

BACKGROUND INFORMATION

It is estimated that one out of every three Americans will develop cancer sometime during their lifetime. Individuals in the general population have a lifetime risk of developing colorectal cancer of approximately 6%. While it is difficult to determine the exact cause of cancer in an individual, the majority of cancer is thought to be due to a combination of factors such as chance events, the aging process, or environmental exposures. About 5 to 10 percent of cancer cases are caused by a hereditary predisposition that is passed on within a family.

We look for several features in families to try to determine whether or not there is a hereditary cancer predisposition in the family. These include:

- Multiple family members affected with the colon cancer or colon polyps
- Earlier than average ages of diagnosis
- Multiple primary cancers in the same individual (such as two primary colon cancers)
- Cancer occurring in multiple generations

Inherited traits are characteristics, such as eye color or hair texture, that are passed from one generation of a family to the next. These traits are passed on in the form of genes. Genes are located on structures called chromosomes. Individuals typically have 46 chromosomes in every cell of the body, and they come in pairs. The chromosome pairs numbered 1 through 22 are the same between men and women and the last pair determines our gender: XX for female and XY for male. One copy of each chromosome pair (and therefore each gene) comes from our mother and the other from our father. Similarly, we pass on one copy of each chromosome pair to our children.

There are hundreds of genes located on each chromosome. Genes make proteins that are necessary for the proper growth and development of the body. Each gene is made up of DNA, which is the information that codes for a particular trait or condition. If you think of a gene as being a very large book, DNA is like the alphabet that makes up the words and sentences in the book. When a gene is altered, it simply means there is a typographical error (typo) in the book. This alteration makes the gene unable to function properly. Alterations can be as large as an entire chapter missing from the book, or as small as a single letter change within a word.

GENETICS OF MYH-ASSOCIATED POLYPOSI

We know of a few genes that when altered, may give an individual in increased chance to develop certain types of cancer. These types of genes are called cancer predisposition genes. Some families with an inherited predisposition to colorectal cancer have a condition called MYH-Associated Polyposis (MAP). MAP is associated with alterations (or “mutations”) in the *MYH* gene. Two common alterations account for approximately 87% of all *MYH* alterations in the Northern European population (called Y165C and G382D).

Individuals with MYH-Associated Polyposis (MAP) are at an increased risk of developing multiple colon polyps and colon cancer. The number of polyps seen in individuals with MAP is typically <100. The precise colon cancer risks for individuals with MAP are not yet known.

INHERITANCE

MAP is inherited in an autosomal recessive manner. In order for an individual to have MAP, he or she must have inherited **TWO** altered copies of the *MYH* gene (one copy from each parent). Recall that individuals have two copies of the *MYH* gene, one received from their mother and the other received from their father. If an individual has one normal copy of the *MYH* gene and one altered copy of the *MYH* gene, that individual is said to be a “carrier” of the gene for MAP. If two parents who are carriers have a child, there is a 1 in 4 (25%) chance that they will **BOTH** pass on the altered *MYH* gene copy to the child (see figure below). Therefore, each child has a 1 in 4 (25%) chance of having MAP if both parents are carriers. Similarly, the siblings of a person with MAP have a 1 in 4 (25%) chance of having MAP. A person with MAP can only have a child with MAP if his or her partner is a carrier or is also affected (therefore, he or she has at least one altered *MYH* gene).

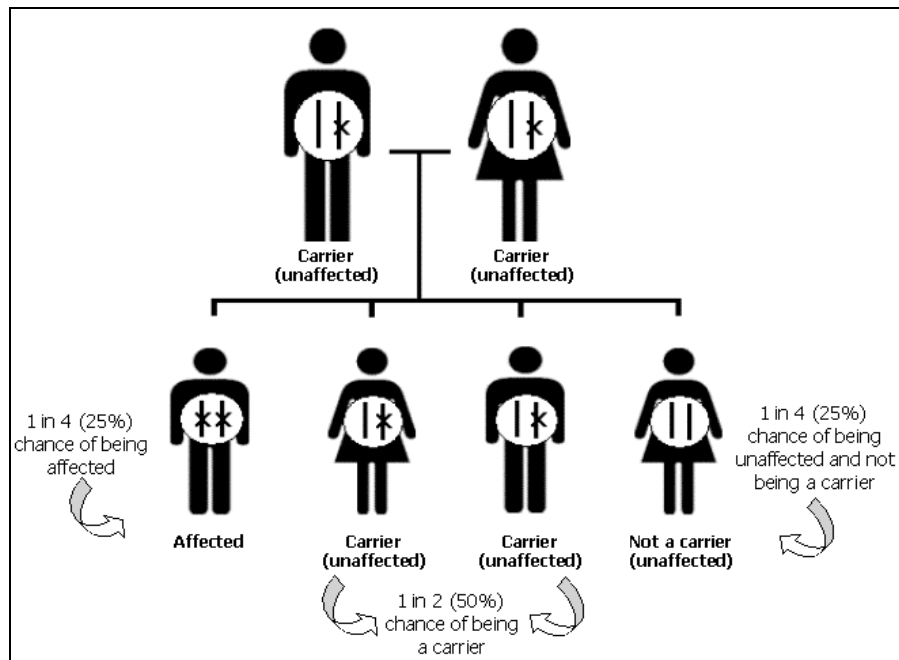


Figure 2: Autosomal recessive inheritance

GENETIC TESTING

Genetic testing involves taking a blood sample and checking the DNA pattern of a gene for an alteration. The cost of genetic testing is often covered by health insurance, but is dependent upon the individual insurance plan. Coverage information can usually be determined prior to proceeding with the test. Results of genetic testing are most informative if an individual who has been diagnosed with cancer is tested first. Genetic testing for cancer predisposition gene mutations should be accompanied by genetic counseling to determine the appropriateness of genetic testing based on the personal and family history of cancer, as well as the pros, cons, and limitations of testing.

OTHER ISSUES

There are advantages and disadvantages to having genetic testing for *MYH* gene alterations. These issues will affect individuals differently, which is why we encourage you to consider the possible ramifications before proceeding with genetic testing.

Potential advantages

- The results of the test can help individuals tailor their cancer screening and management appropriately. For example, an individual who has a positive test result may be recommended to have more frequent screening or prophylactic surgery.
- Results can also help family members clarify their risks of developing cancer and alter their current screening, if indicated.
- The uncertainty of potentially having a gene alteration can also be alleviated by genetic testing results.

Potential disadvantages

- Individuals may be more anxious if they find they have a *MYH* gene alteration because of the uncertainty of when and if cancer will develop.
- An individual's test result can have an impact on other family members and might lead to strained relationships within the family.
- While insurance companies will often cover the cost of testing for alterations in the *MYH* gene, the test can be quite expensive if an individual is responsible for covering all or part of the cost of testing.

Another concern for some individuals is the possibility of genetic discrimination. Genetic discrimination is the misuse of genetic information (*MYH* test results, for example) by employers, health insurers, life insurers and disability insurers. To date, there have been no documented cases of individuals suffering from genetic discrimination due to hereditary cancer syndrome genetic testing in terms of health insurance. There are laws (both national and state) that provide protection against genetic discrimination in health insurance and employment. Unfortunately, these laws do not yet protect against genetic discrimination in life insurance, disability insurance, or long-term care insurance.

If you are interested in scheduling an appointment to discuss this information with a genetic counselor, please call 781-744-3982.