MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER

Attenuated Familial Adenomatous Polyposis Syndrome: Information for families with a pathogenic variant in the *APC* gene

The purpose of this handout is to give you detailed information about your genetic test result which you may read and discuss with your medical providers. Researchers will continue to study the APC *gene, so please check in with your medical providers once a year to learn of any new information that may be important for you and your family members. (Please see the last page for a glossary of medical terms which are underlined in this document.)*

You have a pathogenic variant in the *APC* gene. This means you have **Attenuated Familial Polyposis syndrome** (also known as **AFAP syndrome**).

What is hereditary cancer?

- Cancer is a common disease. One out of every 3 people in the United States will develop some type of cancer in his or her lifetime.

- About 5-10% of cancers (up to 1 in 10) are hereditary. A hereditary cancer occurs when a person is born with a pathogenic variant (also known as a mutation) in a gene that increases the chance to develop certain types of cancer. A pathogenic variant can be passed on from one generation to the next.

- Typically, families with AFAP syndrome have one or more of the following features:
  - Many colon polyps (also called polyposis), typically ranging from 10 to less than 100.
  - Colon cancer diagnosed in the 50's-60's.
  - Multiple family members with colon polyposis or colon cancers.

What is a pathogenic variant?

- DNA is our genetic material which is passed on from parent to child. It contains the instructions for how our bodies develop, grow, and function. A gene is a small piece of DNA which has a specific job to do in the body. Some genes determine features like eye color or height, while other genes are involved with our health.

- We all have variations in our genes that make us different from one another. Most of these variations do not change the way our genes work. However, some variations do prevent a gene from working correctly. This type of variation is called a pathogenic variant or mutation.

Why does having this pathogenic variant cause an increased risk for cancer?

- The job of the *APC* gene is to prevent cancer. It is called a tumor suppressor gene. When working correctly, tumor suppressor genes help to prevent cancer by controlling the growth and division of cells.

- People born with AFAP syndrome have only one working copy of the *APC* gene, so their risk for cancer is higher than average.

What are the cancer risks linked to this pathogenic variant?

- People with AFAP syndrome also have a higher risk for pre-cancerous polyps in the colon, called adenomas. An adenoma is a pre-cancerous growth, and if it is not removed it can grow into a colon cancer.

- People born with an *APC* gene pathogenic variant (who have AFAP syndrome) have higher risks for certain types of cancer which are outlined in the table below.

Table**: Lifetime Cancer Risk (chance to get cancer at any time during life)**

	People who do not have an *APC* gene pathogenic variant	People who have AFAP syndrome
Colon cancer	4-5%	Up to 70%*
Small intestinal (duodenal) cancer	<1%	4-12%
Papillary thyroid cancer	<1%	<2%

National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Colorectal Guideline, Version 1.2020
*These risks are based on people who did not have regular screening and/or other treatments such as risk-reducing surgery.

- The numbers above are shown as a range. This is because not all families/individuals have the exact same degree of risk. Risks may be affected by the environmental factors, lifestyle, personal medical history, family cancer history, and other genetic or unknown factors.

- In addition, people with AFAP may also have non-cancerous features such as: bony growths known as osteomas (typically in the jaw or skull), dental problems (such as extra teeth or dental tumors), unusual pigmentation in the eye which does not cause vision problems (CHRPE), gastric fundic gland polyps and soft tissue tumors (epidermoid cysts, fibromas and desmoid tumors). It is unclear how often these features occur in people with AFAP, if at all.

Is it possible to fix the pathogenic variant?

Unfortunately, it is not yet possible to fix a pathogenic variant in the *APC* gene. However, it is possible to change your medical care and certain things in your lifestyle. Your provider(s) will work with you to discuss these options and create a medical care plan that is right for you.

What are the medical care recommendations?

The medical care recommendations for people with AFAP syndrome are divided into three categories: **surveillance**, **surgery**, and **medications**.

Surveillance:

The purpose of surveillance (also referred to as 'screening') is to diagnose cancer at as early a stage as possible. Although scientists and physicians can't prevent a cancer from developing, early detection is important. When a cancer is detected early, it is more likely to be treated successfully. There are very good surveillance methods for some, but not for all types of cancer.

The table below outlines surveillance recommendations for individuals with AFAP syndrome (adapted from the National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Colorectal Guideline, Version 1.2020). *Please note that these are general guidelines. Specific guidelines for individual patients and families may differ.*

Cancer type	Surveillance recommendations
Colon cancer	Colonoscopy and polypectomy every 1-2 years beginning in the late teens. If multiple adenomas found, discuss timing of colectomy. Surveillance after a colectomy varies depending on type of surgery.
Small intestinal (duodenal) cancer	Yearly upper endoscopy (EGD), beginning around age 20-25.
Thyroid cancer	Yearly thyroid examination, beginning in late teens.

Risk-reducing surgery options:

The goal of risk-reducing surgery is to reduce the risk of cancer by removing healthy tissue before cancer develops. This is also called prophylactic surgery. Risk-reducing surgery does not eliminate the chance to get cancer, but it does greatly lower the chance.

- **Colectomy:** This surgery removes all or part of the colon (large intestine) to lower the risk of colon cancer. Colectomy is usually necessary once a person develops a large number of polyps that cannot be managed through colonoscopy alone. The timing of a colectomy depends upon age, number of polyps, and other factors. There are different types of procedures for removal of the colon and/or rectum which should be discussed with a gastroenterologist and specially trained surgeon. Most colectomy operations do not require a permanent external bag.

Medications (Chemoprevention):
In some cases, medication may be prescribed to lower the chance of developing cancer.

- **Sulindac:** Some research shows that an NSAID called sulindac may stop colon polyps from growing. However, there is still much to be learned about the use of sulindac in people with AFAP syndrome, and it may or may not be right for you. **The use of sulindac is not appropriate for everyone and should <u>not</u> be taken without talking to your healthcare providers first.**

Who should I see for my medical care?

It is important to find health care providers you trust for long-term follow-up care. Your primary care providers may be able to provide some of this care. In some cases, you may need to see specially trained medical providers. We are happy to provide you with referrals to specialists at Mass General as needed.

How can I live a healthy lifestyle to lower my risk of developing cancer?

Everyone should follow a healthy lifestyle, but this may be even more important for someone with an increased risk of cancer. According to the American Cancer Society, a healthy lifestyle includes:

- Avoiding tobacco.
- Maintaining a healthy weight.
- Participating in regular physical activity.
- Keeping a healthy diet with plenty of fruits and vegetables.
- Limiting yourself to no more than 1-2 alcoholic drinks per day.
- Protecting your skin and eyes from the sun.
- Knowing your own body and medical history, your family history, and your risks.
- Having regular check-ups and cancer screening tests.

What are the chances that my family members also have the pathogenic variant?

- **Your children:** Each of your children has a 50% chance to inherit the normal (working) copy of the *APC* gene and a 50% chance to inherit the *APC* gene pathogenic variant (the non-working copy). Given that colonoscopy screening begins in the late teens, you should consider genetic testing for your children before age 20.

- **Your siblings and other relatives:** In most cases, brothers and sisters of a person with an *APC* gene pathogenic variant have a 50% chance to have the same pathogenic variant. Additionally, other family members (such as parents, cousins, aunts, uncles) may also be at risk to have the pathogenic variant.
    - Up to 20% of individuals with AFAP syndrome have a *de novo* (or “new”) pathogenic variant, meaning that they are the first in the family to have the pathogenic variant. Siblings of individuals who have a *de* novo pathogenic variant have only a small risk to have the *APC* pathogenic variant. However, even if a *de novo* pathogenic variant is suspected, genetic counseling and testing is still recommended for siblings.

- **Family planning:** People with an *APC* gene pathogenic variant may have concerns about passing the *APC* gene pathogenic variant to a child. There are reproductive options that can be used to lower the chance of passing an *APC* gene pathogenic variant to a child. If you are interested in learning more about these options, please contact your genetic counselor for a referral.

The letter you received from your genetic counselor will give more specific recommendations about which relatives are candidates for genetic testing. However, please feel free to contact us with any further questions.

Where can I find additional information?

Feel free to contact us if you have any questions or would like additional resources. Some people find it useful to speak with other people with AFAP syndrome who have similar concerns. We would be happy to arrange this for you if you are interested.

The following is a list of additional sources of information:

Center for Cancer Risk Assessment
Mass General Cancer Center
www.massgeneral.org/ccra
(617) 724-1971

American Cancer Society
www.cancer.org
(800) 227-2345

Hereditary Colon Cancer Takes Guts
www.hcctakesguts.org
info@HCCTakesGuts.org
(312) 787-4412

National Cancer Institute's Cancer Information Service
www.cancer.gov/aboutnci/cis
(800) 4-CANCER

Glossary of cancer genetics terms:

- Cell: The basic structural and functional unit of any living thing. Each cell is a small container of chemicals and water wrapped in a membrane. The human body is made up of 100 trillion cells forming all parts of the body such as the organs, bones, and blood.

- DNA: Deoxyribonucleic acid, or DNA, is the genetic material that is passed on from parent to child, which gives the instructions for how our bodies develop, grow, and function on a daily basis.

- Early detection: The process of finding cancer when it is just starting to develop.

- Gene: A gene is a small piece of DNA that gives instructions for a specific trait.

- Inherited trait: A character or feature that is passed on from a parent to a child.

- Lifetime cancer risk: The chance that a person will develop cancer in his or her life. This is sometimes defined as the chance of developing cancer by the age of 75 or 80.

- Pathogenic variant: A change in a gene that prevents it from working correctly. Also called mutation.

- Risk-reducing surgery: Surgery to remove healthy tissue or organs before cancer develops. Also called prophylactic surgery.

- Surveillance: Screening tests or procedures to look for early signs of cancer development or cancer returning (recurrence).

- Syndrome: A set of signs and symptoms that appear together and characterize a disease or medical condition.

- Tumor suppressor gene: When working correctly, tumor suppressor genes prevent cancers from developing by controlling the growth of cells.