Hereditary Cancer Testing: Is it Right for You?

This workbook is designed to help you decide if hereditary cancer testing is right for you. Testing should be completed with a trained healthcare provider.

Introduction

Most cancer occurs by chance. This is often called “sporadic cancer.” In some families we see more cancer than we would expect by chance alone. Determining which of these families have cancer related to an inherited gene mutation is important, as the cancer risks in hereditary cancer families are much higher than the general population.

Sporadic Cancer - Cancer which occurs by chance. People with sporadic cancer typically do not have relatives with the same type of cancer.

Familial Cancer - Cancer likely caused by a combination of genetic and environmental risk factors. People with familial cancer may have one or more relatives with the same type of cancer; however, there does not appear to be a specific pattern of inheritance (eg, the cancer risk is not clearly passed from parent to child).

Hereditary Cancer - Cancer occurs when an altered gene (gene change) is passed down in the family from parent to child. People with hereditary cancer are more likely to have relatives with the same type or a related type of cancer. They may develop more than one cancer and their cancer often occurs at an earlier than average age.
Personal and Family History*

Check all that apply:

☐ Ten or more cumulative colorectal adenomatous polyp(s)
  Number: ________ Age: ________

☐ A previously identified MYH or APC mutation in the family

Adenomatous polyposis syndromes are inherited conditions that are associated with the development of multiple polyps in the colon and rectum. Mutations in the APC gene cause familial adenomatous polyposis (FAP) or attenuated FAP (AFAP). Patients who have a mutation in the APC gene can have tens to hundreds of colon polyps (adenomas), a greatly increased risk of colorectal cancer, and an increased risk for other associated cancers. An APC mutation can be inherited from either your mother or father.

MYH-associated polyposis (MAP) is a hereditary condition that causes an increased risk for colorectal cancer and colorectal polyps. MAP is caused by mutations in the MYH gene. Mutations in the MYH gene are inherited in an autosomal recessive pattern, meaning individuals with MAP have mutations in both of their MYH genes (one from each parent). Individuals with MAP often do not have a family history of colon cancer or colon polyps in family members (although siblings may be affected).

*Assessment criteria based on medical society guidelines. For these individual medical society guidelines go to www.MyriadPro.com

Cancer Risks for People Who Have an APC or MYH Gene Mutation(s)

<table>
<thead>
<tr>
<th>Gene Mutation Carrier Risk</th>
<th>General Population Risk¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal cancer in FAP</td>
<td>approximately 100%</td>
</tr>
<tr>
<td>Colorectal cancer in AFAP</td>
<td>80%-100%</td>
</tr>
<tr>
<td>Duodenal cancer</td>
<td>5%-12%</td>
</tr>
</tbody>
</table>

APC gene mutation carriers have a slightly elevated risk over the general population of developing cancers of the pancreas, thyroid, stomach, and brain. Liver cancer risk in children is also increased.

Because of the numerous colorectal adenomas that occur in MAP, the colorectal cancer risk is known to be significantly increased. Additionally, it is possible that risks of other cancers, such as small bowel, may be increased as well.

1. Risk by age 70
2. Not available
Managing Risk for *APC* Mutation Carriers*

**INCREASED SURVEILLANCE**

<table>
<thead>
<tr>
<th>SITE</th>
<th>PROCEDURE</th>
<th>AGE TO BEGIN</th>
<th>REPEAT TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon-FAP</td>
<td>Sigmoidoscopy or colonoscopy</td>
<td>10-15 years</td>
<td>Annually</td>
</tr>
<tr>
<td>Colon-AFAP</td>
<td>Colonoscopy</td>
<td>Late teens or early 20s (depending on age of polyp development in the family)</td>
<td>1-3 years</td>
</tr>
<tr>
<td>Colon-After colon surgery</td>
<td>Endoscopy of remaining rectum, ileal pouch, or ileostomy</td>
<td>After colon surgery</td>
<td>6 months to 3 years (depending on polyp number and type of surgery)</td>
</tr>
<tr>
<td>Duodenum and stomach</td>
<td>Baseline upper endoscopy (including side-viewing examination)</td>
<td>20-25 years</td>
<td>1-4 years</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Physical exam and consideration of ultrasound</td>
<td>Late teens</td>
<td>Annually</td>
</tr>
</tbody>
</table>

Screening for other FAP/AFAP-related cancers (brain, pancreatic, hepatoblastoma, etc.) may be considered. Please speak to your healthcare provider.

*For reference and supporting data on risk factors and medical management visit www.MyriadPro.com/references

**SURGICAL MANAGEMENT**

- **FAP**—Preventive removal of the colon and rectum is recommended. The timing of surgery is based on the number/size of polyps.
- **AFAP**—Preventive removal of the colon and the rectum may be recommended depending on the number of polyps.

**CHEMOPREVENTION**

- Medications may be used to reduce the number of polyps in any rectum tissue that remains after colon surgery.
Managing Your MAP Cancer Risks*

Options for reducing cancer risk are available whether or not you have already had a diagnosis of cancer and/or polyps (adenomas). It is recommended that you be managed according to these guidelines, depending on the number of colorectal polyps (adenomas) in you and your family members. Discuss these options with the appropriate medical professionals to determine how you will manage your cancer risks.

## INCREASED SURVEILLANCE

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<th>PROCEDURE</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Colon—Small polyp (adenoma) burden, manageable by colonoscopy</td>
<td>Colonoscopy</td>
<td>25-30 years</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Colon—Large polyp (adenoma) burden</td>
<td>Counseling regarding surgical options</td>
<td>Varies based upon polyp (adenoma) burden</td>
<td>N/A</td>
</tr>
<tr>
<td>Colon—After colon surgery</td>
<td>Endoscopy of any remaining colon and rectum</td>
<td>After colon surgery</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Duodenum and stomach†</td>
<td>Upper endoscopy and side viewing duodenoscopy</td>
<td>30-35 years</td>
<td>3-5 years</td>
</tr>
</tbody>
</table>

†Patients who have small bowel polyps (adenomas) should follow FAP small bowel screening guidelines.

## SURGICAL MANAGEMENT

- Preventive removal of the colon and rectum may be recommended depending on the number of adenomas (polyps).

*For references and supporting data on risk factors and medical management, visit www.MyriadPro.com/references*
**Testing Options**

- **COLARIS AP**\(^{\text{PLUS}}\) *(AFAP, FAP, and MAP)*:  
  Sequence and large rearrangement analysis of the \(APC\) and \(MYH\) genes.

- **Single Gene Testing:**  
  Sequence and large rearrangement analysis of one of the \(APC\) or \(MYH\) gene.

- **Single Site Testing:**  
  Mutation specific analysis for individuals with a known AFAP, FAP, or MAP mutation in the family.

**Possible Test Results**

- **Positive Result** → **Increased Cancer Risk**  
  Medical management based on recommendations for gene mutation carriers

- **Negative Result**  
  
  - A gene mutation has been previously identified in the family *(Single Site Analysis)* → **No Increased Cancer Risk**  
    Medical management based on general population cancer screening recommendations
  
  - No gene mutation has been previously identified in the family *(Comprehensive Analysis)* → **Cancer Risk Not Fully Defined**  
    Medical management based on personal and family history of polyps and cancer

- **Uncertain Variant** → **Cancer Risk Not Fully Defined**  
  Medical management based on personal and family history of polyps and cancer

Patients who test positive for one \(MYH\) gene mutation do not have \(MYH\)-associated polyposis (MAP), but may have a small increased risk for colon cancer.
It’s a Family Affair

- *APC* and *MYH* gene mutations are passed on in a family
  - If you have gene mutations in either of these genes, your parents, your children, and your brothers and sisters may also have the same gene mutation
  - Other relatives such as aunts, uncles and cousins may also be at risk to carry the same gene mutation(s)
- Testing is the only way to identify gene mutation carriers
- It is important to share genetic test results with family members
- Individuals may have different viewpoints and reactions to genetic testing

Benefits and Limitations

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
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<tr>
<td>Personalized hereditary cancer risk assessment</td>
<td>Testing does not detect all causes of hereditary cancer</td>
</tr>
<tr>
<td>Appropriate medical management to help reduce cancer risk</td>
<td>A negative result is most helpful when there is a known mutation in the family</td>
</tr>
<tr>
<td>Important information for family members to help determine their risk</td>
<td>Some genetic variants are of unknown clinical significance</td>
</tr>
<tr>
<td>Reduced anxiety and stress</td>
<td></td>
</tr>
</tbody>
</table>

Health Care Coverage

Insurance coverage for genetic testing of at-risk patients is excellent, with the majority of patients covered for testing. The average patient payment for an integrated COLARIS AP test, including patient who pay nothing, is less than $100.*

For information regarding Myriad’s Patient Financial Assistance Program visit [www.MyriadPro.com](http://www.MyriadPro.com) or contact Customer Service at 800-4-MYRIAD (800-469-7423).

*Test prices may be confirmed by calling Myriad Customer Service at 800-469-7423. Unmet deductibles are always the responsibility of the patient.
Privacy

Federal laws (HIPAA and GINA) and laws in most states prohibit discrimination regarding employment eligibility, health benefits, or insurance premiums based solely on genetic information. Additionally, it is Myriad’s policy that test results are disclosed only to the ordering healthcare professional or designee, unless the patient consents otherwise.

Next Steps

☐ Pursue testing
  ☐ Schedule follow-up appointment for results disclosure
    Date: ____________________________  Time: ____________________________
☐ Decline testing-Medical management based on personal and family history of cancer
☐ Undecided

Who to contact with questions: ____________________________

Additional Resources

Colorectal Cancer Network
A support network for individuals and families touched by colon cancer that promotes awareness, screening, and early detection programs as well as legislative actions.
www.colorectal-cancer.net
301-879-1500

Colon Cancer Alliance
The Colon Cancer Alliance (CCA) is a national patient advocacy organization dedicated to ending the suffering caused by colorectal cancer.
www.ccalliance.org
877-422-2030 (toll free)

Myriad Genetic Laboratories, Inc.
www.MySupport360.com
800-4-MYRIAD (800-469-7423)
E-mail: helpmed@myriad.com
www.HereditaryCancerQuiz.com