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
Other	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%
Thyroid	To age 80[3, 4, 5]	2.6%-8.5%	1.1%
Hepatoblastoma	To age 5[1, 2, 3]	1%-2%	<0.001%

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Gastric	To age 80[1, 2, 3, 6]	1.3%, but significantly higher in Japanese and Korean populations	0.6%
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, 7]	10 to 15 years	Annually
	Colorectal surgical evaluation and counseling.[1]	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	Patient education about the importance of quickly seeking medical attention for symptoms of desmoid tumors.[1]	Individualized	NA
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
Thyroid	Thyroid ultrasound[1, 7]	16 years	Every 2 to 5 years, or consider more often if there is a family history of thyroid cancer
Hepatoblastoma	Consider liver palpation, abdominal ultrasound, and alpha-fetoprotein (AFP) measurement.[1, 7]	Infancy	Every 3 to 6 months during first 5 to 7 years of life
Gastric	Consider screening for patients with high risk features.[1]	Individualized	Individualized
Central Nervous System	Patient education about the importance of quickly seeking attention for signs and symptoms of neurologic cancer[1]	Individualized	NA
	Physical examination[7]	Childhood	Annually

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 in childhood, 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.[8]

References

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