

Risk Assessment of Colorectal Cancer

Cancer of the colon and rectum (CRC) is the third most common cancer and the second leading cause of cancer-related death in the United States. It occurs with equal frequency in males and females and, in most cases, is preventable. The most common risk factor for CRC is a family history of CRC. However, most colorectal cancer develops in individuals who are at average risk and it generally begins as a pre-malignant polyp (growth). CRC can be prevented by identifying and removing these polyps by screening sigmoidoscopy or colonoscopy before cancerous changes occur. Early detection is the key to improved survival and treatment outcomes.

How do I know if I am at increased risk for colon cancer?

You may be at increased risk for CRC if:

- you have more than two first-degree relatives (parent, sibling, child) with either CRC or adenomatous polyps (abnormal, mushroom-like growths on the colon) occurring in at least two generations
- individuals in your family have had CRC before age 50
- you have a strong family history of cancer of the colon, ovary, endometrium, brain, small bowel, renal pelvis, ureter, and stomach.

What are hereditary colon cancer syndromes?

Hereditary colon cancer is broadly divided into two types: polyposis (having multiple polyps or growths) and nonpolyposis. Hereditary CRCs have an autosomal dominant pattern of inheritance, which means that first-degree relatives of individuals with a hereditary predisposition to CRC have a 50% chance of inheriting this susceptibility.

Familial Adenomatous Polyposis (FAP) accounts for less than 1% of all CRC. Patients with FAP develop 100s to 1000s of colon polyps at a young age and often have a strong family history of CRC. This disease occurs as a result of defects in the adenomatous polyposis coli (*APC*) gene.

Hereditary Nonpolyposis Colorectal Cancer (HNPCC) accounts for approximately 3-6% of all CRC. Patients with HNPCC tend to have tumors on the right side of the colon and develop colon cancer at an early age, usually under the age of 50, and may have a strong family history of CRC. Family history may also reveal individuals with other cancers such as ovarian, endometrial, or stomach.

Familial clustering of CRCs is still a possibility even when FAP and HNPCC are ruled-out. Individuals with first-degree relatives with colon cancer have a two- to four-fold increased risk of the disease. CRCs in such families may represent a less severe type of familial risk. Genes for these types of CRCs have not yet been identified but are being investigated.

What can I do if there is hereditary CRC in my family?

Screening is recommended earlier and more often for people with a family history of CRC or polyps, and for people with a personal history of inflammatory bowel disease to detect pre-

malignant changes or CRC at the earliest stage possible, when it is most likely to be treated and cured.

Recent studies have demonstrated that individuals who are of Ashkenazi Jewish ancestry have a 6% chance to have a specific “mild” genetic alteration in the *APC* gene known as I1307K. If there is a family history of CRC, there is an increased chance of having this genetic alteration. People who inherit this alteration have approximately double the lifetime risk of developing colorectal polyps and cancer.

What will happen during an appointment to evaluate my cancer risk?

For individuals with a family history or personal history that is suggestive of a hereditary predisposition to CRC, genetic counseling is available to discuss risk-reduction strategies, specialized screening tests, and the availability of genetic testing. The risk assessment team will provide an estimation of a person’s risks for specific cancers based upon age, family history, and other risk factors. It is important to provide the cancer risk team with accurate family history information including the types of cancers in your family and the ages at which they occurred. It is helpful to obtain medical records and death certificates whenever possible in order to verify each cancer diagnosis.

The cancer risk team will discuss the possible role of genetics in a person’s family, cancer screening and cancer risk reduction recommendations, and will provide information about the availability of genetic testing for certain cancers. Identifying individuals with an inherited basis for their cancer allows at-risk relatives to obtain genetic counseling and pre-symptomatic screening. Intensive surveillance and preventative treatment, when available, can be offered to individuals found to be at increased risk for CRC. Family members identified as not having inherited the cancer-causing gene would no longer need to have increased surveillance since the risk for CRC would return to that of the average population.

Genetic Testing

Genetic testing to determine if an individual or family has a hereditary susceptibility to colon cancer is offered to appropriate families following cancer risk assessment. Currently, genetic testing is available for FAP, HNPCC, and a few other rare cancer syndromes, but not for other forms of hereditary CRC. Mutation testing is most informative when performed on a family member who has had cancer. Testing may first involve obtaining a piece of the tumor that was removed or a blood test. If a mutation is identified in that individual, this will assist with their cancer surveillance. Once a mutation is identified in a family, other family members can be tested for that specific mutation. Traditionally, the consideration of genetic testing takes place in a multi-step format. The individual considering testing should have a complete educational session with a genetic counselor. At this appointment the risks, benefits, and limitations of genetic testing are reviewed extensively.

It is important for individuals being tested to understand the value of the information that testing provides, how it will affect future surveillance for them and other family members, and the impact that this information will have on themselves and their children. A second appointment may then be scheduled to return to the clinic to ask additional questions and have

blood drawn (unless blood is drawn at the first visit). The results of testing typically take several weeks at which time a third appointment is scheduled to review these results.

Management options for patients at moderate-to-high risk for colorectal cancer

Cancer surveillance recommendations and strategies will be made based upon the outcome of a patient's cancer risk evaluation. For individuals who are considered to be at increased risk for CRC, recommendations may include more frequent colonoscopies beginning at a younger age, screening for additional cancers that may occur more frequently in families with hereditary CRC, and the consideration of prophylactic removal of the colon. Preventative surgery options should be discussed with specialists. Additionally, chemoprevention agents such as anti-inflammatories (aspirin) are being developed and studied to help prevent the formation of polyps. The risks and benefits of chemoprevention should also be discussed with a specialist. There are also clinical trials that patients may be eligible to participate in that are studying drugs that may reduce risk for colorectal cancer.

Insurance discrimination and confidentiality

Many people are concerned that genetic testing will be used by employers or insurance companies to discriminate against those at increased risk for cancer. Legislation exists to protect individuals in large group health insurance plans, but this has not been sufficiently tested in court. Furthermore, life and disability insurance policies are not protected. Many individuals choose not to inform their insurance companies about the testing in order to avoid this issue and choose to pay for testing out of pocket. This is an important issue that can be discussed with the cancer risk assessment team. There is no reason to be concerned about insurance discrimination following a genetic counseling/cancer risk assessment appointment. Individuals seek genetic counseling for a multitude of reasons and it has not been known to adversely affect insurability.

Confidentiality is of paramount importance in cancer risk assessment. Most risk evaluation programs have careful safeguards to help ensure that family and medical history information, as well as genetic testing results, are not released to anyone without written consent from the individual concerned.

For more information or to schedule an appointment, please contact:

The University of Chicago Cancer Risk Clinic
(773) 834-2661 or toll free 1-866-RSK-CLIN (775-2546)