

## *What is the process of gene testing?*

Each step is usually not followed exactly, but the following is a good idea of the order in which to go about the testing.

- Deciding if a Genetic Test is Appropriate
- Genetic Counseling
- Testing
- Getting the Results
- Disclosure of the Results to Other Family Members
- Follow-up Medical Care

## *Does this sort of thing actually happen?*

Although most of us might not know somebody who has gotten genetically tested, the following is an example of what could happen (following the previously mentioned steps) if testing was done.

Consider the case of 35 year old Mary, whose mother died of colon cancer at age 50, whose cousin died of colon cancer at age 45, and whose uncle was diagnosed with colon cancer a year ago (at age 52). In this example you will see all of the different pieces of the genetic testing process.

## **Deciding if A Genetic Test Is Appropriate**

The first question that should be asked is, "Is genetic testing appropriate?" For Mary and her doctor the first step to answering that question was the collection of Mary's family medical history. Mary had to call a few relatives to confirm cancer diagnoses and the ages that people were diagnosed with the cancer. While talking to her aunt, she found out that another cousin had been diagnosed with endometrial cancer. Mary's doctor suggested that she collect medical records from her family members to help confirm the history. To do this, Mary sent medical release forms to the hospital that treated her mother and to her living uncle with cancer.

Upon review of Mary's history, it was clear to her doctor that there were many people in her family who had developed colon cancer at an early age. Mary's doctor felt that the pattern of cancers seen (colon and endometrial) fit a pattern of Hereditary Nonpolyposis Colorectal Cancer (HNPCC).

For HNPCC, there is a screening test called MSI testing that may be done before genetic testing. A positive MSI test gives clues that there may be an HNPCC mutation. MSI testing is done on tumor samples. Mary's doctor explained this test to Mary and the implications for her and her family. Because Mary herself did not have cancer, Mary's doctor (with Mary's permission) requested tumor tissue from Mary's mother's tumor for MSI testing from the hospital where she had her colon cancer surgery. After a few months, the results from MSI testing were completed. Mary's doctor explained that Mary's mother's tumor was MSI-high, which suggested that her mother might have had a mutation in one of the genes causing HNPCC.

The next question was who in the family, if anyone, should be tested for the actual genes involved in HNPCC. Mary wanted to be tested, but her doctor explained that if she tested negative they would not know if she was negative because she did not inherit the mutation in the family or if the mutation was in a gene that was not being tested. Mary agreed to ask if her affected uncle Evan would be willing to go through genetic testing first. If Evan tested positive, then Mary could go through testing. Evan agreed to consider testing, but wished to be seen at a medical facility closer to where he lived. Mary's doctor suggested the name of a cancer center close to where Evan lived.

## **Genetic Counseling**

Evan and his wife met with a genetic counselor at the cancer center to learn more about genetic testing and hereditary cancer. The genetic counselor explained what HNPCC was, how genes are inherited, what a mutation is, and other basic genetics relating to hereditary colon cancer. She reviewed different outcomes for the testing: a positive test, a negative test, and an indeterminate test result. She also discussed different options available to individuals who test positive and medical recommendations for Evan if he were to test negative.

Evan's wife was worried about how this might affect their children and grandchildren. One of their children had previously died of colon cancer and another one had endometrial cancer. They had a third child who had not had cancer. The genetic counselor explained that if the test result was positive that their living children could be tested for the mutation

in the family. If it was negative, they would be "off the hook" and back to population risk. If the test was positive, surveillance guidelines would be recommended for them.

Evan asked about insurance discrimination based on genetic testing. The counselor said that although there were no good studies showing that genetic discrimination happened, they could keep his result confidential if he did not use his insurance to pay for the test.

Evan and his wife reviewed their concerns and questions with the genetic counselor. Evan wanted black and white answers: should he be tested or not. However, the genetic counselor could only tell him that this was a very personal decision and should be made based on and what benefit it might provide for Evan and his family, and with a thorough understanding of the risks involved. Ultimately, Evan decided to go through genetic testing for HNPCC to benefit his children, grandchildren, nieces and nephews.

## Testing

For the test, Evan had a tube of blood drawn by the nurse in the laboratory near the genetic counselor's office. He decided to pay for the test himself by using a credit card. Before sending the sample by Federal Express to the laboratory where the testing was to take place, the genetic counselor checked that the name on the tube was correct. The genetic counselor also included brief information on the family history for the laboratory.

When the sample arrived, the laboratory technician logged in the sample and gave it a laboratory identification number. She also checked which test was being requested and checked to ensure that the family history matched the request. The next day DNA was extracted from the tube and over the next few weeks the lab sequenced the common genes that cause HNPCC. When a change was found in one of his genes, the laboratory resequenced the DNA to confirm their result. To further ensure accuracy, the laboratory director reviewed the data and the result, and double-checked all the identification numbers. The result was sent back to Evan's genetic counselor with an explanation that the change in the gene was likely to be the cause of Evan's syndrome.

## Getting the Results

Evan returned to the genetic counseling clinic to receive his genetic test result. His niece Mary and his wife came with him. The genetic counselor that had seen Evan before told him that his genetic test had come back positive. There was now a known mutation in the family that could explain the colon and endometrial cancers. The genetic counselor reviewed the value of this test. Evan is at increased risk for a secondary colon cancer. Because of this, it is recommended that he have regular colonoscopies. He is also at slightly increased risk for some upper GI cancers.

The counselor explained that this mutation was likely the cause of the colon cancer and endometrial cancer seen in two of Evan's daughters. She recommended that his two living children get screening for HNPCC-related cancers.

Although Evan was upset that he had passed on a faulty gene to his daughter who had died of colon cancer, his wife consoled him that now they could do something to protect their two younger children.

## Disclosure of Results to Other Family Members

Because Evan was found to have a mutation known to cause HNPCC, other relatives in his family could now be tested for the same mutation. The genetic counselor reviewed the pros and cons of genetic testing for Mary. If Mary tested negative for the mutation in the family, she would be at the same risk for colon cancer as other people in the general population. If she carried the same mutation as her uncle, Mary would be at elevated risk for colon, ovarian, and endometrial cancers and would be recommended to undergo vigilant surveillance for those cancers. Mary decided that she would benefit from testing.

Mary had her blood drawn and sent to the same laboratory that conducted the testing for her uncle.

Because the laboratory only needed to look for the one mutation in the family rather than screening the genes for HNPCC for mutations, the test was less expensive and much quicker. After a few weeks, Mary met with her doctor for results of the test. She did not inherit the mutation that her uncle and mother had shared.

Other family members, such as Mary's brother and sister, however were still at risk for inheriting the mutation. With her doctor's help, Mary drafted a letter to send to all of her at risk family members. The letter discussed the family's increased risk for colon and other cancers and that testing was available. Contact numbers for Mary and the cancer center where Evan had his testing were also included.

Mary's sister Alice decided to have testing. Her brother Tom decided that he would not have testing at this point, but would have regular colonoscopies for screening. Alice was found to carry the same mutation in the HNPCC gene as her uncle.

### **Follow-Up Medical Care**

Because Evan and Alice tested positive for a known mutation, they were given specific medical recommendation for cancer screening. They were also told about a clinical trial involving a drug, similar to aspirin, that was thought to slow down the growth of precancerous polyps. Alice was interested in learning more about clinical trials and her doctor provided her with information.

In addition to regular medical care, Evan and Alice were encouraged to call their doctor or the cancer center annually to find out if anything new was known about HNPCC. Because genetic testing is new and medical information on genetic disorders is evolving, family members and individuals who have gone through testing need to keep in contact with medical personnel who can update them on any changes. For affected individuals who tested negative, additional genetic tests may be offered if new genes are discovered that are involved in that disorder. Also, medical interventions and recommendations will change over time as more is learned about the effectiveness of various preventative and treatment strategies. Some testing centers may offer the latest in clinical trials or be able to relay the results of clinical trials that are relevant to mutation carriers or high-risk individuals.

In addition to keeping in contact with your doctor and local cancer center, you can also keep informed of new treatments, discoveries, and clinical trials by becoming a member of Genetic Health.