Familial Adenomatous Polyposis (FAP)

Brought to you by the *National Society of Genetic Counselors, Cancer Special Interest Group*

What you should know about Familial Adenomatous Polyposis

Familial Adenomatous Polyposis (FAP) is a rare genetic condition that increases a person's chance of developing cancer, mainly colon cancer. Less than 1% of all colon cancer diagnoses are due to FAP. The main feature of FAP is the presence of hundreds to thousands of polyps in the colon. Polyps may also develop in the stomach and small intestine. The type of polyp associated with FAP is called an adenoma. An adenoma is a precancerous polyp that can become malignant (cancerous). In classic FAP, adenomas usually begin developing in teenagers or young adults. Some individuals with FAP present with a milder form of FAP, referred to as attenuated FAP (AFAP). These individuals typically have fewer than 100 polyps (average of 30), which may develop at later ages than classic FAP. FAP and AFAP are both caused by mutations in the *APC* gene.

Cancer Risks and Features Associated with Familial Adenomatous Polyposis

Cancer Type	FAP Lifetime Cancer Risk
Colon	100% (classic FAP); ~70% (attenuated FAP)
Small bowel/Duodenal	4-12%
Stomach/Gastric	0.5-1.3%
Pancreatic	<1%
Thyroid (typically papillary thyroid carcinoma)	<2%
Brain/CNS (typically medulloblastoma)	<1%
Liver (hepatoblastoma)	1-2% (rare after 6 years of age)

Other features: Individuals with FAP may also develop polyps in the stomach (fundic gland polyps) and small bowel, harmless freckle-like spots on the inside of the eye called Congenital Hypertrophy of Retinal Pigment Epithelium (CHRPE), desmoid tumors (tumors of connective tissue), osteomas (bony growths on the skull and jaw), epidermoid cysts (cysts on the skin), extra teeth or dental abnormalities. Individuals with AFAP are less likely to have these additional features.

Genetics and Inheritance of Familial Adenomatous Polyposis

Genes are our body's instructions. They provide our body with information about how to grow and develop. When there is a mutation in a gene, it can cause the gene to no longer function correctly. Each person has two copies of every gene. One copy is inherited from their mother and the other copy is inherited from their father.

FAP is due to a mutation in the *APC* gene. Cancer risks associated with FAP are inherited in an autosomal dominant manner. This means that children, siblings and parents of individuals with an *APC* mutation have a 50% (1 in 2) chance of having the mutation as well. Both males and females can inherit an *APC* mutation and can pass it on to their children.

Most people with FAP inherit the condition from one of their parents who has a mutation in the *APC* gene. However, about 20-30% of the time, an individual with FAP is the first person in the family to have the condition (*de novo*).

The location of the mutation within the *APC* gene can affect whether a person has FAP or AFAP, and therefore how likely it is for them to develop certain FAP features.

Managing Cancer Risks

- **Screening**
  - Annual colonoscopy beginning around age 10 – 15 years. For AFAP, colonoscopy beginning in late teens, then every 1-2 years.
  - Upper endoscopy beginning around age 20 – 25 years (frequency depends on number of polyps).
  - Annual thyroid exam starting as a late teenager (ultrasound imaging may be considered).
  - Annual physical exam with abdominal palpitation.
  - Additional individualized screening may be recommended based on family medical history.
- **Surgery**
  - If polyps can't be managed by colonoscopy, or if colon cancer occurs, surgery to remove the entire colon (colectomy) and connect the small intestine to the rectum or anus is recommended. Sometimes this reconnection is not possible, and a colostomy bag is needed.

When to Consider Evaluation for Familial Adenomatous Polyposis

- Family history information is important when determining the chance that a family or individual has FAP or another genetic condition. At minimum, individuals should be evaluated for FAP if they have:
  - A family member with FAP
  - 11 or more adenomatous colon polyps in their lifetime
  - Rare medical findings (benign or cancerous) that can be associated with FAP (for example, CHRPE)

Genetic Counseling

In many families, the cancer history may be due to a combination of genetic and environmental factors. In addition, other genetic conditions (i.e. other gene mutations) may appear clinically similar to *APC* mutations**.** For this reason, a detailed review of the family history by a genetics professional is important before pursuing genetic testing. A genetic counselor can help determine which, if any, genetic tests may be helpful for a family and review the benefits, risks and limitations of genetic testing. Genetic testing is usually performed through a blood or saliva sample.

Genetic test results can be complicated and are most useful when interpreted by a genetics professional in the context of an individual's personal and family history. To locate a genetic counselor near you, please visit www.nsgc.org and click on the 'Find a Genetic Counselor' link.

Genetic Discrimination

The Genetic Information Nondiscrimination Act (GINA) was signed into federal law in 2008. GINA prohibits health insurers and most employers from discriminating against individuals based on genetic information (including the results of genetic tests and family history information). According to GINA, health insurance companies cannot consider genetic information to be a preexisting condition, nor can they use it to make decisions regarding coverage or rates. GINA also makes it illegal for most employers to use genetic information in making decisions about hiring, firing, promotion, or terms of employment. It is important to note that GINA does not offer protections for life insurance, disability insurance, or long-term care insurance. More information about GINA can be found by contacting a local genetic counselor or by visiting www.ginahelp.org.

Resources

- Hereditary Colon Cancer Foundation: https://www.hcctakesguts.org/
- Genetics Home Reference: https://ghr.nlm.nih.gov/condition/familial-adenomatous-polyposis

References

- GeneReviews: *APC*-Associated Polyposis Conditions. https://www.ncbi.nlm.nih.gov/books/NBK1345/ [Updated 2017 Feb 2]
- National Comprehensive Cancer Network, NCCN Clinical Practice Guidelines for Genetic/Familial High-Risk Assessment: Colorectal v. 3.2019, retrieved from www.nccn.org