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CANCER GENETICS & PREVENTION

FAMILIAL ADENOMATOUS POLYPOSIS (FAP)

PATIENT INFORMATION

What is Familial Adenomatous Polyposis syndrome (FAP)?
FAP is a condition that increases one's risk of developing polyps in the gastrointestinal tract, colorectal cancer, and other less common cancers (see chart below). Gastrointestinal polyps are small growths that occur along the inside wall of the small or large bowel. There are several different types of polyps. The most common type of polyp seen in individuals with FAP is an adenoma. This is considered a pre-cancerous polyp which, if not removed, may turn into a cancer. In the classic form of FAP, individuals may develop hundreds to thousands of polyps in their lifetime.

FAP affects different people in different ways. Even within the same family, it is possible for people to have a different type of FAP including the attenuated form of FAP (AFAP). Individuals with AFAP have fewer polyps and a later age of onset of colorectal cancer (average about 50-55 years instead of 40 years), compared to those with "classic type" FAP. Below are the lifetime risks of cancer in people with **classic FAP** without screening or follow-up, as compared to the general population.

Cancer	FAP Risk	General Population Rik
Colorectal	~100%	5-6%
Small bowel: duodenum/ampulla	4-12%	<1%
Thyroid (primarily papillary)	2%	<1%
Pancreas	~2%	<1%
Brain (primarily medulloblastoma)	<1%	<1%
Liver/Hepatoblastoma (under age 5)	1.6%	<1%
Bile duct	Low, but increased	<1%
Stomach	<1% (Western culture)	<1%

[Reference: NCCN Guidelines Version 2.2013 FAP]

There are other non-cancerous features associated with FAP, including:

- benign bony growths (known as osteomas), typically on the jaw or skull
- benign unusual pigment in the eye known as congenital hypertrophy of the retinal pigment epithelium or CHRPE
- dental abnormalities, including extra or missing teeth
- skin findings, such as fluid-filled cysts or fibromas
- soft tissue (desmoid) tumors, usually of the abdomen or abdominal wall
- polyps in the stomach that are benign (fundic gland polyps)
- adenomas of the small bowel (duodenum)
- adrenal masses

In AFAP, some of the other features of FAP may be present, but the eye findings and desmoid tumors are rare.

Some other types of FAP are:

- **Gardner syndrome:** Individuals with a history of Gardner syndrome multiple adenomatous polyps and for non-cancerous bony growths (osteomas) and soft tissue tumors.

- **Turcot syndrome:** Individuals with Turcot syndrome have features of FAP plus brain tumors.

What causes FAP?
About 90% of people with classic FAP carry a change or alteration in the Adenomatous Polyposis Coli *(APC)* gene. There are also some families with FAP who have a gene alteration that cannot be found by today's technology.

If a person has a harmful alteration (a mutation) in the *APC* gene, then they are at risk for developing the cancers seen in FAP. All of us have two copies of almost every gene (one from each parent), so even if one is altered, the other one can work normally. However, if the second copy of the gene is damaged by chance, the cell no longer has a working copy of the gene to help protect it from uncontrolled cell growth. This uncontrolled growth over time can cause polyps and cancer to form.

How is FAP inherited?
FAP is inherited in an "autosomal dominant" manner. Autosomal means that both men and women can have FAP and pass it on to their children. Dominant means that it takes only one altered copy of a gene in order to cause FAP. An alteration in the *APC* gene can be inherited from a parent like other family traits. In about 20% of people (1 out of 5) with FAP, the alteration in the *APC* gene is not inherited from their parents, but instead occurs as a brand new change in that person.

Some individuals are diagnosed with FAP based on their medical and family history, even if they do not carry a detectable alteration in the *APC* gene. This is especially true for individuals with attenuated FAP.

If you have an altered *APC* gene, here are the chances that other relatives might have inherited it:

- **Your Children –**50% risk for each child

- **Your Mother or Father –** almost a 50% risk. In most cases, you would have inherited the altered gene from either your mother or your father. In about 20% of people with FAP, neither parent will have the altered gene because it has developed as a brand new genetic event/mutation in you.

- **Your Brothers and Sisters –** 50% risk if one of your parents has the alteration. If neither of your parents carries the alteration, then your siblings have a very low risk of having the alteration.

- **Your Nieces and Nephews –** 25% risk if one of your parents has the alteration.

- **Your Grandchildren –** 25% risk overall; 50% risk if their parent has the alteration; 0% risk if their parent does not have the alteration.

- **Your Aunts and Uncles –** 25% risk for the side of the family which has FAP; no increased risk for relatives on the other side of the family. If it is not clear which side of the family has FAP, then relatives on both sides of the family should be offered genetic testing.

- **Your First-Cousins –** 12.5% risk for the cousins on the side of the family which has FAP; no increased risk for cousins on the other side of the family. If it is not clear which side of the family has FAP, then relatives on both sides of the family should be offered genetic testing.

How is FAP managed?
There are a number of medical recommendations to help manage these increased risks that should be considered. Although we do not currently have any perfect strategies for reducing cancer risks, we do know that by close monitoring, colon cancer may be prevented. With close monitoring, if colon cancer does develop, it can be detected in their earliest stages, when it is most amenable to treatment. A screening test is one that is done in an effort to identify cancer (or pre-cancerous changes) early. Risk reduction strategies are used to try to prevent cancer.

Screening:
Annual physical exam
Polyps and gastrointestinal cancer
- colonoscopy annually (beginning at age 10-15 years or sometimes later depending on the family history)
- upper endoscopy (every 1-4 years or with symptoms, frequency depends on number of polyps found)

Thyroid cancer
- thyroid examination annually (with physical exam or ultrasound as needed)

Liver/Hepatoblastoma
- abdominal examination (with physical exam and ultrasound) and measurement of alpha fetoprotein (aFP) level (a blood test) every 3-6 months, from birth until age 5

For certain families or individuals:
- desmoid tumor screening
- small bowel screening

Risk Reduction:
For individuals with FAP, the number of polyps forming can become overwhelming and too difficult to remove or follow over time. In these cases, it is recommended that individuals with FAP discuss surgical options to reduce the risk of cancer.
- The type of surgery that is recommended for individuals with FAP is called a colectomy, and involves removing the colon. This surgery can be performed in slightly different ways, and we recommend that you discuss the benefits and risks of these surgeries with a colorectal surgeon. For individuals with FAP, the goal is that colectomy should occur before colorectal cancer develops. Individuals with "classic type" FAP often need to consider this surgery at a

younger age than someone with the attenuated form of FAP. Most often patients go on to live healthy, active lives and do not require a colostomy "bag".

- Chemoprevention with non-steroidal anti-inflammatory drugs (NSAIDs) including a medication called sulindac, may be recommended for some patients. At this time, it is recommended for patients who have had a colectomy but continue to form adenomas in the remaining gastrointestinal tract.

Where can I find more information?

Dana Farber Cancer Institute, Cancer Genetics & Prevention
www.dana-farber.org/cancergenetics

Cancer.net
http://www.cancer.net/patient/Cancer+Types/Familial+Adenomatous+Polyposis

Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA)
http://www.cgaicc.com/

Colon cancer alliance
http://www.ccalliance.org/

American Cancer Society
www.cancer.org

National Cancer Institute
www.cancer.gov

References:

- NCCN Guidelines Version 2.2013 Familial Adenomatous Polyposis
- PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002-. Genetics of Colorectal Cancer (PDQ®): Health Professional Version. [Updated 2012 Jul 20]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK65788/