The Ribbon

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Hereditary Breast Cancer: Current Information, Services Available, and Related Research

The questions of inherited predispositions to breast cancer are intimately related to the questions of breast cancer and environmental risk factors. As the National Action Plan on Breast Cancer and the American Society of Clinical Oncology pointed out in their joint 1997 report, "multiple genetic and environmental factors likely influence the extent to which a risk factor for breast cancer plays a role in any one individual." Despite tremendous increases in knowledge in the past several years about specific genetic mutations, we are at the beginning stages of understanding genetic/environment interactions. Nevertheless, for an individual woman today, the recent advances in identification of genetic mutations and the accompanying available testing present new options and new dilemmas.

In this issue of ***The Ribbon****, we feature four complementary articles:*

- *a background article on hereditary breast and ovarian cancer*
- *an article which outlines New York State's uniquely far-reaching cancer genetic services*
- *an overview of a genetic and epidemiologic research study which is making an important start in examining the differences in environmental risk factors between women with and without certain genetic predispositions, and women with these inherited predispositions who do not develop cancer*
- *a Research Commentary providing an overview of genetically-influenced increased susceptibility to ionizing radiation, a risk factor for breast cancer*

What Do We Know About Hereditary Breast Cancer?

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Q. ***How common is hereditary breast and ovarian cancer?***

A. In 1999, more than 180,000 women will be diagnosed with breast cancer and about 27,000 women will be diagnosed with ovarian cancer in the US. Approximately 44,000 women will die due to breast cancer, while 13,500 will die due to ovarian cancer. An estimated five to ten percent of these breast and ovarian cancers are thought to be hereditary or due to an inherited predisposition. A woman with an inherited predisposition has an increased risk to develop both diseases. It is important to remember that most breast and ovarian cancers are *not* hereditary.

Q. How is a predisposition to develop breast and ovarian cancer inherited?

A. Each cell in our body has twenty-three pairs of chromosomes, for a total of forty-six. One chromosome from each pair comes from our mother and the other comes

from our father. Each chromosome is composed of thousands of genes. Our genes carry the instructions for our growth and development and can determine such physical traits as hair, eye, and skin color. They can also determine whether or not we are predisposed to develop cancer. In 1994, the first major breast and ovarian cancer predisposition gene, BRCA1 or "Breast Cancer 1", was isolated on chromosome 17. A year later, the second major breast and ovarian cancer predisposition gene, BRCA2 or "Breast Cancer 2", was isolated on chromosome 13. In their functional form, both genes are thought to act as brakes on cell growth and are called *tumor suppressor genes*. An inherited change or mutation in either gene can cause the brakes to fail allowing cells to grow in an uncontrolled manner. This uncontrolled cell growth can lead to the development of cancer. Therefore, a woman with an inherited mutation in either BRCA1 or BRCA2 will be more likely to develop breast and/or ovarian cancer. It is important to remember that not every woman with an inherited mutation in either BRCA1 or BRCA2 will develop breast and/or ovarian cancer.

Q. What is the risk of inheriting a mutation in BRCA1 or BRCA2?

A. A mutation in either BRCA1 or BRCA2 is inherited in an autosomal dominant fashion. This means that an individual needs to inherit only one copy of either gene with a mutation to be predisposed to develop cancer. Each child of a BRCA1 or BRCA2 mutation carrier would have a 50%, or one in two, chance of inheriting the mutated gene and a predisposition to develop cancer. Alternatively, each child of a BRCA1 or BRCA2 mutation carrier would have a 50%, or one in two, chance of inheriting the functional or non-mutated gene. It is important to remember that both men and women can inherit and pass on mutations in BRCA1 and BRCA2.

Q. How significant is a family history of breast and/or ovarian cancer in predicting the presence of a mutation in either BRCA1 or BRCA2?

A. Although some individuals found to have a mutation in either BRCA1 or BRCA2 do not have a family history of breast and/or ovarian cancer, most do. About half of families with hereditary breast cancer have mutations in BRCA1, while most of the remaining families have mutations in BRCA2. Most families with histories of hereditary breast and ovarian cancer have mutations in BRCA1, while a smaller, undefined percentage have mutations in BRCA2. An undefined percentage of hereditary breast and/or ovarian cancer families may have mutations in as yet unidentified cancer predisposition genes. Families with mutations in BRCA1 or BRCA2 can have many women from several generations with breast cancer, as well as women with ovarian cancer. Some women may develop both breast and ovarian cancer. Cancers of the colon and prostate have also been seen in families with BRCA1 mutations, while male breast cancer, melanoma, and cancers of the gallbladder, prostate, pancreas, and stomach have been seen in families with BRCA2 mutations.

Clues which increase the likelihood that a cancer-susceptibility mutation is present in a family include:

- A positive family history of breast and/or ovarian cancer (in three or more first- or second-degree relatives on the same side of the family);
- Early age of onset (especially before age 45) of breast cancer in the patient or any close (first- and/or second-degree) relative;
- A patient or family member with ovarian cancer (at any age) in addition to one or more family members with breast cancer (at any age);
- Bilateral or multifocal breast disease or multiple primary tumors (at least one involving the breast) in the patient or family member;
- Breast cancer in a male patient or a male family member; and
- Ashkenazi Jewish descent with a family history of one or more cases of breast or ovarian cancer at any age.

Taken from the "Genetic Susceptibility to Breast and Ovarian Cancer: Assessment, Counseling and Testing Guidelines", American College of Medical Genetics Foundation with Support from the New York State Department of Health, 1999**.**

Q. What should Jewish women know about BRCA1 and BRCA2?

A. Several hundred different mutations have been identified in both BRCA1 and BRCA2. Recent studies have shown that two mutations in BRCA1 (called *185delAG* and *5382insC*) and one mutation in BRCA2 (called *6174delT*) are more common in individuals of Ashkenazi (Eastern or Central European) Jewish ancestry. Scientists estimate that these three mutations account for most of the inherited predisposition to breast and ovarian cancer seen in the Ashkenazi Jewish population. Additionally, these mutations were found in 1/40, or 2.5%, of Ashkenazi Jews unselected for family history. This is far greater than the estimated frequency of all mutations in BRCA1 and BRCA2 in the general population. This phenomenon can most likely be explained by the presence of these mutations in one or many founders of the Ashkenazi Jewish population several generations ago and is referred to as *founder effect*. For example, the 185delAG mutation in BRCA1 is thought to have occurred about 40 to 50 generations ago and is

estimated to be 1500 to 2000 years old. Other ethnic groups also have mutations in BRCA1 and BRCA2 that are more common in their respective populations due to this same phenomenon.

Q. What is cancer genetic counseling?

A. Genetic counseling is an essential component of cancer risk assessment and the genetic testing process and involves:

- A review of medical records
- A detailed discussion of an individual's medical and family histories
- A brief introduction to genetics and cancer
- An assessment of an individual's risk(s) to develop cancer
- An assessment of an individual's risk to carry a mutation in a cancer predisposition gene
- A discussion of the risks, benefits, and limitations of genetic testing
- Recommendations for cancer screening

In order to discuss this information in detail and facilitate an informed decision about genetic testing, a typical cancer genetic counseling session can last up to two hours and additional sessions are sometimes necessary.

Q. Describe the genetic testing process for BRCA1 and BRCA2.

A. Mutations in BRCA1 and BRCA2 can be detected by obtaining a blood sample. Sometimes stored tissue samples can be used. This analysis can take several weeks to complete and cost up to $2400. Any individual of Ashkenazi Jewish ancestry who decides to undergo genetic testing for mutations in BRCA1 or BRCA2 is initially tested for the three common mutations described above. This test generally costs about $400 to $500 and the results are usually ready within three to five weeks. Many medical insurers are now covering the cost of genetic testing for BRCA1 and BRCA2 for men and women at increased risk to carry a mutation in either gene. Several research studies throughout the United States also offer genetic testing for BRCA1 and BRCA2 for no fee.

Q. If an individual is found to have a mutation in BRCA1 or BRCA2, how does this impact his or her risk to develop cancer?

A. The average woman has an estimated lifetime breast cancer risk of 10 to 12% and an estimated lifetime ovarian cancer risk of 1 to 2%. A woman who inherits a mutation in BRCA1 has an estimated lifetime breast cancer risk of up to 85% and an estimated lifetime ovarian cancer risk of up to 60%. A woman found to have a mutation in BRCA1 who already has breast cancer now has an increased risk to develop cancer in her other breast. BRCA1 mutations may also be associated with an increased risk for prostate cancer in men and colon cancer in men and women. A woman who inherits a mutation in BRCA2 also has an estimated lifetime breast cancer risk of up to 85% and an estimated lifetime ovarian cancer risk between 15 and 30%. A woman found to have a mutation in BRCA2 who already has breast cancer may also have an increased risk to develop cancer in her other breast. BRCA2 mutations are also associated with an increased risk for breast cancer in men. *It is important to remember that the cancer risks associated with inherited mutations in BRCA1 and BRCA2 are still being studied and recent data has shown that the risks for breast and ovarian cancer may be overestimated in some families.*

Q. If a woman is found to have a mutation in BRCA1 or BRCA2, what are her options?

A. Such a woman is advised to participate in a breast cancer screening program that involves monthly breast self-examination, more frequent physical breast examinations by her gynecologist and/or breast surgeon, as well as mammography. Ovarian cancer screening is also recommended and involves a pelvic examination, a specific blood test called CA-125, and a transvaginal ultrasound examination. Prophylactic mastectomy and oophorectomy are also options considered by some women. However, the extent of breast and ovarian cancer risk reduction after prophylactic surgery is not yet fully known. Colon cancer screening is also recommended and involves digital rectal examination, fecal occult blood testing, and sigmoidoscopy and/or colonoscopy. Currently, researchers are also studying chemopreventive agents like *tamoxifen, raloxifene*, and oral contraceptives and their effectiveness in reducing breast and ovarian cancer risk both in women in the general population and in women with mutations in BRCA1 and BRCA2.

Q. If a man is found to have a mutation in BRCA1 or BRCA2, what are his options?

A man found to have a mutation in BRCA1 or BRCA2 is advised to undergo colon cancer screening as described above. Prostate cancer screening is recommended for men found to have mutations in BRCA1 and involves digital rectal examination and a specific blood test called PSA (prostatic specific antigen).

Q. Will I face discrimination by my employer or health and life insurer if I undergo genetic testing?

A. Many individuals considering genetic counseling and genetic testing for BRCA1 and BRCA2 ask this question. Federal legislation in the form of *The Health Insurance Portability and Accountability Act of 1996* or HIPAA and legislation in many states address the issue of genetic discrimination by group health insurers. However, discrimination by employers and life insurers is not addressed by HIPAA and different states have different laws addressing these issues. For more information, contact your state government or a health professional in your area providing genetic counseling and genetic testing.

Q. How can I learn more about genetic counseling and genetic testing for BRCA1 and BRCA2?

A. Genetic counseling and genetic testing for BRCA1 and BRCA2 is available at several centers throughout the US and New York. To find a genetic counselor or other health professional in your area with an expertise in cancer genetics, contact the National Cancer Institute at 1-800-4-CANCER or visit the National Society of Genetic Counselors' Resource Link at http://www.nsgc.org/Resource_link.html

Cancer Genetics Services in NYS

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The Genetics Education and Information Program is located within the Bureau of Chronic Disease Services at NYS Department of Health. This article will focus on our activities relating to cancer genetics. Other cancer services programs within the Bureau are the Breast and Cervical Cancer Screening and Early Detection Program, the Colorectal Cancer Screening Program, the Prostate Cancer Education Initiative, and the Ovarian Cancer Information Program. The Genetics Program aims to educate NYS clinical and public health providers about genetic risk assessment, counseling and testing for a variety of cancers and to improve coordination and collaboration among genetic counselors and other professionals providing these services. Availability of DNA testing for BRCA1 and BRCA2 and media attention to the Human Genome Project have led to significant public interest in this rapidly evolving area. However, a small number of studies and significant anecdotal evidence indicate that providers are not yet sufficiently knowledgeable in this area.

Clinical Genetics Guideline

Supported by a grant from the NYS Department of Health, the American College of Medical Genetics convened a multidisciplinary group to develop and disseminate a document entitled *"Genetic Susceptibility to Breast and Ovarian Cancer – Assessment, Counseling and Testing Guidelines"*. The teams were made up of representatives of professional societies, such as the American College of Surgeons, the National Society of Genetic Counselors, the American College of Radiology and the Medical Society of the State of New York, as well as advocacy groups such as the National Association of Breast Cancer Organizations. The guidelines provide background information, an algorithm outlining a recommended protocol, a sample family history questionnaire, an extensive justification section, and complete references. They present a balanced view of the benefits vs. burdens of genetic testing. The document suggests that a brief three generation family history should be drawn up for every patient seen by a primary care provider or non-genetics specialist so that those who would benefit from further risk assessment and discussion can be identified. The document describes the extensive genetic counseling required prior to genetic testing, but does not stipulate which patients should be referred to a genetic counselor or other specialist. The primary care provider may choose to handle certain cases or certain aspects of each case.

According to the Guidelines indications for consideration of genetic testing include:

- *Three close relatives on the same side of the family with breast or ovarian cancer*
- *Having a family member with an identified mutation*
- *Age of onset < 45 in the patient or close relative*
- *One or more cases of ovarian cancer at any age and one or more cases of breast cancer at any age*
- *Multiple primary or bilateral breast cancer*
- *Breast cancer in a male relative*
- *Ashkenazi Jewish descent and family history of breast or ovarian cancer at any age*

The Guidelines are now posted on the Department of Health website at www.health.state.ny.us – click on "information for providers"; "clinical guidelines". You can order a copy of the Executive Summary by contacting Skye Brown at (518) 486-2215.

Genetic Counseling Services

In NYS, we are fortunate to have many genetic counselors, distributed around the state, whose entire practice is focused

on cancer genetics. Genetic counseling is a communication process which deals with the human problems associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family. The process of genetic counseling involves an attempt by one or more appropriately trained individuals to help the affected individual or family to:

- Comprehend the medical facts, including the diagnosis, probable cause of the disorder, and the available management;
- Appreciate the way heredity contributes to the disorders, and the risk of recurrence in specified relatives;
- Understand the alternatives for dealing with the risk of recurrence;
- Choose the course of action which seems to be appropriate in view of their risk, their family goals, and their ethical and religious standards, and to act in accordance with that decision; and
- Make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder.

-- American Society of Human Genetics, 1975.

Genetic counselors working in the area of cancer review the family and personal medical history, facilitate collection and interpretation of medical records to confirm specific cancer diagnoses in relatives, provide comprehensive risk assessment, and discuss available options, including genetic testing, specific surveillance strategies, medical and/or surgical prophlaxis, etc. NYS genetic counselors specializing in cancer genetics work in the following institutions:

Albany Medical Center
Albert Einstein College of Medicine
Beth Israel Medical Center
Binghamton Genetic Counseling Program
Central Suffolk Hospital
Columbia-Presbyterian Medical Center
Long Island Jewish Medical Center
Memorial Sloan-Kettering Cancer Center
Mt. Sinai Medical Center
New York Breast Cancer Study at Sarah Lawrence College
New York University School of Medicine
North Shore University Hospital
Roswell Park Cancer Institute
St. Luke's – Roosevelt Hospital Center
Staten Island University Hospital
Strang Cancer Prevention Center
SUNY Health Science Center at Syracuse
University of Rochester Medical Center
Winthrop University Hospital

Most clinical geneticists and genetic counselors in the state see patients who are uninsured or underinsured. Fees are based on a zero-based sliding fee scale. No NYS resident should forego genetic counseling because of an inability to pay. Specific contact information is available from the Cancer Information Service at 1-800-4CANCER or call the Bureau of Chronic Disease Services at (518) 474-1222.

NYS Cancer Genetics E-mail List

To improve coordination and collaboration among those providing cancer genetic services in NYS and those interested in learning more about these issues, we initiated an e-mail list in February 1999. We are currently sending approximately five – ten messages per week to more than 125 geneticists, genetic counselors, public health administrators, Healthy Women Partnership technical advisors, members of NYS Cancer Advisory Groups, advocates, etc. The list keeps participants informed about relevant scientific articles, research projects, new clinical initiatives, and educational programs. Our goal is to expand the list to include more non-geneticists, and to encourage participants to keep each other informed through this means. To join our list, contact us at (518) 474-1222, or send an e-mail message to KXG03@health.state.ny.us.

Other Educational Activities

Genetics Education and Information Program staff and cancer genetic counselors in the state are available to lecture on this topic to your class or group. The Bureau has organized workshops on cancer genetics at the Division's Annual Meetings and presented to various Healthy Women Partnerships around the state. Since our program is unique in the US, we have also been asked to speak at many national meetings about incorporating genetics into chronic disease/adult health programs.

What's Next?

We are in the process of setting up a Genetics Working Group to help us to organize genetics services and strengthen ties with the various chronic disease programs. The Working Group will spearhead the development of a strategic plan which will guide our efforts and perhaps serve as a model for similar activities in other states. We specifically would like to increase our program's visibility and improve collaboration between genetics clinicians and the Healthy Women Partnerships. This will be accomplished through increased educational opportunities and piloting of a genetics risk-scoring tool in one of our partnership sites.

Report on the New York Breast Cancer Study

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Women who inherit specific mutations in the BRCA1 and BRCA2 genes are predisposed in their lifetimes to develop breast and ovarian cancer, as well as other possible cancers. Some women with inherited mutations, however, do not develop any cancer. And for women with cancer, age at onset, disease progression and lifestyle factors vary widely, even in the same family.

The goal of the New York Breast Cancer Study is to help answer such questions surrounding inherited breast and ovarian cancer. This genetic and epidemiological project is designed and directed by two leaders in cancer genetics and genetic counseling: Mary-Claire King, PhD, American Cancer Society Professor and Laboratory Director in the Division of Medical Genetics at the University of Washington in Seattle, and Joan H. Marks, MS, Creator and Director Emerita of the Health Advocacy and the Human Genetics Masters Programs at Sarah Lawrence College in Bronxville, New York.

King and Marks united in the mid-1990s soon after the isolation of the BRCA1 and BRCA2 genes and at the rise of genetic counseling as a recognized service in cancer care. King and Marks amassed a team of medical specialists in the metropolitan New-York area and in 1996 began searching for the three most common BRCA1 and BRCA2 mutations in Jewish women and families with breast cancer and evaluating the lifestyle and social factors which may impact cancer development.

Today, the study has enrolled over 800 participants and has expanded to include 13 medical centers: Albert Einstein College of Medicine, Beth Israel Medical Center, Columbia Presbyterian Medical Center, Memorial Sloan-Kettering Cancer Center, New York University Medical Center and Strang Cancer Prevention Center in New York City; North Shore University Hospital on Long Island; White Plains Hospitals Center in White Plains, New York; Stamford Hospital/Bennett Center in Stamford, Connecticut; Hackensack University Medical Center in Hackensack, New Jersey; and three private oncology/radiology practices in New York City.

Integrating molecular genetics, genetic counseling and epidemiology, the investigators seek to identify genetic and environmental factors important in the control of breast or ovarian cancer and to apply what is learned from Jewish families in New York to the general population of individuals confronting the reality of breast and ovarian cancer in their lives.

The Genetic Mission

A primary goal of the New York Breast Cancer Study is to determine the actual (empiric) risk of breast cancer, ovarian cancer, or both, by age, among women who carry one of the three founder BRCA1 or BRCA2 mutations in the Jewish population. These mutations are 185delAG and 5382insC in the BRCA1 gene, and 6174delT in the BRCA2 gene.

To date, 650 women have joined the study, with more enrolling every day. Each collaborating medical center identifies eligible women from their patient population and invites them to participate. Eligible women must be Jewish, diagnosed with invasive breast cancer between 1994 and the present, and living in the New York area. Women do not need a family history of cancer to participate, limiting the bias of family history in the assessment of BRCA gene mutations.

Enrollment procedures are carefully designed. Women are first offered genetic counseling to assess their family and lifestyle histories and to review the benefits and limitations of genetic testing. Participants may either receive their test results or enroll anonymously and may withdraw at any time. Participation is free of charge, and test results are protected by a Certificate of Confidentiality from the National Institutes of Health.

Each participant signs an informed consent and provides a blood sample for genetic testing. Genotyping for the three founder BRCA mutations is carried out at the University of Washington. Results are returned through a post-test consultation with the genetic counselor and medical team at the participant's hospital, ensuring that each woman understands the implications of her results and receive appropriate medical follow-up.

Epidemiological Aims

Epidemiological goals of the study include identifying the differences in environmental risk factors between women with and without BRCA gene mutations who develop breast and/or ovarian cancer and women with mutations who remain cancer free. These comparisons may uncover environmental influences on breast/ovarian cancer that are preventable and thus may imply new routes towards fighting these diseases.

Toward these aims, all participants are asked to complete a specially designed questionnaire on their breast and ovarian health history, hormonal and reproductive history, social history, diet, exercise, smoking and alcohol use, and radiation, pesticide and related chemical exposures. For

anonymous participants, questionnaires and blood samples are numbered so that test results can still be linked to environmental risk factors for epidemiological analysis.

Family Testing

When a participant is found to carry a BRCA mutation, the next phase of the study involves genetic counseling and testing for this family, with the goal of better understanding the inheritance and penetrance of these gene mutations and identifying other types of cancers that may be associated.

The first step is determining which side of the family the mutation originated and then inviting into the study those relatives who may be carriers. Relatives are contacted by a genetic counselor with the help of the original study participant, and may enroll no matter where they live or whether or not they have had cancer. Genetic counseling and blood sampling are coordinated in each relative's local area. Relatives complete the study questionnaire and may receive their test results or participate anonymously. Several hundred relatives have now enrolled in the study from across the United States and Canada, Israel, France, Sweden and England.

Longer Term Goals

Long term goals of the project include examining whether other mutations in the BRCA genes, or other genes all together, can explain the cancer histories in families that do not to carry a common BRCA mutation.

Another goal is to assess the impact of genetic counseling in the cancer predisposition testing process via a questionnaire on patients' perceptions of this experience and the influence of genetic test results on future cancer care choices.

Current graduate students of the Human Genetics Program at Sarah Lawrence College also serve as research assistants, gaining necessary training in cancer counseling as well as in developing and managing clinical genetics research.

Maintaining sensitivity to the needs of participants remains a consistent focus. An Advisory Board of cancer patients and professionals provides oversight to the study, in particular to issues of patient's rights.

Over the next year, the study will continue collecting invaluable research data for the medical community while at the same time benefiting women and families with cancer. With its carefully designed objectives, the inclusion of relatives in the project, and the comprehensive counseling and testing services offered to each individual, the New York Breast Cancer Study remains unique to research of its kind.

As Research Coordinator for the New York Breast Cancer Study, Jessica oversees the activities at all collaborating centers, counsels patients, and is the primary coordinator of family enrollment. Jessica also organizes the data on each participant and extracts DNA from all blood samples for genetic testing. For more information on inherited breast cancer or the New York Breast Cancer Study, please contact Jessica Mandell at (914) 395-2239.

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Genetically-Influenced Susceptibility to Ionizing Radiation

Think about recommending routine screening for a large number of healthy people for early detection of some dreaded disease like breast cancer. What criteria would you consider appropriate for this recommendation? You would surely want the screening to be effective at saving lives, reasonably accurate (i.e. not miss real cancers and minimize false positives), and reasonably safe. This article is about general population screening of healthy women by annual mammograms; it is not relevant to those with personal or strong family histories of cancer or to patients who have detected a lump or other abnormality.

Is general population screening by mammography effective at saving lives?

- Eight large scale randomized controlled studies have shown that such screening for women over 50 can reduce breast cancer deaths in this population by 25 to 30% within five to six years.
- It is widely agreed that there is no benefit for screening women under 40.
- There is great controversy about such screening for women between 40 and 49. Premenopausal women have much lower risk of breast cancer and they have denser breasts, which make it harder to interpret their mammograms. With one exception, controlled trials have shown that the rate of death from breast cancer was the same in the screened group as in the control group for seven to nine years following initiation of screening.

Is general population screening by mammography reasonably accurate?

- 80% to 90% of women with known breast cancer show positive results on mammograms. This means that 10 to 20% of breast cancers go undetected by mammograms.
- About one in five to one in ten biopsies done on the basis of suspicious mammograms reveal cancer. This means that 80% to 90% of biopsies are done on women who do not have breast cancer.

What are the risks of mammographic screening?

One of the harmful consequences of routine mammograms relates to the high rate of false positives. Since 80%-90% of biopsies are done on women who do not have breast cancer, thousands of healthy women have biopsies and some of them have medical complications. The other major harmful consequence, DNA damage, is the focus of the rest of this article.

The X-rays used to make mammographic images also cause some small amount of damage to your DNA. Most people have wonderful repair systems that are capable of repairing the damaged DNA. Moreover most cells have a surveillance system that prevents a cell from copying its DNA if it is damaged. However, a small percentage of the population have inherited deficiencies in their repair systems and/or their surveillance systems. For these individuals the unrepaired damage increases their risk of cancer of all types.

An example of an inherited defect in DNA repair

Ataxia telangiectasia (AT) is a rare genetic disease characterized by neuromuscular degeneration, immune system dysfunction, and a 100 times greater risk of cancer than the general background rate. The elevated cancer risk results from an extreme sensitivity of AT patients to X-rays and the fact that they continue making new DNA even when their DNA is damaged.

To inherit AT disease you must inherit a bad copy of the gene from both your parents. If you inherit just one bad copy of the gene, you are a carrier. Although individuals having the full blown AT disease are rare, about 1% of the population are carriers. It is significant that AT carriers are sensitive to radiation—not as sensitive as those of AT patients but more so than most people. Their cells are more damaged by radiation than non-AT cells and the repair system in their cells is three times slower. AT carrier women have about a three- to four-fold increased risk of breast cancer compared to women without this mutated gene. Exposure to X irradiation, for example from diagnostic X-rays or from occupational exposure, probably increases the risk of breast cancer in carrier women. It has been suggested that more cases of breast cancer may occur in women with mutated AT genes than to women with altered BRCA 1 and 2 genes. Most importantly, for the 1% of women who are carriers of an AT mutation, mammography may significantly increase their risk of breast cancer.

It is likely that in the next 10 years clinical tests will become available that will identify AT carriers and perhaps women with other genetic susceptibilities to X-rays. Such women will be advised to avoid routine mammograms. Even though they will represent only a few percent of the population, since there are 32 million American women between 40 and 79 we are talking about hundreds of thousands of women who in the future may be advised **not** to have routine mammograms.

Conclusion

For women over 50 at average risk of breast cancer, routine mammograms are probably worthwhile. Since the benefit of routine screening for women under 50 has not been documented and since at least several percent of the population are genetically sensitive to damage by X-irradiation, it seems advisable for premenopausal women to consult their doctors as to their personal risk factors before deciding whether to have routine mammograms.

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Prepared by Rita Calvo, Ph.D., Senior Lecturer, Molecular Biology and Genetics. Prof. Calvo teaches courses in Human Genetics and Genetics and Society, Cornell University

BCERF's Rural Initiative: Reaching Out to Women Across New York State

This summer BCERF launched a new educational initiative to bring breast cancer risk reduction information to rural women. The centerpiece of the project is a special display designed for use at fairs, farm shows and other local settings across the state.

The display features a self-guided, touch-screen computer program that includes the images and voices of farm and rural women modeling risk reduction strategies. The computer screen is presented as a "window" in a country kitchen, with cheerful wallpaper, real curtains and a farm view. By touching the computer screen, viewers can access information on a variety of breast cancer topics that may be most relevant to them, including reducing exposure to pesticides and chemicals, diet and lifestyle factors, early detection and answers to some frequently asked questions.

In August and September the display was featured at events including Empire Farm Days in Seneca

At the Central NY Farm Progress Show in Herkimer on September 15-16, 1999, BCERF partnered with Bassett Healthcare to provide breast cancer risk reduction and screening information to rural women.

Falls, the New York State Fair, and the Central New York Farm Progress Show in Herkimer. At the two farm shows, BCERF collaborated with medical professionals who provided clinical breast exams and/or information on mammography to fairgoers. This model combines information on screening with risk reduction, giving women more complete messages about breast health. Over 300 people interacted with the exhibit during these events, bringing questions about breast cancer risk and diet, family history, chemical safety and exercise.

The display was developed following six months of research and study with rural women and professional partners, including Cornell Cooperative Extension, the New York State Department of Health, the New York Center for Agriculture, Medicine and Health (NYCAMH), and the Cancer Information Service of the National Cancer Institute.

Prepared by Mary Maley, BCERF Health Educator

"We Need to Know"

Ad Hoc Discussion Group

"Learning Together"

"How do educators and advocates get reliable scientific information to their audiences?" This was just one of the questions discussed at BCERF's Ad Hoc Discussion Group meeting at the New York Hospital-Cornell Medical Center, White Plains last month. About 35 people representing Cornell Cooperative Extension (CCE), breast cancer advocacy groups, pesticide applicators and legislative and state agency representatives attended the October 13 meeting.

Open Discussion on Topics for 2000
Four individuals presented topics of concern to themselves and the organizations they represent. Those topics were reliable science and the precautionary principle, and, food safety and right-to-know. The purpose of this discussion was to help select Ad Hoc topics for the coming year.

Reliable Science and the Precautionary Principle. Miriam Goodman of the Huntington Breast Cancer Action Coalition told the group that physicial changes in the environment and release of toxic substances have had a large impact on human health in a variety of ways. Existing guidelines and regulations have not done the job of protecting us, and we must take a different approach. The precautionary principle states that:

- people have a duty to take action to prevent harm
- the burden of proof of harmlessness rests with the proponent
- before using a new process or chemical we must examine alternatives
- decisions must be open, informed, democratic and inclusive.

Rose Marie Williams of the Cancer Awareness Coalition emphasized the need to examine sources of scientific data, where the funding comes from, the role of the media, and how science and government policy intersect. She advocated for the precautionary principle as a "new paradigm."

Active discussion followed and comments addressed the need for personal responsibility in environmental decision-making in all areas, such as whether people are also willing to give up or use less gasoline, and other petroleum products and chemicals since all might impact adversely on health. The question remained as to when to act; how much scientific information is needed for policy making?

Liz Siaba of CCE of Nassau County discussed some challenges faced by extension educators in sharing reliable science with consumers. She said that we have the responsibility to advise and guide people. But the public doesn't want the "PhD-level course", so educators must know how to recognize what constitutes good science. For example, did the researcher follow guidelines and are the results replicable? Later in the meeting, this dialogue continued. The group asked Liz how she as an educator responds to questions about proper use of pesticides. Is there a vehicle for making recommendations and changes on what we use? Walter Schroeder, Director, NYSPAC, asked about the health effects for applicators, and commented for the need for good research on this exposed population.

Food Safety and Right-to-Know. Laura Weinberg of the Ecological Commission of the Town of North Hempstead, raised concerns about genetically engineered food, and hormones and food. She would like to see labeling of genetically modified foods so that consumers would be protected. Rose Marie Williams raised concerns about bovine growth hormone, and Miriam Goodman noted that genetically-altered corn and soy are in many products that we eat.

Pesticide Use and Sales Registry
Robert Haggerty, Supervisor, Pesticide Reporting Section, Bureau of Pesticide Management of the NYS Department of Environmental Conservation (DEC), provided an update

continued on page 12

Cornell University Program on Breast Cancer and Environmental Risk Factors in New York State (BCERF)

FACT SHEETS

Single copies available at no cost. For multiple copies please contact BCERF (address below).

General Information on Breast Cancer

__*FS # 3*—Understanding Breast Cancer Rates

__*FS # 5*—The Biology of Breast Cancer

__*FS # 6*—Tumor Supressor Genes - Guardians of Our Cells

__*FS # 9*—Estrogen - What is the Relationship?

__*FS #10*—Estrogen - What Factors Affect a Woman's Exposure to Estrogen?

Diet and Lifestyle

__*FS # 8*—Childhood Life Events

__*FS #13*—Alcohol

__*FS #18*—Fruits and Vegetables

__*FS #19*—Exercise

__*FS #27*—Dietary Fat

__*FS* #29—Breast Feeding

CRITICAL EVALUATIONS OF PESTICIDES AND BREAST CANCER

Critical Evaluations are available on the BCERF web page as portable document files (pdf), and can be accessed on the BCERF web site (see address below).

If you would like to order a hard copy please indicate below and send your check payable to Cornell University for **$3.00 each**, to cover the cost of reproduction and mailing.

__#1 2,4-D
__#2 Lindane
__#3 Heptachlor and Heptachlor Epoxide
__#4 Chlordane
__#5 Simazine
__#6 Cyanazine
__#7 Dichlorvos
__#8 Atrazine
__#9 Chlorpyrifos

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Pesticides and Breast Cancer Risks

__*FS # 2*—DDT, DDE and the Risk of Breast Cancer

__*FS #11*—An Evaluation of Chlordane

__*FS #12*—An Evaluation of Heptachlor

__*FS #14*—An Evaluation of 2,4-D

__*FS #15*—An Evaluation of Lindane

__*FS #16*—An Evaluation of Simazine

__*FS #17*—An Evaluation of Cyanazine

__*FS #20*—An Evaluation of Dichlorvos

__*FS #23*—An Evaluation of Atrazine

__*FS #26*—An Evaluation of Chlorpyrifos

__*FS #28*—An Evaluation of Diazinon

Pesticide-Related Issues

__*FS # 4*—Reducing Pesticide Exposure in the Home and Garden: Alternatives and Proper and Legal Use Resource Sheet

__*FS #7A*—Reducing Potential Cancer Risks from Drinking Water--*Part I: Contaminant Sources and Drinking Water Standards*

__*FS #7B*—Reducing Potential Cancer Risks from Drinking Water--*Part II: Home Water Treatment Options*

__*FS #21*—Avoiding Exposure to Household Pesticides: Protective Clothing

__*FS #22*—Safe Use and Storage of Hazardous Household Products

__*FS #24*—Consumer Concerns About Pesticides in Food

__*FS #25*—Pesticide Residue Monitoring and Food Safety

__*FS #30*—Resources for Information on the Health Effects of Pesticides and Responding to Pesticide Poisonings

__*FS #31*—Integrated Pest Management Around the Home and Garden

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on the 2nd Annual Report on the Pesticide Use and Sales Registry. The data for 1998 is still being entered into the system, therefore the report is a "snapshot of where we were on June 1." When all the data is finalized for calendar year 1998 that information will be available on their website (www.dec.state.ny.us/website/dshm/prl). The report contains information on six million applications and sales. As of February 1 Bob reported a 75% compliance rate as compared to a 50% compliance rate during the same time last year. As of the report date, the compliance rate was 95% for applicators and 97% for commercial permittees.

Groundwater Monitoring Program on Long Island

Maureen Serafini, Chief, Pesticide Product Registration Section of the NYS DEC, reported that untreated water from wells showed contaminants at low levels, whereas the public water supply did not show contamination. Many of the pesticides that were found were from pesticide products that are no longer registered for use on Long Island. This project, now into its third year, is a partnership of US Geological Survey and the Suffolk County Department of Health Services. 2,300 water samples have been collected from the highly agricultural areas of western New York and in Nassau and Suffolk counties.

BCERF Update

June Fessenden MacDonald, Director of BCERF updated the group on BCERF's activities in research, education and outreach. BCERF's Interactive Computer Display was also at the meeting. Most of the attendees tested the display and it was well received. Highlights of June's report included:

- Eight Critical Evaluations completed and 30 fact sheets available.
- BCERF Educational Tool Kit consisting of five modules offering strategic opportunities for risk reduction to be developed within a year.

MARK YOUR CALENDARS!

The next Ad Hoc Discussion Group meeting will take place in February 2000 in Albany, NY.

Ad Hoc Discussion Group meetings are open to any and all stakeholders to come together to discuss issues related to breast cancer and environmental risk factors.

The Ribbon is published by the Cornell Program on Breast Cancer and Environmental Risk Factors in New York State. Comments are welcome; contact the Editor

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