of refining chemoprevention." ●

**FOR MORE INFORMATION**, contact the Cancer Prevention Center at (713) 745-8040. For information about enrollment in the STAR trial through M. D. Anderson, call (713) 792-8064. Participants must be 35 years old or older, postmenopausal, at increased risk for breast cancer, and have no history of breast cancer.



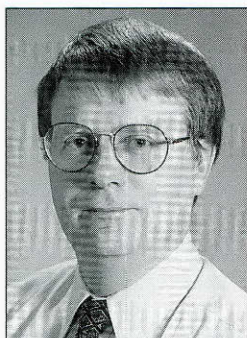


## DiaLog

### Understanding Risk: A Prerequisite for Making Informed Decisions

**Gordon B. Mills, M.D., Ph.D.**  
Chairman, Department of  
Molecular Therapeutics

The exciting results of the Breast Cancer Prevention Trial illustrate how important it is for women to understand the meaning of elevated cancer risk. New approaches to cancer prevention such as tamoxifen, along with more aggressive alternatives such as prophylactic surgery, are not without physical and psychological consequences, and making the right decision about which approach is most appropriate requires a thoroughly informed and educated patient.



Every woman is aware that she is at risk for the development of breast and ovarian cancer, and many can quote lifetime risks for the general population. However, the ability to define one's own personal lifetime risk of breast and ovarian cancer may be much more limited. In our own studies of women attending the Breast and Ovarian Cancer Genetic Predisposition Clinic, we found that women routinely overestimate their lifetime risk of breast cancer by at least threefold. Translating the lifetime risk estimates normally quoted in the lay and scientific literature (approximately 10% for breast cancer and 1.4% for ovarian cancer) into the chance that cancer will

develop in a specific woman this year, in the next five years, or in the next ten years is very difficult. On an individual basis, the chances are binomial: 100% or 0%. That is, cancer either will or will not develop.

So, when a woman is told that she has an abnormality in BRCA1 or BRCA2, what does this mean in terms of her risk this year or in the next five years? It may not mean much if she is in her teens or 20s, when the effects of the BRCA1 and BRCA2 genes rarely manifest. It may mean a lot to a woman in her 40s, when her risk of breast cancer may be as high as 1% to 2% per year.

A woman's concept of risk is affected by her life experiences. High risk may mean something completely different to a woman who has watched her mother suffer and die of breast cancer than to a woman who has never had an experience with cancer. Physicians must therefore be able to explain risk in the appropriate context for each patient.

By improving how we communicate risk to our patients, we can give women the information they need, based on their personal and family history, to effectively evaluate their risk of breast and ovarian cancer in terms consistent with their lifetime experiences. Only then can we help women determine which prevention options, if any, are most appropriate for them.

*Paula Rieger, M.S.N., and Christie Graham, M.H.A., contributed to this article.*

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