

OncoLog

Teen-Savvy Smoking Prevention

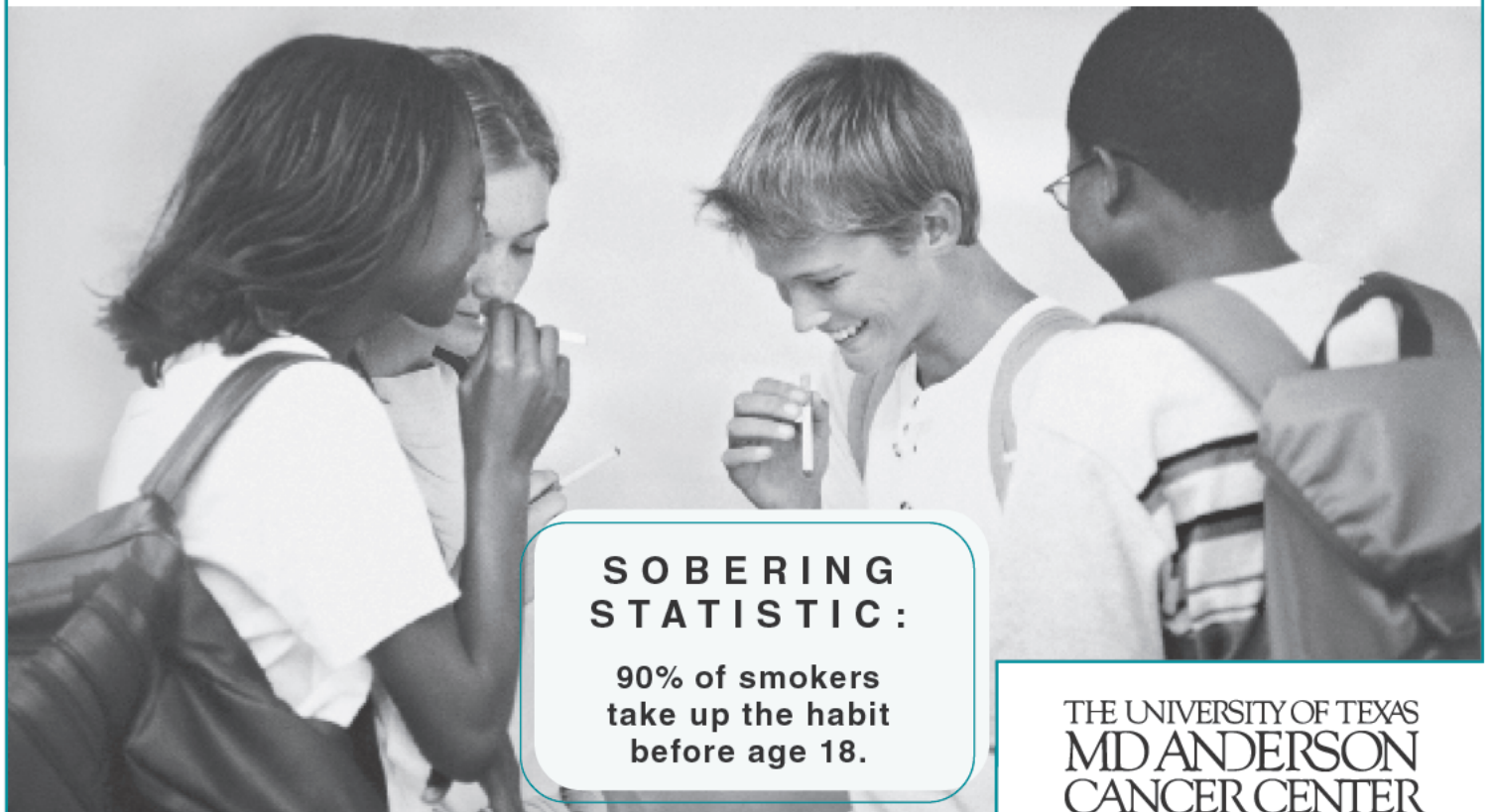
Teens are intrigued by a hip new, Web-based, interactive smoking cessation program.

by Karen Stuyck

When most people hear the words “smoking prevention,” they don’t think of computer games. But ASPIRE is just that—an interactive multi-media CD-ROM used as part of a curriculum to convince

teenagers to stop smoking—or better yet, never start.

ASPIRE (“A Smoking Prevention Interactive Experience”) provides smoking cessation awareness for high school students using captivating *(Continued on next page)*



SOBERING STATISTIC:

**90% of smokers
take up the habit
before age 18.**

THE UNIVERSITY OF TEXAS
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Teen-Savvy Smoking Prevention

(Continued from page 1)

graphics and a video game feel. The program was originally designed as a research project in Houston-area schools, but portions of the program are now available online for kids to access any time, according to the project's creator, Alexander Prokhorov, M.D., Ph.D., an associate professor in the Department of Behavioral Science at The University of Texas M. D. Anderson Cancer Center. (www.mdanderson.org/aspireonline)

"Student response to the program was overwhelming," he said. "Now that we've completed the study, we're eager to let parents, teachers, and most of all, teens, know that help is available."

ASPIRE's interactive multi-media CD-ROM includes quizzes, a video game, animated scenarios, and videos of other teenagers confronting smoking dilemmas. ASPIRE shows students why smoking is harmful and offers specific help on how to stop. Each part of the curriculum is modified for individuals, depending how they answer questions about their behavior and attitudes toward smoking. Once the student's stage of readiness to change is identified, ASPIRE offers eight educational tracks to meet the students' individual needs. Thus, someone who is only thinking about starting to smoke would see different scenarios and get different information than another student who is already smoking and not sure that he wants to quit.

While young people are a notoriously difficult audience for stop-smoking programs, they are an important group to reach since 90% of smokers start smoking before age 18. Part of the problem in interesting younger smokers in quitting is that young people tend to think of themselves as invincible. "Younger smokers usually don't yet have smoking-related physical problems, and telling them that smoking increases their chances of dying of lung cancer at 40 or 50 just doesn't work," Dr. Prokhorov said. "In addition, adolescent smokers often don't want their parents to know that they smoke."

...telling [younger smokers] that smoking increases their chances of dying of lung cancer at 40 or 50 just doesn't work."

– Dr. Alexander Prokhorov



Different approaches are needed to reach younger smokers than those traditionally used with adults. Lung cancer statistics, for instance, may not be compelling to these students, but they are very interested in how smoking may affect their athletic performance or how it can lead to impotence, infertility, or complications during pregnancy—factors that might affect them now or in the near future.

Increasingly, M. D. Anderson researchers are designing tobacco cessation programs for specific populations. Realizing that different groups of people respond to stop-smoking programs in different ways, the scientists tailor clinical trials to determine the best approach for each audience. Recent stop-smoking research projects, for instance, have focused on pregnant women, teenagers, Spanish-speaking people, and college students. Several of Dr. Prokhorov's smoking cessation projects are designed for young people; ASPIRE, for instance, is targeted specifically for high school students.

The video game component of ASPIRE has players making a journey up a steep mountain to find their place on Mount Aspire. Along the way, students reach Decision Point, Commitment Peak, Action Steppes, Perseverance Gorge, Balance Bluff, Temptation Quarry, and Independence Overlook. Each stopping place on the mountain gives students a variety of information and a chance to make

decisions. At Temptation Quarry, for instance, they learn that the three main motivations for teen smoking are social reasons, addiction, and mood alterations such as calming down or help in coping with difficult situations.

Three animated monkeys show how to stop smoking using the three R's: **Recognize** what kinds of things tempt you to smoke, such as a specific time of day or being around certain types of people; **Remember** why you want to quit, such as wanting to be a better athlete or deciding "I want to respect Number One"; and **React** to the situation without smoking.

Furthermore, students are able to interact with the program and find myriad ways to cope with their own specific temptations. For instance, if a teenager is having a hard time dealing with social pressures such as smoking at parties or not knowing what to say when friends offer a cigarette, he can click the icon with this temptation on the screen. In a variety of scenarios—videos of other teens discussing the issue, an animated ballpark stand where each character has a different phrase on how to say no if friends are pressuring him to smoke—he can pick up ideas.

The student learns that it's smart to avoid situations where people are smoking. But if friends are smoking around him, it's a good idea to have phrases ready. Maybe he'll want to ask for support: "Dude, I'm trying to quit smoking. Do you mind?" Or perhaps



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he'll opt for being direct ("It's not my thing."), changing the subject ("Want a carrot?"), or using humor ("No way, man. Cigarettes kill trees. Smoke veggies, not cigarettes."). The coping devices, illustrated by other kids implementing the approaches, include having positive plans, using humor, being smart, ignoring the invitation to smoke or changing the subject, being direct, and asking for support.

About 1,600 students from Houston area high schools completed the ASPIRE program. Eighteen months after completing the program only 2% of ASPIRE students had become new smokers, compared with 6% of a control group. "We showed that the program changes kids' perceptions of tobacco," Dr. Prokhorov

said. "It increases their self-efficacy in quitting smoking or in not starting."

Dr. Prokhorov's passion to help young people give up or avoid smoking has not stopped with high school kids. Another study is designed to help college students quit smoking by having them look at their own health and by showing them how smoking has affected their lung and bronchial function.

"We tried to make 'invulnerable' students feel more vulnerable," he said. Using spirometry, a lung function test, students can see the age of their lungs. "Quite a lot of the students who smoked exhibited decreased lung function, which frequently translated into a 19 year old having the lungs of a

(Continued on page 4)

Eighteen months after completing the program only 2% of ASPIRE students had become new smokers, compared with 6% of a control group.

Teen-Savvy Smoking Prevention

(Continued from page 3)

30 year old," Dr. Prokhorov said. A carbon monoxide meter showed students how smoking increases their carbon monoxide level, which adversely affects athletic performance. Students who later quit smoking were happy to see their individual respiratory symptoms improve, their carbon monoxide levels go down dramatically, and their lung age decrease.

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"Students were intrigued by the program; it held their interest," Dr. Prokhorov said. "Many student participants said they would recommend the program to friends and family members."

Dr. Prokhorov's group is now developing a Web-based smoking cessation program specifically for middle school students. The program will use some elements of ASPIRE such as quizzes, games, flash animation, and video clips. "We want this program to be edgy, full of animation and videos," Dr. Prokhorov said. He hopes that an adolescent, for instance, who feels pressured to try smoking, can go to the ASPIRE program on the Internet and choose from menu options to see how to cope. Since the program can be accessed at any time, Dr. Prokhorov hopes this "cyber support" will help make a real difference in teens' attitudes toward smoking. ●

FOR MORE INFORMATION, contact Dr. Prokhorov at (713) 745-2382. Portions of the ASPIRE program can be found online at www.mdanderson.org/aspireonline.

Considering Prophylactic Surgery, Part II

In the April issue, we looked at the pros and cons of prophylactic surgery for women with BRCA1 or BRCA2 mutations.

Here, we discuss thyroidectomies or colectomies for people who carry mutated genes that put them at high risk for certain cancers.

by Ellen McDonald

Undergoing prophylactic surgery to prevent a cancer caused by a genetic mutation is a life-altering event, however effective the operation may be.

This is the issue faced by people with multiple endocrine neoplasia type 2 (MEN2), familial adenomatous polyposis (FAP), or hereditary nonpolyposis colorectal cancer (HNPCC). All three conditions result from inherited or spontaneously mutated genes and can often be effectively treated with well-timed prophylactic surgery.

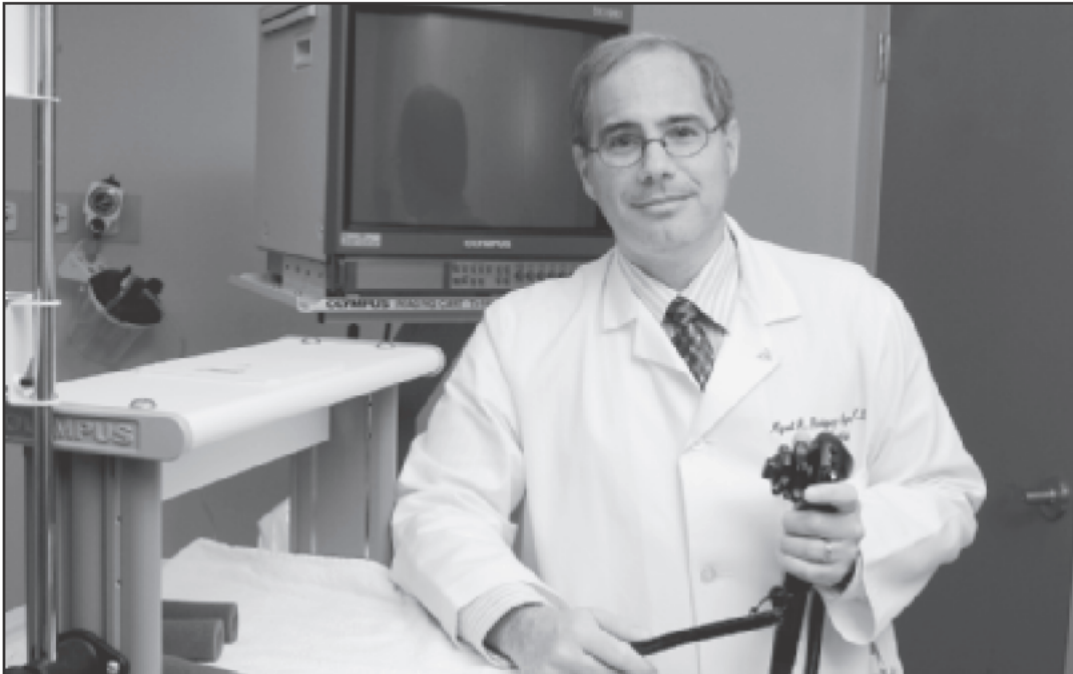
MEN2 is characterized by medullary thyroid carcinoma, pheochromocytoma, and hyperparathyroidism. A well-timed thyroidectomy, usually in childhood, can often prevent the development—or at least the spread—of cancer.

"Surgery to remove the thyroid gland is always recommended when a *RET* mutation is detected," said Robert F. Gagel, M.D., a professor in the Department of Endocrine Neoplasia and Hormonal Disorders and the head of the Division of Internal Medicine at M. D. Anderson Cancer Center. He explained that the disease manifests itself in two forms: MEN2A and

MEN2B, the latter being a more aggressive form that typically results from a spontaneous mutation and that all too often is not diagnosed until after tumor growth and metastasis have occurred. Because of the aggressive nature of MEN2B, thyroidectomy should be performed as early in life as possible—at 6 months or sooner in some cases.

"It is hard to cure a child with MEN2B," Dr. Gagel admitted. "However, children with MEN2A can be cured, assuming they have a thyroidectomy at a relatively young age. Our best estimate is that we can cure approximately 85% of MEN2A patients by removing the thyroid gland before the age of 13," remarked Dr. Gagel.

"However, an intriguing question currently under study at M. D. Anderson and elsewhere is whether we can cure 100% of these patients by removing the thyroid by age 5. Some evidence suggests that it's possible to cure at least 95% of them. But given that the genetic test that definitively identifies people with this mutation has been available for only 10 years, we probably won't really have the answer to this question for another 20 years or more."



“Retrospective studies have shown that the surgery can improve survival time [of people with FAP] by approximately 20 years,” said Dr. Rodriguez-Bigas, who is holding a flexible sigmoidoscope.

Suzanne Shapiro, a genetic counselor in the Department of Surgical Oncology, explained that timing of prophylactic thyroidectomy is key for children with MEN2A—early enough in life to prevent the development or metastasis of medullary carcinoma and yet late enough to minimize the number of years daily thyroid hormone replacement therapy will be required.

“Appropriate timing also depends on a family’s specific experience with the disease,” she added. “Some parents may not feel comfortable waiting until a child is 5 years old, especially if there’s a family history of aggressive thyroid cancer. Timing of the surgery, therefore, shouldn’t be set in stone, but should be based on the current literature, family medical history, and the parent’s wishes.”

One parent who knew no hesitation is ██████████, whose own thyroid cancer led to a diagnosis of MEN2A in 2003. Prior to that, no one in her family had suspected the presence of a familial genetic mutation, although in retrospect she believes that her paternal grandmother and other family members may have died of complications of MEN2A.

“At first it was scary finding out that I had the disease, extremely so,” ██████████

explained, “but I did my own research, asked a lot of questions, and learned everything I could about it.” She persuaded everyone in her large family to be tested, and five of them, including two of her daughters, ages 11 and 21, were found to carry a *RET* mutation. She encouraged her daughters to undergo prophylactic thyroidectomies, the results of which showed very little cancer development and no lymph node involvement in either daughter.

While age is not as major a factor for familial adenomatous polyposis (FAP) or hereditary nonpolyposis colorectal cancer (HNPCC), the treatment approach certainly is. Prophylactic colectomy is widely accepted as the optimal treatment for patients with FAP, a genetic syndrome associated with a germline mutation in the *APC* gene. The surgery typically involves removal of the abdominal colon and an abdominal or total colectomy. It may also involve removal of the rectum and connection of the small bowel reservoir to the anus to establish bowel continuity. The type of procedure performed depends on many factors, but more importantly on the location and number of polyps, which can range from the hundreds to the thousands.

“Most patients who carry such a mutation will develop cancer by age 50 without the surgery,” said Miguel A. Rodriguez-Bigas, M.D., a professor in the Department of Surgical Oncology at M. D. Anderson. “Retrospective studies have shown that the surgery can improve their survival time by approximately 20 years.”

Nevertheless, the data are not so clear regarding HNPCC. “Prophylactic surgery is more controversial in the management of HNPCC, or the Lynch syndrome,” Dr. Rodriguez-Bigas continued, “because there are as of yet no data showing a major improvement in survival time with the surgery, and 15 to 20% of people with HNPCC

will not develop colorectal cancer.” (Despite its name, HNPCC is not a type of colorectal cancer but a disorder that puts those affected at higher risk for colorectal cancer, and these people will develop polyps before they develop cancer.)

Therefore, based on the individual circumstances of the case and his judgment as a surgeon, Dr. Rodriguez-Bigas may offer prophylactic surgery as an option to patients with HNPCC. Such patients are identified by having both the requisite family history of non-FAP-related colorectal cancer and a genetic mutation in a mismatch repair gene, such as *hMSH2*, *hMLH1*, or *HMSH6*.

“We generally try to see patients with either disorder as early as possible,” noted Patrick M. Lynch, M.D., an associate professor in the Department of Gastrointestinal Medicine and Nutrition. “Ideally, we’d like to see patients before they have any signs of disease, such as polyps, bleeding, or obstruction.

“In the case of FAP, we currently have a clinical trial specifically designed for children with the genetic mutation. The trial includes a fairly active chemoprevention program and close

(Continued on page 6)

Considering Prophylactic Surgery

(Continued from page 5)

Our genetic counselors

work closely with physicians throughout this process and will track families with the genetic mutations through several generations.”

— Dr. Patrick M. Lynch

surveillance, usually with colonoscopy, to study whether we can postpone the day when prophylactic colectomy will be needed. Our genetic counselors work closely with physicians throughout this process and will track families with the genetic mutations through several generations.”

Despite recommending that patients delay the surgery until their polyp burden is at least moderate, Dr. Lynch always encourages the patient and, if applicable, the patient's parents, to get to know the surgeon long before the need for surgery exists. “This gives them ample opportunity to get a second opinion if desired, discuss the type of surgery required based on the trajectory and progression of the polyp involvement, bond with the doctor, and prepare themselves emotionally for the physical and psychological consequences of the surgery.”

Although he hopes that advances in medical treatment will one day make prophylactic colectomy—which even in the best of circumstances is a radical treatment—unnecessary, Dr. Lynch believes that until that day comes, he best serves his patients by giving them this time to prepare. ●

FOR MORE INFORMATION, contact Dr. Gagel at (713) 792-6517, Dr. Rodriguez-Bigas at (713) 745-4955, or Dr. Lynch at (713) 794-5073.

IN BRIEF

Breast Cancer Gene May Be Vaccine Target

A GENE THAT APPEARS TO HELP regulate normal embryonic development somehow becomes overexpressed in breast cancer cells, according to a new study conducted by Laszlo Radvanyi, Ph.D., associate professor of breast and melanoma medical oncology at M. D. Anderson, and scientists at Sanofi Pasteur's Cancer Vaccine Program in Toronto, Canada. The study was recently published in the August 2, 2005, issue of the *Proceedings of the National Academy of Sciences*. Researchers hope to use the cancer-specific protein to train the immune system to specifically attack breast cancer cells.

“There is a tremendous need for new molecular targets to treat breast cancer,” Radvanyi says. “There are very few bona fide targets that are exquisitely specific for breast cancer. We believe this is one of them.”

While doing a large-scale genetic screen, Radvanyi and his collaborators zeroed in on the gene, called TRPS-1, which is found at high levels in all forms of breast cancer. After identifying TRPS-1, they showed that T-cells trained to detect TRPS-1 would attack and kill breast cancer cells containing the protein in laboratory experiments. “This immune response against breast cancer is exciting because our protein expression analysis showed that TRPS-1 appears to be overexpressed only in cancers and not in normal tissue, making an immune response potentially very specific for the tumor only,” Radvanyi says.

Researchers will next try to understand what the protein's targets are inside the cell. “If we understand its targets, in addition to vaccines targeting TRPS-1,

we might also be able to design inhibitors that disrupt its action, which could be clinically important given its early appearance in breast cancer,” Radvanyi says.

Potential “Weak Link” Between Virus and Liver Cancer Discovered

RESEARCHERS AT M. D. ANDERSON have uncovered a crucial molecular link between a viral infection and development of a common and fatal form of liver cancer. In the process, they have identified a possible way to treat this disease as well as a number of other cancers.

In findings reported in *Molecular Cell*, Mien-Chie Hung, Ph.D., professor and chair of the Department of Molecular and Cellular Oncology, and his team traced the pathway by which the hepatitis B virus leads to the development of hepatocellular carcinoma. They found that it “turns off” the enzyme GSK-3 β , which acts to suppress tumor formation and inhibit the spread of cancer.

GSK-3 β could prove to be the Achilles heel for liver cancer and other tumors—including breast, colon, kidney and stomach—that use a similar “pathway” to cancer development, the researchers say.

“This study identified a novel mechanism for how hepatitis B primes liver cells to turn cancerous, and what we found has potential relevance for other cancers as well,” says Hung. “We think it may be possible in the near future to develop novel therapeutic approaches for treatment of . . . cancers, including development of gene therapy and a small molecule that will activate GSK-3 β .” Hung collaborated with researchers from Baylor College of Medicine in Houston as well as Germany, Taiwan, and China. ●



From Patient to Patient: Real-World Coping Tips

Have you recently been diagnosed with a serious illness like cancer? Wondering how to cope? We asked cancer patients, members of the Anderson Network, to share some of their real-world coping tips.

Educate yourself.

- Educate yourself, through your doctor, the Internet, the library, and the other many cancer resources, about your disease and treatment so as to feel more in control and less overwhelmed.”
- Become informed about your type of cancer and disease—learn about the disease, and learn the ‘vocabulary’ of your cancer. In other words, understand the terms so that you can better process what the doctors and health care professionals are saying. This also will help you to frame questions better in order to probe for more information or clarification. You don’t have to try to become an expert overnight, but start checking out Web sites, books, and support groups to begin understanding the disease.”
- Understand the staging of your disease as soon as it is known. This gives you a marker to use in asking questions.”

Ask questions.

- An old Chinese proverb says, ‘To know the road ahead, ask those coming back.’”

- Take someone with you to doctors’ appointments for the express purpose of taking notes and helping you ask questions. Make up your list of questions ahead of time. Don’t always wait to ask the doctor the questions—you can ask nurses and physician assistants some of the questions also. Sometimes they have a little more time to answer, or you can use them to practice a question for the doctor. They can sometimes help you to frame the question.”

Reach out to others.

- The best coping strategy for me was to talk with all my friends!”
- Do use support networks to talk with others with your disease who can share tips and stories about how they survived.”
- Counseling and support groups are important in helping you realize that you are not alone.”
- Make sure that you have a network of friends (besides your family) to talk to and vent.”
- Get involved with organizations that deal with your disease. Giving back works for so many.”
- Don’t try to handle the disease of cancer by yourself, but if you find it hard to talk with someone, try writing your feelings down.”

Stay positive and forward looking.

- Remember that you are still the same person you were before you were diagnosed. You now just happen to have cancer. Don’t look too far into the future; just aim to get through the day. Remember that no disease


“To know the road ahead, ask those coming back.”

is 100% fatal. Why shouldn’t you be the survivor?”

- Remove yourself from negative people! This is a huge help. As a cancer patient, you have to remain positive and forward looking. Being around negative people and situations will not enhance your healing process.”
- Don’t dwell on others’ stories of people they know that died of your disease or had bad experiences. Don’t dwell on the mortality rates that are published on the Internet.”
- I wrote down all the bad things about breast cancer, how I felt about the negative aspects (scared for my daughters, sad, etc.). Next, I wrote down the good things about breast cancer (many treatment options, etc.) and known truths about breast cancer (many women have survived it, etc.). I then formed an action plan to get me through the experience by determining what I wanted to have and be at the end of the treatment and the action steps to get me there (positive attitude, etc.).” ●

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

 **(800) 392-1611, Option 3,** within the United States, or

 **(713) 792-3245** in Houston and outside the United States.

June 2005
R. Williams

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DiaLog

Enrolling Patients in Prevention Trials

Therese B. Bevers, M.D.
Associate Professor, Department
of Clinical Cancer Prevention

For many years, the number one killer of Americans was heart disease. However, with heart disease-related deaths declining—attributable, at least in part, to improved prevention strategies—cancer now holds the dubious distinction of being the number one killer of Americans.



Clinical trials are critical to helping us identify not only better treatments but also preventive strategies. As a result of two decades of advances in the science of cancer prevention, our ability to detect cancer at ever earlier stages, including at the molecular level, means we can now identify—and even treat—some precancers, instead of waiting for the full-blown disease to develop. Clinical trials in cancer prevention hold out the promise that we might one day be able to identify a person's cancer risk profile at an early age and prescribe individually tailored risk-reduction strategies that may prevent the development of the disease. If we are to do this, however, we must encourage many more people to take part in cancer prevention trials.

Currently, only 3% of eligible adults are enrolled in any cancer clinical trials, but primary care physicians have enormous power to change that when it comes to

prevention trials. They hold tremendous persuasive powers for getting patients involved because patients care about what their doctors have to say. Physicians are also key to ongoing participant compliance because patients need the support of their doctors to deal with possible side effects and remain involved in the trial.

Enrolling in prevention clinical trials benefits not only patients but also primary physicians. Prevention trials typically provide risk assessment for a specific type of cancer, which allows patients, and their doctors, to learn about risks and management options. Furthermore, primary physicians can be certain that patients on clinical trials are being monitored very closely, often by experts in the field, for development of the disease. Finally, physicians can be assured that patients have access to the newest and best cancer prevention interventions and treatments—often long before they become commercially available.

Overall, involvement in prevention clinical trials is critical if we are to reduce the number of cancer-related deaths in America. Primary care physicians can play an important role in encouraging patients to become involved in cancer prevention clinical trials. Such encouragement and resulting participation will not only help reduce the number of cancer-related deaths in America but will ultimately help us develop ways to put an end to cancer before it begins. ●

OncoLog

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Published by the Department of Scientific Publications-234,
The University of Texas M. D. Anderson Cancer Center,
1515 Holcombe Boulevard, Houston, Texas 77030,
713-792-3305.

Made possible in part by a gift from the late Mrs. Harry
C. Wiess.

Circulation: 25,000

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