

CGC UPDATE

FALL 2003
Patient Newsletter

NEWSLETTER OF THE CANCER GENETIC COUNSELING PROGRAM AT YALE

FALL 2003

Happy Autumn! Our program had a happy & productive summer that included training a graduate student in genetic counseling and producing a video for BRCA carriers making difficult choices. Both of these wonderful projects were sponsored by patient and foundation donations! Thank you to all who participated and best wishes.

Sincerely,

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Gynecological Surgery Decision-Making for BRCA1 and BRCA2 Carriers

Women who carry mutations in BRCA1 or BRCA2 have a high lifetime risk of developing ovarian and "ovarian-type" cancers. The lifetime risk for a mutation carrier to develop ovarian cancer ranges from 15-60%, depending on the population studied; however, even the lowest end of this range is much greater than the general population risk of 1-2%. Ovarian cancer is very difficult to detect at an early, treatable stage (even when using CA-125 and transvaginal ultrasounds). Therefore, it is recommended that women who carry BRCA mutations consider having their ovaries and fallopian tubes removed by the time they are forty and are done having children¹.

BRCA carriers are at risk for ovarian cancers, and cancers of the fallopian tube and peritoneum (a thin membrane that lines the abdominal cavity). Therefore, all BRCA carriers who opt for prophylactic surgery should have their ovaries AND fallopian tubes removed (bilateral salpingo-oophorectomy = BSO)². This surgery reduces the risk of ovarian and fallopian tube cancers in BRCA carriers by >90%. It also significantly reduces the *future risk* of breast cancer, particularly in young women who have the surgery before they go through menopause³⁻⁴.

There has been debate about whether BRCA carriers are also at risk for endometrial cancer, and should therefore be offered total abdominal hysterectomies (TAH-BSO) (removal of the uterus, cervix, ovaries, and fallopian tubes). There is a rare, aggressive form of uterine cancer called Uterine Serous Papillary Carcinoma (USPC) that closely resembles ovarian and peritoneal cancer under the microscope. It has been reported in a few women who have tested BRCA positive⁵; however, a study of Jewish women with endometrial cancer (including 17 cases of USPC) did not show an excess of BRCA mutations⁶.

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Gynecological Surgery Decision-Making for BRCA Carriers ***(continued from page 1)***

In a separate study of 56 non-Jewish women diagnosed with USPC, none (0/56) were found to carry a BRCA mutation⁷. If a relationship does exist between BRCA mutations and endometrial cancer, the risk for endometrial cancer appears to be low and is not significantly elevated over that of the general population⁸. Some have argued that removing the ovaries and fallopian tubes alone may leave at-risk stumps of fallopian tube that are still attached to the wall of the uterus. However, BSO has been shown to reduce the risk of ovarian and fallopian tube cancers by >90%. *It is therefore premature to offer total abdominal hysterectomy as the **only** prophylactic surgical choice for BRCA carriers.*

Ultimately, the patient must decide whether she wants BSO or TAH-BSO. Some important points to consider and discuss with your physician:

- Do you have any other indication for TAH (e.g. fibroids, endometriosis)?
- If you have your uterus removed and want to take hormone replacement therapy, you may be a candidate for estrogen alone (instead of combined with progestin). Estrogen alone may be associated with a lower risk of subsequent breast cancer than combined hormone replacement therapy.
- Tamoxifen is associated with a small, but increased risk of uterine cancer. If you have your uterus removed, this risk will be eliminated if you ever need to take tamoxifen.
- BSO is a smaller surgery than TAH-BSO. It is usually done laparoscopically and is an outpatient procedure. TAH-BSO generally requires hospitalization and is associated with a longer recovery time than BSO. TAH-BSO is also associated with more complications. Please speak to your physician about the risks/benefits of each procedure.
- Studies have shown that BSO, alone, significantly reduces the risk of ovarian and breast cancer in BRCA carriers.

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| 1. Rebbeck TR J Clin Oncol 2000; 18(21):100s-3s. | 5. Hornreich G et al. Gyn Oncol 1999;75:300-4. |
| 2. Aziz S et al. Gyn Oncol 2001; 80:341-5. | 6. Levine DA et al. Gyn Oncol 2001;80:395-8. |
| 3. Rebbeck TR. et al. N Engl J Med; 346(21):1616-22. | 7. Goshen R. et al. Gyn Oncol 2000;79: 477-81. |
| 4. Kauff ND et al. N Engl J Med; 346(21):1609-15. | 8. Boyd J. Gyn Oncol 2001; 80:337-40. |

Yale Cancer Genetic Counseling Clinics

Yale

Mondays at 55 Church Street, Suite 800B (203) 764-8400

Greenwich, CT

Once a month at the Bendheim Cancer Center, Greenwich Hospital (203) 764-8400

Norwalk, CT

Once a month at the Whittingham Cancer Center, Norwalk Hospital (203) 852-2148

Danbury, CT

Once a month at the Praxair Cancer Center, Danbury Hospital (203) 764-8400

Research Updates

Multiple Colorectal Polyps and Mutations in the MYH gene

NEJM 2003; 348(9): 791-799.

This study tested patients with multiple adenomatous colon polyps (3-100) or classic familial adenomatous polyposis (FAP) (a hereditary cancer syndrome in which patients develop >100 adenomatous colon polyps) for mutations in a newly discovered gene called MYH. All patients with FAP had previously tested negative for mutations in the APC gene (which typically causes FAP). This study found that overall ~1/3 of patients with 15 or more adenomatous colon polyps had mutations in both copies of the MYH gene. This means that mutations in the MYH gene are inherited in a recessive pattern (i.e. individuals need to carry mutations in both copies of the gene in order to be at risk for the disease). The researchers conclude that MYH gene testing may be considered in patients with 15 or more adenomatous colon polyps. *However, clinical testing is not currently available in the U.S. and we have limited data on the clinical care of patients with MYH gene mutations.* Stay tuned for more information...

MRI screening for breast cancer in high-risk women

Proceedings of the American Society of Clinical Oncology May 2003, abstracts 4, 5, 362.

These 3 studies examine the usefulness of MRI as a screening tool for breast cancer among BRCA carriers and/or women at high risk to carry a BRCA mutation. All of them found that MRI is very sensitive¹ (sensitivity ranged from 71-100%) and both studies comparing MRI to other screening methods (mammograms, clinical breast exams, and ultrasound) found that MRI detected more breast cancers than the other methods. However, the specificity² of MRI was more variable. MRI was more specific than mammograms in one study but less specific than mammograms in another study. Overall, these studies agree that MRI is an appropriate screening tool for women at high risk. However, two of the studies caution that MRI may result in a significant number of false positive test results and unnecessary biopsies.

¹Sensitivity - the rate at which the test result is positive when the disease is present. In this case, if a test has a higher sensitivity, then more breast cancers will be detected by that screening test.

²Specificity - the rate at which the test result is negative when the disease is not present. A higher specificity means a lower rate of false positive results whereas a lower specificity means a higher rate of false positive results.

Familial Pancreatic Cancer and BRCA2

JNCI 2003; 95(3): 214-221.

Cancer Research 2002; 62: 3789-3793.

These studies found that a significant proportion (12-18%) of families with familial pancreatic cancer (families where 2-3 or more close relatives - i.e. parent and child or 2 or more brothers and/or sisters - have had pancreatic cancer) carried a BRCA2 mutation. None of the families with identifiable BRCA2 mutations in these studies had a history that was classic for hereditary breast-ovarian cancer. Both studies conclude that BRCA2 testing should be considered in families with familial pancreatic cancer.

Resources

On the web:

www.cancerquest.org

This website produced by the Emory University Department of Biology provides a thorough overview of cancer biology including normal cell biology and changes in the cell that lead to cancer. Detailed information about cancer diagnosis and treatment, new areas of research, and clinical trials is also included. Although all technical terms are defined in a glossary and excellent illustrations accompany the text, some readers may find the text difficult to understand due to the level of detail and the use of technical terms.

www.cdc.gov/DES

Diethylstilbestrol (DES) is a medication that was prescribed to pregnant women from 1938-1971, primarily to prevent miscarriages. This website from the Centers for Disease Control and Prevention (CDC) provides current information representing over 30 years of research on the health risks associated with DES exposure. It has separate sections for women who took DES during pregnancy and for men and women who were exposed to DES before birth (in the womb).

From the bookshelf:

Show Me: A Photo Collection of Breast Cancer Survivors' Lumpectomies, Mastectomies, Breast Reconstructions, and Thoughts on Body Image- Second Edition

Penn State Milton S. Hershey Medical Center, 2001

As the title suggests, this book features 30 breast cancer survivors' experiences with surgical treatment and reconstruction. It includes color photographs of the results of various surgical and reconstruction options and comments from patients and their partners about their experiences. The book is available from their website (www.hmc.psu.edu/womens/showme/index.htm) for \$25 (including shipping and handling). The website also includes sample stories of 7 of the patients featured in the book.

Straight Talk About Breast Cancer: From Diagnosis to Recovery, A Guide for the Entire Family

Suzanne W. Braddock, MD et al

Addicus Books, Inc., 1994

This book is broken up into chapters that take the reader through every stage of breast cancer: from diagnosis to treatment, surgery, and reconstruction. This is a detailed educational resource packed with information but it also offers helpful questions for patients to ask their physicians for more information about their *personal* situation. Alongside the text are comments from other women about their personal experiences with breast cancer. The text was published in 1994, and while much of it is still current, please keep in mind that we are more knowledgeable about breast cancer now than we were when this book was published.

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Upcoming Events

Fall 2003

October 8 and November 12

6pm

Understanding Cancer Lecture Series

Yale New Haven Hospital East Pavilion Cafeteria

This is a free lecture series for patients and their families.

Please call 1-877-YALEMDS for reservations or more information.

November 2, 2003

Y-Me Breast Cancer Symposium

Yale Medical School

For more information about this annual, day-long event, please call 203-483-8200.

Resources (continued from page 4)

In Mommy's Garden: A Book to Help Explain Cancer to Young Children

Neyal J. Ammary and illustrated by Christopher Risch

Canyon Beach Visual Communications, 2003

This is a 31-page colorfully illustrated book designed to help young children (ages 3-7) understand cancer and its treatment. In this story, the mother explains to her young daughter that her cancer "is like the weeds that grow in our flower garden." The book expands on this simple concept to explain cancer treatments and their side effects. The characters are illustrated without facial features and with a neutral skin color (light brown) to give a multiethnic appearance. Although the book is simple enough for most young children to understand, some parents may wish to alter the word choice to reflect their own family values and their child's level of understanding. This book is available for \$17.45 (\$14.95 + \$2.50 shipping and handling). To order, please contact Neyal Ammary at InMommysGarden@yahoo.com.

Your Contribution to Research...

The field of cancer genetics is a young one, and recent genetic discoveries over the past 8-10 years have made clinical genetic testing a reality for several types of cancer. However, because the field is so new, we are lacking long-term data in many areas (the effect of prophylactic surgery or chemopreventive drugs on carriers of cancer susceptibility genes, the percentage of carriers who develop cancer by a certain age, etc.). In order to contribute to research in these areas while also protecting your confidentiality, we have created the Coded Information Sharing protocol. This protocol allows us to share unidentified patient data (pedigree data, clinical data, pathology information) with researchers *without* the patient identifying information (names, dates of birth, addresses, unit numbers) that may compromise confidentiality.

Also, if you qualify for a research trial, our program may contact you to let you know about the trial. We will not give your confidential patient identifying information to any researchers without your written permission. In these ways, we aim to contribute to research while protecting your confidentiality.

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