The Cancer Genetics Program at **The Cancer Institute at Alexian Brothers Hospital Network**

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In the past decade as our knowledge of cancer genetics and inherited cancer susceptibility has increased, cancer genetic risk assessment and testing has become a viable healthcare option for more American patients. The majority of women who pursue genetic testing do so to see if they carry mutations that could be passed on to their children. However, cancer genetic testing has far-reaching ramifications for patients and their families and can help guide decisions about future screening and prevention, as well as medical management options. While genetic testing isn't right for everyone, at Alexian Brothers, we believe that all appropriate patients should be given the option.

A genetics nurse clinician is an integral part of the Cancer Genetics Program at the Cancer Institute at Alexian Brothers Hospital Network.

In 2001 The Cancer Institute at Alexian Brothers Hospital Network in Elk Grove Village, Ill., made a commitment to develop a cancer genetics program. The key to our program's success has been to start slowly, adding to our program as physicians, high-risk nurse educators, and administrators have become comfortable with the new program.

We began our cancer genetics program with a focus on education, counseling, and testing for BRCA1 and BRCA2 genes. Between 5 percent and 10 percent of women with breast or ovarian cancer develop their disease because they have inherited a mutated copy of either of two genes, called BRCA1 and BRCA2.[1(p72)] Genetic testing to identify abnormalities in these genes provides an opportunity for enhanced medical management for these women and their relatives.

Genetic testing should be performed only after an individual has received detailed education and counseling about its benefits and limitations from a healthcare professional. Individuals interested in having their family history assessed for a possible hereditary risk of cancer should talk with their physician, nurse educator, or genetic counselor that specializes in cancer genetics.

The Alexian Brothers' Program

The cancer genetics program at Alexian Brothers consists of the following elements:

- Screening/family history
- Pre-test counseling and education
- Follow-up counseling, informed consent, and blood draw from appropriate patients
- Post-test counseling
- Medical management follow-up.

The American Society of Clinical Oncology (ASCO) guidelines for the appropriate use of genetic tests for predisposition to cancer recommend that genetic testing be offered only when an individual has a strong family history of cancer or early onset of the disease; the test can be

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adequately interpreted; and when the test result will influence medical management of the patient or family members. Informed consent, as well as counseling before and after the testing, are critical components of the genetic testing process.

Screening. The screening process at Alexian Brothers' cancer genetics program begins either with an initial phone interview or with the referring physician. The screening process aims to provide people with a risk assessment to determine if they should undergo genetic testing. Much can be gained from the assessment regardless of whether genetic testing is pursued. The high-risk nurse educator may conduct a preliminary screening interview by phone and then ask the patient to bring additional family history information and reports to a pre-test counseling appointment.

The hallmark characteristic of hereditary breast cancer is young age at diagnosis.[2] All women who have been diagnosed with breast cancer before age 50 should have their family history evaluated for additional signs of a hereditary susceptibility.[2] Accurately assessing family history for women with breast cancer diagnosed at a young age, or ovarian cancer at any age, is extremely important in order to identify the possibility of hereditary risk.[3]

Family history features that increase the chance of finding a BRCA1 or BRCA2 mutation include[3]:

- Diagnosis of breast cancer before age 50
- Ovarian cancer at any age
- Women who have had bilateral breast cancer
- Women who have had both breast cancer and ovarian cancer
- Male breast cancer.

In some instances, family history may not provide adequate information for screening purposes. For example, a young woman with breast cancer may have few or no female relatives, or perhaps both of her parents were only children. In this example, the woman's young age at diagnosis warrants making genetic testing an option.

Because BRCA1 and BRCA2 mutations are more common among certain ethnic groups, in the screening process all patients are asked about their ethnic background. For example, approximately 1 in 40 individuals of Ashkenazi Jewish ancestry carry a mutation in BRCA1 or BRCA2 as compared to 1 in several hundreds in the general U.S.[1 (pp82-85)] This higher prevalence is the result of a "founder effect," the phenomenon of specific genetic mutations becoming more common in populations that have been isolated over long periods of time for geographic, social, or religious reasons. Founder mutations have also been identified in several other populations, including among Icelanders, Finns, Dutch, and French-Canadians. [1 (pp82-85)]

The Cancer Institute at Alexian Brothers Hospital Network offers genetic testing for BRCA1 and BRCA2 mutations to any woman of Ashkenazi Jewish ancestry who was diagnosed with breast cancer before age 50 or ovarian cancer at any age.

Pre-Test Counseling. After the screening process, patients identified at high risk can schedule a pre-test counseling appointment. For this appointment the patient meets with the high-risk nurse educator for about an hour to an hour-and-a-half.

Pre-test counseling about the benefits and limitations of genetic testing is essential. Unlike other diagnostic tests, the identification of hereditary susceptibility to malignancy has significant implications not only for the person being tested but also for that person's relatives. Genetic testing is crucial to identify women who carry a mutation in either BRCA1 or BRCA2 and who would benefit from the screening and preventative options.

Recent studies of women with mutations in the BRCA1 and BRCA2 genes have demonstrated the effectiveness of several interventions designed to reduce the risk of cancer specifically for this group of women.[4] Moreover, women who learn that they did *not* inherit a BRCA mutation previously identified in their family clearly benefit as well. These individuals are at no increased risk despite their family history, making increased screening or other interventions unnecessary.[3] Studies have shown that people who pursue genetic testing and learn they do not carry their family's mutation have less anxiety and depressive disorders compared to individuals who are at high risk and chose not to be tested.[5]

In pre-test counseling, patients are educated about the features of a hereditary cancer in their family; the implications of positive, negative, or variant of uncertain significance test results; and the options for cancer screening and prevention based on the family's risk level and test results. Psychosocial assessment, including the patient's perception of risk and motivation for pursuing genetic testing, is completed prior to the blood sample being drawn. Patients are given the opportunity to discuss the various psychosocial issues that may arise when reviewing the family's cancer history and considering genetic testing.

Medical management options are discussed in detail during pre-test counseling by both the physician and cancer genetics nurse educator. Specific recommendations have been made for the medical management of women who learn that they carry mutations in BRCA1 or BRCA2, including increased surveillance; chemoprevention such as the use of tamoxifen; or risk-reducing sur-

Clinical Research Supports Genetic Testing

Normally, the BRCA1 and BRCA2 genes are responsible for proteins that repair damage in other genes, thus preventing the accumulation of mutations that can lead to cancer. Reflecting on the important role of these genes, inheritance of only one mutated copy of BRCA1 or BRCA2 leads to a greatly increased risk of developing cancer.

A mutated copy of either gene may be inherited from an individual's father or mother. Many women are not aware that breast and ovarian cancer occurrences on both the maternal and paternal sides of the family are important. In fact, 50 percent of women with hereditary risk have inherited the predisposing mutation from their father, and in most such women, little or no history of breast or ovarian cancer exists on the mother's side of the family. If a person is carrying a mutation in either BRCA1 or BRCA2, each child has a 50 percent chance of inheriting the mutation.[1(pp22-27)]

Studies have shown that if a woman inherits a mutated copy of either BRCA1 or BRCA2, her chance of developing breast cancer before the age of 50 approaches 50 percent, unless measures are taken to address that risk. By age 70, her risk increases to 87 percent, whereas the average risk of breast cancer is approximately 10 percent by this age.[13] The risk of ovarian cancer is also greatly increased (from less than 2 percent to between 27 percent and 44 percent) in women who carry mutations in these genes.[13]

Although the risk is greatly increased for women who learn they carry a mutation in either BRCA1 or BRCA2, the development of cancer is not a certainty. Whether or not a woman develops breast or ovarian cancer depends not only on the BRCA1 or BRCA2 mutation, but also the relationship with mutations that may occur in other genes, environmental, and lifestyle factors.

In addition to large risks of breast and ovarian cancers, BRCA2 mutations may be associated with increase risks of other cancers, for example, pancreatic, gallbladder, bile duct, stomach, malignant melanoma, and prostate cancer. The extent to which BRCA1 mutation carriers are at increased risk of other cancers, however, has been less clear.[3]

gery, such as removal of the ovaries and fallopian tubes.[6]

After the pre-test counseling session, patients are sent home with written information and educational videotapes to review individually or with family members. The genetic nurse educator coordinates verification of insurance coverage for genetic testing, with permission from the patient.

Insurance Coverage and Employment Issues. Genetic testing for mutations in the BRCA1 and BRCA2 genes is done through Myriad Genetics Laboratories in Salt Lake City, Utah. The cost of the test is $2,975 for the first family member who pursues full sequencing. Most insurance companies cover between 80 to 90 percent of the cost of genetic testing. If a patient tests positive for a mutation, the cost is $350 for subsequent relatives who decide to be tested for their family's specific mutation.

Many individuals who seek information about genetics and cancer express concern about the implications of a positive test for insurance and employment. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) prohibits group health plans from denying or limiting coverage based on genetic information, and a majority of states have passed laws or have legislation pending to provide further protection against "genetic discrimination." Recent studies have demonstrated that genetic susceptibility testing is no more likely to result in adverse consequences for health insurance or employment than other medical tests.[7]

Life insurance, on the other hand, is viewed much differently than health insurance. Patients who undergo genetic testing for cancer predisposition may find obtaining life insurance difficult after testing. For this reason, at Alexian Brothers, we recommend that all patients pursuing cancer genetic testing have life insurance in place prior to testing.

Informed Consent and Blood Draw. For patients who decide to pursue genetic testing, a second appointment is scheduled. During this visit, the patient meets with both a physician and the genetics nurse educator. This appointment allows patients to ask any additional questions and to complete the informed consent forms before a blood sample is drawn for genetic testing.

The results of a BRCA1 and BRCA2 genetic test are generally available in about three weeks. For patients undergoing testing, we schedule a follow-up post-test counseling appointment in four weeks' time. That allows the physician and nurse educator one week to review the test results prior to meeting with the patient. We suggest that patients bring a family member to this post-test appointment.

Post-Test Counseling. Genetic test results are given during a post-test counseling office visit. This appointment provides the opportunity to address all questions and psychosocial issues as they arise, and to make concrete plans for follow-up. A woman who tests positive for a BRCA1 or BRCA2 mutation will typically have several follow-up discussions with various physicians, for instance, primary care, oncologist, surgeon, obstetrician/gynecologist, to decide which screening and preventative options will most benefit her.

Breast cancer screening recommendations for women who test positive for a BRCA1 or BRCA2 mutation include increased surveillance, annual mammography starting as early as age 25, and clinical breast exams at least twice a year.[8] Many recent studies have shown that MRI of the breasts may be a more sensitive screening method for mutation carriers.[9] Although MRI screening has yet to become standard care, women carrying a BRCA1 or BRCA2 mutation may have the

option to participate in ongoing research studies.

One medical management option might include the use of tamoxifen, a selective estrogen receptor modulator (SERM) that has been shown to reduce the risk of breast cancer by 45 percent in "high risk" women, and remains an option for mutation carriers who have completed childbearing.[10] For women who have already had breast cancer, tamoxifen may reduce the risk of a contralateral breast cancer by 50 to 75 percent.[10]

Finally, prophylactic bilateral mastectomy has been shown to reduce the risk of breast cancer by 90 percent or more in women carrying a BRCA1 or BRCA2 mutation.[11]

Unfortunately the data have been dismal regarding the efficacy of screening methods to detect early-stage ovarian cancer. A National Institutes of Health consensus panel on ovarian cancer recommended that women who test positive for a BRCA1 or BRCA2 mutation be offered annual measurement of serum CA-125 and transvaginal ultrasound of the ovaries, although neither modality has a high enough sensitivity and specificity to be considered a reliable screening test for early-stage disease.[6] The development of novel screening methods for women at high risk of ovarian cancer remains an active area of research.

In addition to reducing the risk of ovarian cancer by 95 percent, removal of the ovaries has also been shown to reduce the risk of breast cancer by at least 50 percent in women with a mutation in either BRCA1 or BRCA2.[12] Finally, the use of oral contraceptives remains an option for risk reduction for mutation-positive women who are not yet ready to have their ovaries removed, although the data is controversial.[12]

Additional Follow-Up. After the post-test counseling appointment, the genetic nurse educator usually calls patients within the next one to two days to check in and see how they are doing. At Alexian Brothers, we follow up with our patients as long as needed.

Expanding the Cancer Genetics Program

Today, the cancer genetics program at Alexian Brothers offers services in two locations: The Cancer Institute at Alexian Brothers Hospital Network, Elk Grove Village and St. Alexius Medical Center, Hoffman Estates. Our cancer genetics program now provides risk assessment, education, counseling, and testing, when appropriate, for patients and families at risk for breast, ovarian, colon, melanoma, and pancreatic cancers. Our goal has been for every patient at The Cancer Institute to have a comprehensive risk assessment.

The surgical, medical, and radiation oncologists are instrumental in our cancer genetics program. High-risk educators who work in a cancer genetics program must have a strong oncology or genetics background. Identifying, counseling, and testing patients for hereditary cancers is a complex paradigm. A cancer high-risk educator must understand oncology and cancer syndrome patterns and have the skill to interpret pathology information.

The cancer risk patient educator must also stay up-to-date with the medical literature, reviewing studies, participating in continuing education associated with cancer genetics, and conducting monthly case study reviews with a certified genetic counselor.

Our cancer genetics program now provides *risk assessment, education, counseling, and testing…*

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