

APC gene

Associated Syndrome Name: Familial adenomatous polyposis (FAP)/attenuated familial adenomatous polyposis (AFAP)

APC Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Colorectal	High Risk
Other	High Risk
Endocrine	Elevated Risk
Gastric	Elevated Risk

APC gene Overview

Familial adenomatous polyposis (FAP)/attenuated familial adenomatous polyposis (AFAP) ^{1, 2}

- Individuals with *APC* mutations have either familial adenomatous polyposis syndrome (FAP) or attenuated familial adenomatous polyposis syndrome (AFAP). The distinction between FAP and AFAP is based on the number of adenomatous polyps found in the patient, as described below.
- Patients with FAP/AFAP have a greatly increased risk for colorectal cancer, often at very young ages.
- Patients with FAP/AFAP are likely to develop large numbers of adenomatous polyps in the gastrointestinal (GI) system, particularly in the colon, rectum, stomach and small bowel. Patients with 100 or more polyps are said to have a diagnosis of FAP and patients with less than 100 polyps are said to have a diagnosis of AFAP. These polyps begin to form at an average age of 16, but can be found in individuals as young as age 7.
- Patients with FAP/AFAP also have a high risk for other cancers, most notably small bowel and periampullary cancer. There are also elevated risks for childhood hepatoblastoma, and cancers of the thyroid and central nervous system (CNS).
- Patients with FAP, and less commonly, patients with AFAP, can have clinical findings other than cancer, such as osteomas, dental abnormalities, congenital hypertrophy of the retinal pigment epithelium (CHRPE) and benign cutaneous lesions. Desmoid tumors, which occur in some individuals with FAP, are the most serious cause of morbidity among affected individuals outside of cancer, and may be triggered by abdominal surgery.
- Although there are high risks for cancer in patients with FAP/AFAP, these risks can be greatly reduced with appropriate medical management. Guidelines from the National Comprehensive Cancer Network (NCCN) are listed below. It is recommended that patients with *APC* mutations and a diagnosis of FAP or AFAP be managed by a multidisciplinary team with experience in the prevention and treatment of the complications associated with hereditary colorectal cancer conditions.

APC gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	FAP to age 21 ^{1, 2, 3}	7%	<0.1%
	FAP to age 50 ^{1, 2, 3}	93%	0.4%
	FAP to age 80 ^{1, 2, 3}	>99%	2.8%
	AFAP to age 80 ^{1, 2, 3}	>70%	2.8%
Other - Desmoid Tumors	To age 80 ^{2, 3}	10%-30%	<0.04%
Small Bowel/Periampullary	To age 80 ^{1, 2, 3}	4%-12%	0.2%
Hepatoblastoma	To age 5 ^{1, 2, 3}	1%-2%	<0.001%
Gastric	To age 80 ^{1, 2, 3, 4, 5}	1.3%, but significantly higher in Japanese and Korean populations	0.6%
Thyroid	To age 80 ^{3, 6, 7}	2.6%-8.5%	1.1%

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Central Nervous System	To age 80 ^{1, 2, 3}	1%	0.5%

APC Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Colorectal	Colonoscopy ¹	10 to 15 years	Annually
	Colorectal surgical evaluation and counseling. ^{1, 8}	Based on cancer diagnosis and/or polyp number, size and histology	NA
	Consider chemoprevention with NSAIDs to reduce adenoma burden after surgery. ¹	NA	NA
Other - Desmoid Tumors	Abdominal MRI or CT ¹	When symptoms are present	At least annually
Small Bowel/Periampullary	Upper endoscopy, with consideration of capsule endoscopy to visualize the entire small bowel ¹	20 to 25 years, or earlier if there is a family history of small bowel adenomas or cancer	Every 3 to 5 years
Hepatoblastoma	Consider liver palpation, abdominal ultrasound, and alpha-fetoprotein (AFP) measurement. ¹	Infancy	Every 3 to 6 months during first 5 years of life
Gastric	Consider screening for patients with high risk features ^{1, 5}	Individualized	Individualized
Thyroid	Thyroid ultrasound ¹	Late teens	Every 2 to 5 years, or consider more often if there is a family history of thyroid cancer
Central Nervous System	Patient education about the importance of quickly seeking attention for signs and symptoms of neurologic cancer ¹	Individualized	NA

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the APC gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

Children should be tested for APC gene mutations by age 10-15 years, when colon cancer screening should begin. If hepatoblastoma

screening is being performed, *APC* genetic testing could be done in infancy.¹

Approximately 20% of individuals with FAP/AFAP have not inherited the *APC* mutation from a parent. In these cases the mutation has developed spontaneously in that individual (a *de novo* mutation). Once this occurs, the children of that individual are each at 50% risk of inheriting the mutation.⁹

References

1. Gupta S, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal. V 1.2023. May 30. Available at <https://www.nccn.org>.
2. Yen, et al. *APC*-Associated Polyposis Conditions. 2022 May 12. In: Pagon RA, et al., editors. GeneReviews® [Internet]. PMID: 20301519.
3. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2023 Mar 24]. Available from <https://seer.cancer.gov/explorer/>.
4. Mankaney G, et al. Gastric cancer in FAP: a concerning rise in incidence. *Fam Cancer*. 2017 16:371-376. PMID: 28185118.
5. Ajani JA, et al. NCCN Clinical Practice Guidelines in Oncology®: Gastric Cancer. V 1.2023. Mar 10. Available at <https://www.nccn.org>.
6. Uchino S, Age- and Gender-Specific Risk of Thyroid Cancer in Patients With Familial Adenomatous Polyposis. *J Clin Endocrinol Metab*. 2016 101:4611-4617. PMID: 27623068.
7. Chenbhanich J, Prevalence of thyroid diseases in familial adenomatous polyposis: a systematic review and meta-analysis. *Fam Cancer*. 2019 18:53-62. PMID: 29663106.
8. Achatz MI, et al. Cancer Screening Recommendations and Clinical Management of Inherited Gastrointestinal Cancer Syndromes in Childhood. *Clin Cancer Res*. 2017 23:e107-e114. PMID: 28674119.
9. Aretz S, et al. Somatic *APC* mosaicism: a frequent cause of familial adenomatous polyposis (FAP). *Hum Mutat*. 2007 28:985-92. PMID: 17486639.

Last Updated on 31-Jan-2024