familial adenomatous polyposis

Familial adenomatous polyposis (FAP) is an inherited disorder characterized by cancer of the large intestine (colon) and rectum. People with the classic type of familial adenomatous polyposis may begin to develop multiple noncancerous (benign) growths (polyps) in the colon as early as their teenage years. Unless the colon is removed, these polyps will become malignant (cancerous). The average age at which an individual develops colon cancer in classic familial adenomatous polyposis is 39 years. Some people have a variant of the disorder, called attenuated familial adenomatous polyposis, in which polyp growth is delayed. The average age of colorectal cancer onset for attenuated familial adenomatous polyposis is 55 years.

In people with classic familial adenomatous polyposis, the number of polyps increases with age, and hundreds to thousands of polyps can develop in the colon. Also of particular significance are noncancerous growths called desmoid tumors. These fibrous tumors usually occur in the tissue covering the intestines and may be provoked by surgery to remove the colon. Desmoid tumors tend to recur after they are surgically removed. In both classic familial adenomatous polyposis and its attenuated variant, benign and malignant tumors are sometimes found in other places in the body, including the duodenum (a section of the small intestine), stomach, bones, skin, and other tissues. People who have colon polyps as well as growths outside the colon are sometimes described as having Gardner syndrome.

A milder type of familial adenomatous polyposis, called autosomal recessive familial adenomatous polyposis, has also been identified. People with the autosomal recessive type of this disorder have fewer polyps than those with the classic type. Fewer than 100 polyps typically develop, rather than hundreds or thousands. The autosomal recessive type of this disorder is caused by mutations in a different gene than the classic and attenuated types of familial adenomatous polyposis.

Frequency

The reported incidence of familial adenomatous polyposis varies from 1 in 7,000 to 1 in 22,000 individuals.

Genetic Changes

Mutations in the *APC* gene cause both classic and attenuated familial adenomatous polyposis. These mutations affect the ability of the cell to maintain normal growth and function. Cell overgrowth resulting from mutations in the *APC* gene leads to the colon polyps seen in familial adenomatous polyposis. Although most people with mutations in

the *APC* gene will develop colorectal cancer, the number of polyps and the time frame in which they become malignant depend on the location of the mutation in the gene.

Mutations in the *MUTYH* gene cause autosomal recessive familial adenomatous polyposis (also called MYH-associated polyposis). Mutations in this gene prevent cells from correcting mistakes that are made when DNA is copied (DNA replication) in preparation for cell division. As these mistakes build up in a person's DNA, the likelihood of cell overgrowth increases, leading to colon polyps and the possibility of colon cancer.

Inheritance Pattern

Familial adenomatous polyposis can have different inheritance patterns.

When familial adenomatous polyposis results from mutations in the *APC* gene, it is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person has one parent with the condition.

When familial adenomatous polyposis results from mutations in the *MUTYH* gene, it is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition.

Other Names for This Condition

- adenomatous familial polyposis
- adenomatous familial polyposis syndrome
- adenomatous polyposis coli
- familial multiple polyposis syndrome
- FAP
- MYH-associated polyposis

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Desmoid disease, hereditary
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1851124/
- Genetic Testing Registry: Familial adenomatous polyposis 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2713442/

- Genetic Testing Registry: Familial multiple polyposis syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0032580/
- Genetic Testing Registry: MYH-associated polyposis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1837991/

Other Diagnosis and Management Resources

- GeneReview: APC-Associated Polyposis Conditions
  https://www.ncbi.nlm.nih.gov/books/NBK1345
- GeneReview: MUTYH-Associated Polyposis
  https://www.ncbi.nlm.nih.gov/books/NBK107219
- Genomics Education Programme (UK): Familial Adenomatous Polyposis
  https://www.genomicseducation.hee.nhs.uk/resources/genetic-conditions-factsheets/item/76-familial-adenomatous-polyposis
- Genomics Education Programme (UK): MYH-Associated Polyposis
  https://www.genomicseducation.hee.nhs.uk/resources/genetic-conditions-factsheets/item/84-myh-associated-polyposis
- MedlinePlus Encyclopedia: Colon Cancer
  https://medlineplus.gov/ency/article/000262.htm
- MedlinePlus Encyclopedia: Colorectal polyps
  https://medlineplus.gov/ency/article/000266.htm
- National Cancer Institute: Genetic Testing for Hereditary Cancer Syndromes
  https://www.cancer.gov/about-cancer/causes-prevention/genetics/genetic-testing-fact-sheet

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Colon Cancer
  https://medlineplus.gov/ency/article/000262.htm
- Encyclopedia: Colorectal polyps
  https://medlineplus.gov/ency/article/000266.htm
- Health Topic: Cancer--Living with Cancer
  https://medlineplus.gov/cancerlivingwithcancer.html
- Health Topic: Colonic Polyps
  https://medlineplus.gov/colonicpolyps.html
- Health Topic: Colorectal Cancer
  https://medlineplus.gov/colorectalcancer.html

Genetic and Rare Diseases Information Center

- Attenuated familial adenomatous polyposis
  https://rarediseases.info.nih.gov/diseases/8532/attenuated-familial-adenomatous-polyposis
- Familial adenomatous polyposis
  https://rarediseases.info.nih.gov/diseases/6408/familial-adenomatous-polyposis
- Gardner syndrome
  https://rarediseases.info.nih.gov/diseases/6482/gardner-syndrome

Additional NIH Resources

- National Cancer Institute: Colorectal Cancer
  https://www.cancer.gov/types/colorectal
- National Cancer Institute: Genetics of Colorectal Cancer
  https://www.cancer.gov/types/colorectal/hp/colorectal-genetics-pdq
- National Human Genome Research Institute: Learning About Colon Cancer
  https://www.genome.gov/10000466/
- National Institute of Diabetes and Digestive and Kidney Diseases: Colon Polyps
  https://www.niddk.nih.gov/health-information/digestive-diseases/colon-polyps

Educational Resources

- American Cancer Society: Colon and Rectum Cancer
  https://www.cancer.org/cancer/colon-rectal-cancer.html
- CDC: Colorectal (Colon) Cancer
  https://www.cdc.gov/cancer/colorectal/

- Disease InfoSearch: Attenuated Familial Adenomatous Polyposis (AFAP)
  http://www.diseaseinfosearch.org/Attenuated+Familial+Adenomatous+Polyposis+%28AFAP%29/661
- Disease InfoSearch: Familial Adenomatous Polyposis (FAP)
  http://www.diseaseinfosearch.org/Familial+Adenomatous+Polyposis+%28FAP%29/2722
- Genetic Science Learning Center, University of Utah
  http://learn.genetics.utah.edu/content/disorders/multifactorial/
- Johns Hopkins Cancer Risk Assessment Program
  http://www.hopkinsmedicine.org/gastroenterology_hepatology/clinical_services/colon_cancer_risk_assessment_clinic.html
- MalaCards: adenomatous polyposis coli
  http://www.malacards.org/card/adenomatous_polyposis_coli
- Mount Sinai Hospital Kid's Corner: FAP & You
  http://www.zanecohencentre.com/gi-cancers/fgicr/kids-korner/fap-a-you
- My46 Trait Profile: Familial Adenomatous Polyposis
  https://www.my46.org/trait-document?trait=Familial%20adenomatous%20polyposis&type=profile
- My46 Trait Profile: MUTYH-Associated Polyposis
  https://www.my46.org/trait-document?trait=MUTYH-Associated%20Polyposis&type=profile
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/familial-adenomatous-polyposis/
- Orphanet: Familial adenomatous polyposis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=733

Patient Support and Advocacy Resources

- American Society of Colon and Rectal Surgeons: Hereditary Colorectal Cancer Registries
  https://www.fascrs.org/hereditary-colorectal-cancer-registries
- Colon Cancer Alliance
  https://www.ccalliance.org
- Colorectal Cancer Coalition
  https://fightcolorectalcancer.org

GeneReviews

- APC-Associated Polyposis Conditions
  https://www.ncbi.nlm.nih.gov/books/NBK1345
- MUTYH-Associated Polyposis
  https://www.ncbi.nlm.nih.gov/books/NBK107219

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22familial+adenomatous+polyposis%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Adenomatous+Polyposis+Coli%5BMAJR%5D%29+AND+%28%28familial+adenomatous+polyposis%5BTI%5D%29+AND+%28FAP%5BTIAB%5D%29+AND+%28colorectal%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- DESMOID DISEASE, HEREDITARY
  http://omim.org/entry/135290
- FAMILIAL ADENOMATOUS POLYPOSIS 1
  http://omim.org/entry/175100
- FAMILIAL ADENOMATOUS POLYPOSIS 2
  http://omim.org/entry/608456

Sources for This Summary

- Attard TM, Cuffari C, Tajouri T, Stoner JA, Eisenberg MT, Yardley JH, Abraham SC, Perry D, Vanderhoof J, Lynch H. Multicenter experience with upper gastrointestinal polyps in pediatric patients with familial adenomatous polyposis. Am J Gastroenterol. 2004 Apr;99(4):681-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15089902
- Baglioni S, Genuardi M. Simple and complex genetics of colorectal cancer susceptibility. Am J Med Genet C Semin Med Genet. 2004 Aug 15;129C(1):35-43. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15264271
- Bienz M. APC. Curr Biol. 2003 Mar 18;13(6):R215-6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12646143
- Cheadle JP, Sampson JR. Exposing the MYtH about base excision repair and human inherited disease. Hum Mol Genet. 2003 Oct 15;12 Spec No 2:R159-65. Epub 2003 Aug 5. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12915454

- Claes K, Dahan K, Tejpar S, De Paepe A, Bonduelle M, Abramowicz M, Verellen C, Franchimont D, Van Cutsem E, Kartheuser A. The genetics of familial adenomatous polyposis (FAP) and MutYH-associated polyposis (MAP). Acta Gastroenterol Belg. 2011 Sep;74(3):421-6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22103048
- Crabtree M, Sieber OM, Lipton L, Hodgson SV, Lamlum H, Thomas HJ, Neale K, Phillips RK, Heinimann K, Tomlinson IP. Refining the relation between 'first hits' and 'second hits' at the APC locus: the 'loose fit' model and evidence for differences in somatic mutation spectra among patients. Oncogene. 2003 Jul 3;22(27):4257-65.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12833148
- Järvinen HJ, Peltomäki P. The complex genotype-phenotype relationship in familial adenomatous polyposis. Eur J Gastroenterol Hepatol. 2004 Jan;16(1):5-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15095846
- Knudsen AL, Bisgaard ML, Bülow S. Attenuated familial adenomatous polyposis (AFAP). A review of the literature. Fam Cancer. 2003;2(1):43-55. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14574166
- Lipton L, Tomlinson I. The multiple colorectal adenoma phenotype and MYH, a base excision repair gene. Clin Gastroenterol Hepatol. 2004 Aug;2(8):633-8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15290654
- Lucci-Cordisco E, Risio M, Venesio T, Genuardi M. The growing complexity of the intestinal polyposis syndromes. Am J Med Genet A. 2013 Nov;161A(11):2777-87. doi: 10.1002/ajmg.a.36253. Epub 2013 Oct 3. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24124059
- Lynch HT, Shaw TG, Lynch JF. Inherited predisposition to cancer: a historical overview. Am J Med Genet C Semin Med Genet. 2004 Aug 15;129C(1):5-22.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15264268
- National Cancer Institute: Genetics of Colorectal Cancer
  https://www.cancer.gov/types/colorectal/hp/colorectal-genetics-pdq
- Rowley PT. Inherited susceptibility to colorectal cancer. Annu Rev Med. 2005;56:539-54. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15660526
- Rustgi AK. The genetics of hereditary colon cancer. Genes Dev. 2007 Oct 15;21(20):2525-38. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17938238
- Sampson JR, Dolwani S, Jones S, Eccles D, Ellis A, Evans DG, Frayling I, Jordan S, Maher ER, Mak T, Maynard J, Pigatto F, Shaw J, Cheadle JP. Autosomal recessive colorectal adenomatous polyposis due to inherited mutations of MYH. Lancet. 2003 Jul 5;362(9377):39-41.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12853198

- Sieber OM, Lipton L, Crabtree M, Heinimann K, Fidalgo P, Phillips RK, Bisgaard ML, Orntoft TF, Aaltonen LA, Hodgson SV, Thomas HJ, Tomlinson IP. Multiple colorectal adenomas, classic adenomatous polyposis, and germ-line mutations in MYH. N Engl J Med. 2003 Feb 27;348(9): 791-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12606733
- Wang L, Baudhuin LM, Boardman LA, Steenblock KJ, Petersen GM, Halling KC, French AJ, Johnson RA, Burgart LJ, Rabe K, Lindor NM, Thibodeau SN. MYH mutations in patients with attenuated and classic polyposis and with young-onset colorectal cancer without polyps. Gastroenterology. 2004 Jul;127(1):9-16. Erratum in: Gastroenterology. 2004 Nov;127(5):1651.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15236166

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/familial-adenomatous-polyposis

Reviewed: October 2013
Published: August 22, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services