

What's Inside

Targeted Therapy:
Treatments for
Hereditary Cancer . . . 2

An Introduction
to Breast
Reconstruction. 3

Voices of FORCE . . . 4

Surviving Breast
Cancer: African-
American Women and
the Importance Of
Genetic Testing 6

GINA: an Update. . . . 7

What's New 8

Staff

Sue Friedman
Exec. Dir., FORCE

Kathy Steligo
Editor

Contributors

Joanne Cabello

Trudy Harris

Tuya Pal, M.D.

Susan Vadaparampil,
Ph.D.

Contact Us

FORCE
16057 Tampa Palms
Blvd. W. #373
Tampa, FL 33647

Tel: 866-288-RISK
Fax: 954-827-2200

info@facingourrisk.org

www.facingourrisk.org

Welcome!

by *Sue Friedman*

Fall is a season of action. Hustling the kids back to school. Cheering our favorite football and hockey teams. Saying goodbye to summer's hectic activities and transitioning our homes for winter.

Here at FORCE, Fall is an equally busy time. September is Ovarian Cancer Awareness Month; October is Breast Cancer Awareness Month. Because so many of our members or their loved ones have been impacted by one or both of these cancers, this time of year is particularly significant to our constituency.

This second edition of *Joining FORCEs* focuses on taking action. Been thinking about collecting a family medical history but never quite been able to get around to it? Try the simple online tool described below; it makes easy work of collecting family medical history to identify genetic factors

National Family History Day: "My Family Health Portrait"

by *Kathy Steligo*

Heart disease, stroke, diabetes, and other common health disorders often run in families. By recognizing the genetic factors that contribute to these diseases, family members can identify their own increased risk and take appropriate preventative actions.

Everyone benefits by gathering their family health history. Collection and interpretation of this information is the most practical personalized tool available. The complex data reflects the interaction of genetic, environmental, cultural, and behavioral factors shared by family members. Health care professionals can use this knowledge to design individualized care programs to prevent disease and promote overall health.

Recent polls indicate the vast majority of people believe family information is important to their health, although most have never attempted to gather such facts. Working with agencies of the U.S. Department of Health and Human Services, Surgeon General Richard H. Carmona,

that contribute to disease. If you're facing mastectomy, our introduction to reconstructive methods will help you sort out your options. From our research desk, we share data supporting the value of exercise to prevent or delay the onset of cancer or reduce the risk for recurrence (and a wonderful personal testimony to the recuperative powers of exercise). We also bring information regarding genetic testing among African-American women, and exciting news from the United Kingdom about PARP Inhibitors—promising new drugs that may kill BRCA tumor cells while sparing healthy cells.

We're here to empower you with information and resources, so you can take action to protect your health. As always, we welcome your thoughts and comments about our newsletter.

M.D., M.P.H., launched the Family History Initiative, a public health awareness campaign to encourage Americans to collect family health data and share it with their physicians. This effort highlights Thanksgiving, a traditional time of family gatherings, as the perfect time to discuss and document family health histories. The first annual National Family History Day was Thanksgiving 2004.

My Family Health Portrait is an easy-to-use tool to help document generations of family members and their health disorders. The program prompts for information and then creates a family tree indicating health problems that may be passed from one generation to the next. The tool can be downloaded in English and Spanish at <http://www.hhs.gov/familyhistory>. A print copy may be ordered by calling 888-275-4772.



Understanding Clinical Trials

Researchers conduct clinical trials to test a new drug for treatment or prevention of disease. The process usually involves three phases of testing:

- **Phase I trials** usually involve a small number of patients and are designed to evaluate safety and optimal dosing of a new drug.
- **Phase II trials** further test a new drug's safety and evaluate its efficacy.
- **Phase III trials** involve a larger number of participants and compare new drugs to current standard treatments. Participants are usually randomly assigned to the group receiving standard treatment or the group receiving the new treatment. Phase III cancer treatment trials do not include a placebo arm (unless there is no standard treatment for that particular cancer). Placebo arms may be included in chemoprevention trials studying drugs that might lower cancer risk in people who do not already have the disease.

BRCA Breast Cancer Trial

Dr. Tutt and Professor Alan Ashworth, in collaboration with the UK National Cancer Research Institute, have also set up an international study testing carboplatin, an established form of chemotherapy in BRCA-associated metastatic breast cancer. This chemotherapy drug also targets the DNA repair defect in BRCA cancers and may prove more effective and better tolerated than standard taxane-based chemotherapy. They hope US centers for women with advanced BRCA breast cancers will soon adopt this Phase II BRCA trial.

References

T Helleday. Curing hereditary breast cancer. Commentary published in *Project Syndicate*, May 2005.

H Farmer, N McCabe, CJ Lord, AN Tutt, DA Johnson, TB Richardson, M Santarosa, KJ Dillon, I Hickson, C Knights, NM Martin, SP Jackson, GC Smith, A Ashworth. Targeting the DNA repair defect in BRCA mutant cells as a therapeutic strategy. *Nature*, April 2005; vol. 434: p. 917-921.

N Turner, A Tutt, A Ashworth. Hallmarks of 'BRCAness' in sporadic cancers. *Nature Reviews Cancer*, October 2004; vol. 4: p. 814-819.

Targeted Therapy: Specific Treatments for Hereditary Cancer

by Kathy Steligo

One of the benefits of genetic research and determining an individual's genetic makeup is the potential for individualized cancer treatment. Hereditary cancers may differ from sporadic, or nonhereditary, cancers in several ways, including which genes are activated, how the cancer develops, and how it responds to treatment. However, no treatment protocols are specific to cancers in BRCA mutation carriers.

Standard cancer therapies often involve chemotherapy to slow the growth of cancerous cells or eradicate them. Chemotherapy is often effective but indiscriminate, damaging healthy cells along with cancerous cells, causing nausea, hair loss and other undesirable side effects. The ideal treatment eliminates cancer cells but spares unaffected cells. Developing such a "smart" drug requires a greater understanding of how cancer cells are unique from other cells and identifying their vulnerabilities.

Targeted therapy, specific treatments for certain cancers based on cellular genetic traits, attacks the unique weakness of cancer cells. This is a growing area of research involving medications that are often more effective with fewer toxic side effects. Herceptin, for example, is a successful targeted therapy for women with aggressive breast cancers that overexpress the Her2neu protein. It has limited use, however, for hereditary cancers associated with BRCA mutations which usually do not overexpress Her2neu. Now a breakthrough discovery in the United Kingdom may one day be just what the doctor ordered for women with BRCA1 and/or BRCA2 mutations: PARP inhibitors, targeted therapy using enzymes that appear to destroy hereditary breast cancer tumors without harming normal cells.

Healthy breast cells have two BRCA

genes, one from each parent. Normally, each cell is capable of correcting DNA damage and keeping cells from growing uncontrollably. This repair function is critical throughout a person's life, correcting accumulative cellular damage caused by aging, environmental factors, and certain hormones and viruses. Cells can function normally if one copy of the gene is damaged, as when a BRCA mutation occurs, because the second copy picks up the repair function. Irreparable damage to both copies of the gene, however, can be the first step in developing cancer, creating an environment for cells to grow uncontrollably and allowing tumors to form. For this reason, women who inherit BRCA mutations are at greater risk for developing breast and ovarian tumors.

PARP inhibitors work by selectively killing cells which have no functioning BRCA gene, preventing cells from

using their backup repair mechanism. Healthy cells which retain their DNA repair capability theoretically would remain unharmed. Preliminary experiments with mice have been encouraging, killing breast cancer cells that lack BRCA function and eliminating tumors. "If our laboratory findings are confirmed in the clinic, we could dramatically improve the treatment of patients with BRCA1 or 2-associated cancers," says Dr. Andrew Tutt, a key researcher.

If trials involving human tumors show similar results, PARP inhibitors may turn out to be significant weapons in the arsenal against cancer, particularly for those with BRCA mutations. The new drugs would likely be used for treatment with chemotherapy, not in place of it. If they successfully treat inherited breast tumors, one day they may also prevent hereditary cancers from developing. And although PARP inhibitors are being studied first on breast cancers, they may

"If our laboratory findings are confirmed in the clinic, we could dramatically improve the treatment of patients with BRCA1 or 2-associated cancers."

continued on page 8

An Introduction to Breast Reconstruction

by Kathy Steligo

If you're facing mastectomy, whether you've been diagnosed with breast cancer or you're acting prophylactically to reduce your risk, you have a decision to make: what will you do about your missing breasts? You may choose to do nothing. Perhaps you prefer to wear prosthetics. Surgical reconstruction offers a more permanent option. Although reconstruction can't replace lost sensation or restore the ability to breastfeed, it can restore a natural profile in and out of clothing.

Generally, reconstruction is completed in three stages over six to eight months. The initial surgery forms breast *mounds*, breasts without nipples. This first stage is the most complex and involves the most recovery. Depending on the procedure used, an additional shorter surgery refines the shape and size of your new breasts and creates nipples. Later tattooing simulates the areolas and completes the process.

For most women, reconstruction can be done anytime. Immediate reconstruction performed with mastectomy surgery is advantageous, however, because it produces minimal scarring and you're never without a breast. Delayed reconstruction, performed months or years after mastectomy, produces good results, but the mastectomy scar remains on the new breast. If your insurance company covers mastectomy, federal law requires that it also pay for reconstruction.

Implants. The least invasive procedure uses implants for shape and volume. Saline implants are quite firm, like a water balloon filled to capacity. Silicone models, although more controversial, have a texture and consistency more like breast tissue. Temporary implants called expanders are first placed under the chest muscles. Over several weeks they are gradually inflated with saline to stretch the skin and muscles. During a subsequent minor surgery, the expanders are replaced with implants. Some physicians use hybrid expander-implants: when fully expanded, they are sealed and remain in place,

eliminating the need for exchange surgery. A newer technique uses AlloDerm®, a processed skin product, to cover and hold the implant in place, eliminating the expansion process altogether.

Implants aren't permanent. Sooner or later they wear out and must be removed and/or replaced. This may occur sooner if the implant leaks or is distorted by hard scar tissue that forms around it. Some implants must be replaced within a year of reconstruction; others may last for 15 years or longer.

Tissue Flaps. Breasts can also be recreated with skin and fat from your back, buttocks, or abdomen (the latter option also provides a tummy tuck). More traditional tissue flap methods utilize the underlying muscle; newer sophisticated methods do not. Breasts made with your own tissue feel and move more naturally than those reconstructed with implants. However, tissue flap procedures are more complex and recovery is more intense—this involves surgery at the chest and the donor site—but the overall reconstruction timeline is shorter. Unlike implants, flaps form full-size breasts during the initial operation. Additional surgery later refines the breast shape and creates the nipples.

Flap reconstruction may be a good choice if your chest has been irradiated or if you want to avoid the lengthy implant expansion process. Implants may be a better solution if you want to avoid a longer recovery from flap surgery or don't want to scar another area of your body.

Four Reconstruction Planning Tips

1. Understand all your options.
2. Consult with several plastic surgeons.
3. Set realistic expectations.
4. Select a surgeon who is experienced with your preferred technique.

Editor Kathy Steligo is author of "The Breast Reconstruction Guidebook" (800-431-1579 or www.breastrecon.com)

The Language of Mastectomy

Learning about mastectomy can be confusing. Here's a quick guide to the different types of mastectomy and when they are used.

Unilateral mastectomy: removal of one breast.

Bilateral mastectomy: removal of both breasts.

Prophylactic mastectomy: removal of healthy breasts to reduce breast cancer risk.

Modified radical mastectomy: now the most commonly performed mastectomy, similar to a total mastectomy (see below), but also includes removal of some underarm lymph nodes. Usually performed when invasive cancer is diagnosed.

Radical mastectomy: once the only treatment for any breast cancer, this procedure removed breast tissue, lymph nodes, and skin, as well as the chest muscle. This procedure is now used only when cancer has spread to the chest muscle.

Total or simple mastectomy: removes breast tissue, nipple, areola, and some skin around the incision. No lymph nodes are removed. This procedure is appropriate for prophylactic mastectomy or when non-invasive cancer is found in more than one quadrant of the breast.

Skin-sparing mastectomy: removes the nipple and areola and most breast tissue, but the rest of the breast skin is left intact to accommodate immediate reconstruction.

Nipple-sparing mastectomy: a type of skin-sparing mastectomy that leaves a woman's natural nipples intact (if they are free of cancerous cells). This procedure leaves more tissue behind than a skin-sparing mastectomy. Most or all nipple sensation is usually lost.

Subcutaneous mastectomy: a type of nipple-sparing mastectomy performed through an incision under the breast. This procedure leaves more breast tissue behind than a nipple-sparing mastectomy.

Study for African-American Women with Breast Cancer

Researchers at the H. Lee Moffitt Cancer Center & Research Institute are conducting a study to determine how genetics may contribute to the higher rate of breast cancer among young African-American women. The study is accepting African-American women throughout the U.S. who were diagnosed with breast cancer before age 50. For additional information about participating in the study, please contact study coordinator Cheryl Miree at 813-745-1766.

Dr. Tuya Pal is a clinical geneticist and an Assistant Professor of Interdisciplinary Oncology at H. Lee Moffitt Cancer Center and Research Institute.

Dr. Susan Vadaparampil is a behavioral scientist and an Assistant Professor of Interdisciplinary Oncology at H. Lee Moffitt Cancer Center and Research Institute.

References

S N Sheinfeld Gorin, J E Heck. New York Physicians against Cancer. Delay in breast cancer diagnosis by race/ethnicity. Abstract #6004 from American Society of Clinical Oncology Annual Conference, May 2005.

K Armstrong, E Micco, A Carney, J Stopfer, M Putt. Racial differences in the use of BRCA1/2 testing among women with a family history of breast or ovarian cancer. *Journal of the American Medical Association*, April 2005; vol. 293, no. 14: 293:1729-1736.

Surviving Breast Cancer: African-American Women and the Importance Of Genetic Testing

by Tuya Pal, M.D. and Susan Vadaparampil, Ph.D.

African-American women in the United States who develop breast cancer are more likely to be diagnosed at younger ages and more likely to die from the disease when compared with Caucasian women.

Many factors may contribute to the higher death rate. According to the American Cancer Society, several studies document treatment differences between African-American women and Caucasian women. Alarming, more African-American women than white women experience a delay in treatment after an abnormal screening, according to data from the American Society of Clinical Oncology's annual meeting. The delay is documented in the largest and most systematic evaluation of disparities based on ethnicity and race, according to researcher Sherri N. Sheinfeld Gorin, Ph.D., of Columbia University Medical Center.

Scientists are exploring the relationship between younger age at diagnosis among African-American women and a variety of factors, including genetic predisposition. Although multiple genes are involved in breast cancer development, BRCA1 and BRCA2 gene mutations are believed to account for the majority of hereditary breast cancers. The likelihood of a mutation is higher when the disease is diagnosed at a younger age. Thus, some breast cancers in young African-American women may be due to a hereditary component.

There is a disparity in access to and use of general preventive healthcare services in the African-American community. The disparity is even greater in access to and use of newer technologies such as genetic testing for hereditary breast cancer risk. A much lower percentage of African Americans are aware of their personal risk of cancer and genetic testing options. Studies indicate African-American women are less familiar with genetic testing and how it might benefit them in making decisions about screening or treatment compared to Caucasian women.

Research led by Dr. Katrina Armstrong at the University of Pennsylvania found African-American women with a family history of cancer are less likely to seek information about genetic testing than Caucasian women. In fact, Caucasian women were almost five times more likely than African-American women to undergo genetic counseling to determine whether or not they should be tested. This difference remained even when women of similar socioeconomic and medical risk backgrounds were compared.

Factors not explored in the study include limited knowledge about genetic counseling and testing among both African-American women and the physicians who care for them. Worries within the African-American community about how genetic information is used may also pose a barrier for advancing knowledge. People may be concerned that their genetic test results will be used against them if they are found to carry one of the hereditary breast cancer gene mutations. Women need to understand that having one of these mutations may increase their risk for developing the disease, but it does not automatically mean they will develop breast cancer.

Because of lower rates of genetic testing among African-American women, it is uncertain whether genetic factors for breast cancer risk are common in the African-American community. This lack of information can complicate interpretation of genetic testing results. However, if more African-American women with certain risk factors were to participate in research involving genetic testing, the information could be used to develop new technologies to help detect and treat their cancers earlier, when chances of cure are more likely.

To increase awareness of inherited cancer syndromes, a strong need for nationwide education exists about the role of genetics in cancer. This is especially true among minority populations.

continued on page 7

Genetic Information Nondiscrimination Act (GINA): An Update

by Sue Friedman

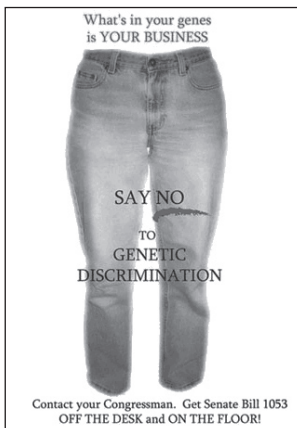
Genetics hold the promise for an era of unparalleled medical possibilities. Genetic testing, for example, can now identify people who carry hereditary mutations and who may be at high risk for diseases such as cancer. But for many people, genetic testing is a double-edged sword. While they may appreciate scientific advances that have created a blood test to determine whether they carry a BRCA mutation or not, many worry a positive test result may be used against them, jeopardizing their jobs or health insurance.

This fear of genetic discrimination may prevent people from talking to relatives or experts about their family history of disease; they may be afraid to undergo genetic testing or to notify health care professionals about their genetic status. Many refrain from participating in research studies, thereby slowing the development of potentially lifesaving treatments or risk-management options.

Although documented cases are rare, genetic discrimination is a common concern for those with a family history of disease. Most states have some laws relating to genetic discrimination, but the amount of protection they offer and how they define genetic information varies from one state to the next. The Health Insurance Portability and Accountability Act (HIPAA) protects people with group insurance from having their rates changed or their insurance dropped because of any preexisting condition. But HIPAA

has many loopholes; it simply isn't broad enough to protect everyone from genetic discrimination in health insurance.

In February, the Senate unanimously passed The Genetic Information Nondiscrimination Act (GINA) of 2005. The bill (S.306) proposes to prohibit discrimination in employment and health insurance based on an individual's genetic information. President Bush subsequently issued a supportive Statement of Administrative Policy. The corresponding House bill (H.R. 1227), however, is still working its way through



Thanks to Becky Fisher for the use of this image.

committee. Introduced in March by Congresswoman Judy Biggert (R-IL), this important legislation now has 126 co-sponsors. But there is still work to be done. Employment trade organizations, specifically the National Association of Manufacturers and the Chamber of Commerce, are actively opposing the bill.

FORCE is proud to be a member of the Coalition for Genetic Fairness (CGF), a partnership of advocates,

industry members, and health professionals who are working hard to increase support for this legislation. Help us move this critically important legislation forward. Voice your opinion to your elected representatives. Call or visit their local office. Together, our actions in support of this bill could move it from political football to actual law.

Surviving Breast Cancer *(continued)*

Ultimately, the benefits of increased participation in cancer genetics research and testing have great potential as genetics-based medicines will likely become available in the near future. However, these benefits will remain unrealized until

efforts increase to bridge racial disparities that contribute to unequal access and use of preventative medical services, which can then lead to reduce disparities in health outcomes.

Why Do We Care?

Genetic medical advances are being discovered with increasing regularity, but our laws aren't keeping pace. A common national framework must be provided; one that prohibits insurers and employers from requiring a person's genetic information or denying coverage or jobs because of that information. For more information about genetic information and discrimination view the brochure written by FORCE and the National Society of Genetic Counselors at www.facingourrisk.org/discrimination. You may order the brochures by calling FORCE at 866-288-7475 or e-mailing info@facingourrisk.org.

The Problems with HIPAA

HIPAA prohibits group insurance companies from denying, canceling, or charging different rates for individuals with preexisting conditions, but it doesn't adequately address genetic information:

- It does not protect people with individual insurance plans.
- It does not prevent insurance companies from requiring people to disclose whether they have had a genetic test, even if the companies are not allowed to use the information against them.
- It does not prevent an insurance company from denying coverage to or increasing rates of its entire group (even if the company cannot discriminate against an individual), based on the genetic test results of an insured person.
- It does not prevent employment discrimination based on a genetic test result.

Take Action

- Find contact information for the House of Representatives at www.house.gov.
- Learn more about the Coalition for Genetic Fairness at www.geneticfairness.org.
- Find more details about advocacy and how to become involved to get this important legislation passed. Visit the FORCE website at www.facingourrisk.org/advocacy.
- Visit The National Human Genome Research Institute's website at www.genome.gov/PolicyEthics/LegDatabase/pubsearch.cfm. Search the legal database to determine your state's laws on this issue.

Our Sponsors

FORCE proudly acknowledges contributions from our sponsors whose generosity make this newsletter possible.

Genome Level

Center for Restorative Breast Surgery
Lani Sinclair in memory of Sherry P.

Chromosome Level

Anonymous Donor
Myriad Genetic Laboratories

Gene Level

Ciphergen Biosystems, Inc.
Dana-Farber Cancer Institute
Friedman Family Trust

DNA Level

Evanston Northwestern Healthcare
The Center for Medical Genetics
Reflections Boutique

If you'd like to learn more about sponsoring FORCE, visit www.facingourrisk.org/sponsorship or call 866-288-RISK, extension 1.

We Want to Hear From You

What's on your mind? What would most help you understand or cope with issues of prevention, diagnosis or treatment? Perhaps you've recently tested positive for a BRCA gene mutation and don't know where to turn. Maybe you're dealing with breast or ovarian cancer, or care about someone who is. Send your input, ideas and comments to info@facingourrisk.org or mail to FORCE, 16057 Tampa Palms Blvd. W. #373, Tampa, FL 33647

FORCE: Facing Our Risk of Cancer Empowered
16057 Tampa Palms Blvd. W. #373
Tampa, FL 33647

Targeted Therapy *(continued)*

prove effective for treating other diseases associated with BRCA mutations, such as ovarian, pancreatic, and peritoneal cancers. Nor will these drugs be limited to mutation carriers. A percentage of sporadic cancers—about 20% of breast cancers and a portion of ovarian and pancreatic cancers—may have inactivated BRCA genes and behave like cancers associated with inherited BRCA mutations. These tumors may also respond to the selective action of PARP inhibitors.

At this point, the toxicity of these drugs is unknown. Nor is it understood whether BRCA mutation carriers may be particularly sensitive to any side effects. And while the earliest test results are promising, researchers suggest tempering enthusiasm with the realities of drug development: once human testing begins, it may take 10 years to bring the new drug to market.

What's New @ FORCE

6th Annual Chat-a-thon

This year's 'round the clock FORCE chat-a-thon is scheduled for October 21 and 22. This popular event increases awareness of hereditary breast and ovarian cancer and raises funds for FORCE. Stop by for a few minutes or stay for a few hours. Everyone is welcome.

Help us make our chat-a-thon a success:

- Log in to www.chat-a-thon.com to join the discussions.
- Become a sponsor (visit www.facingourrisk.org/helping.php#donations).
- Spread the word! "Chat" up the event to friends, family, and physicians.

Because they will not be available any time in the near future, PARP inhibitors are not an option for women presently making treatment decisions.

The first steps in the developmental timeline involving humans are Phase I studies; small trials of PARP inhibitors (consisting of 40 participants) are beginning in the United Kingdom to monitor the medication's safety and establish appropriate oral patient doses. If successful, larger clinical trials with BRCA patients will follow.

Under the best circumstances, funding trials of targeted therapies and finding qualified participants often requires organized, concerted efforts by patient advocacy groups. Meanwhile, we must continue to unite our community and advocate for our population.

Want to volunteer to staff the chatroom or have questions? Contact suefriedman@facingourrisk.org.

*Saturday, October 29 at 12:01 a.m. (EST) through
Sunday, October 30 at 11:59 pm (EST)*
2 days + 2 nights = 4 FORCE!

Save the Date: First Annual Joining FORCES Conference February 10-11, 2006

Our first FORCE conference on hereditary cancer and risk will be held in Tampa early next year. Visit our website or contact us at info@facingourrisk.org, or call 866-288-RISK for details.