Updated December 2019 (NCCN v3.2019)

Familial Adenomatous Polyposis (FAP): *APC* Mutations

Cancer Risks and General Management Recommendations

***APC* Mutation Carrier Cancer Risks**	**General Population Lifetime Cancer Risks**	**Surveillance/Management Recommendations[1-3]**

<u>Colon Cancer</u>
100% (without intervention)
	4.5%	*Surveillance*
		• Colonoscopy (preferred) or flexible sigmoidoscopy every 12 months beginning at age 10-15
		Surgery
		• If a high polyp burden is found that cannot be handled endoscopically, or for those that are unable or unwilling to be followed with colonoscopy, surgery may be recommended.
		• The extent of colectomy may be modified based on the burden of adenoma distribution and number.
		  ○ Total Abdominal Colectomy with ileorectal anastomosis (TAC/IRA) is generally recommended for Attenuated Adenomatous Polyposis (AFAP). Patients that undergo this procedure should still undergo endoscopic evaluation of the rectum every 6-12 months depending on polyp burden.
		  ○ Total proctocolectomy with ileal pouch-anal anastomosis (TPC/IPAA) is generally recommended for FAP and can be considered if dense rectal polyposis is not manageable with polypectomy. Endoscopic evaluations of the ileal pouch are recommended every 1-3 years depending on polyp burden.
		• Management should be individualized to account for genotype, phenotype, and personal considerations.
		Chemoprevention
		• Chemoprevention may facilitate management of the remaining rectum post-surgery. There are no FDA-approved medications for this indication at present. While there are data to suggest that sulindac is the most potent polyp regression medication, it is not known if the decrease in polyp burden decreases cancer risk.

<u>Small Bowel (Duodenal/ Periampullary) Cancer</u>
 	
Small bowel cancer: 4-12%[1]
	<1%	*Surveillance*
		• Baseline upper endoscopy (including complete visualization of the ampulla of Vater) at age 20-25 years (or earlier if colectomy performed before age 20).
		• The frequency of upper endoscopy should be based on duodenoscopic findings/polyp burden. Cap-assisted endoscopy may be adequate for visualization of the ampulla.
		  ○ Stage 0, no polyposis: repeat every 4 years
		  ○ Stage 1, minimal polyposis (1-4 tubular adenomas, size 1-4mm): repeat every 2-3 years
		  ○ Stage 2, mild polyposis (5-19 tubular adenomas, size 5-9mm): repeat every 1-3 years
		  ○ Stage 3, moderate polyposis (>20 lesions, or size >1cm): repeat every 6-12 months

		○ Stage 4, dense polyposis or high grade dysplasia: surgical evaluation, expert surveillance every 3-6 months, complete mucosectomy or duodenectomy, or Whipple procedure if duodenal papilla is involved
Gastric Cancer *Fundic gland polyps*: approximately 50%[2] *Gastric adenomatous polyps*: 10% *Gastric cancer*: 0.5-1.3%[1]	<1%	*Management* • Fundic gland polyps occur in the majority of FAP patients and focal low grade dysplasia can occur but is typically non-progressive. For this reason, specialized surveillance or surgery should only be considered in the presence of high-grade histologic features or for people from geographic areas with high gastric cancer risk. • Patients with high risk gastric lesions that cannot be removed endoscopically should be referred to a specialized center for consideration of gastrectomy. *Surgery* • Endoscopic removal of duodenal adenomas is the standard of care. If polyps are not resectable endoscopically, surgical resection may be considered, particularly if the lesions are villous, larger than 1 cm and/or cause symptoms.
Thyroid Cancer 1-2%	1.3%	*Surveillance* • Annual thyroid examination beginning in the late teenage years. • Annual thyroid ultrasound can be considered, although high-level evidence to support this recommendation is lacking.
Pancreatic Cancer 2%	1.5%	*Surveillance* • No consensus guidelines for pancreatic cancer risk management. • Pancreatic cancer surveillance may be considered on an individual basis. Individuals may consider annual abdominal MRI, annual endoscopic ultrasound (EUS), or enrolling in research protocols to evaluate screening modalities for pancreatic cancer.
Hepatoblastoma 1-2% (from birth to age 5)		*Surveillance* • Liver palpation, abdominal ultrasound, and AFP blood tests every 3 to 6 months may be considered for children from birth to age 5. • Screening in a clinical trial is preferred, as there is limited data regarding these recommendations in FAP.
CNS Tumors <1%	<1%	*Surveillance* • Annual physical examination.
Intra-abdominal desmoids 10-30%[2]		*Surveillance* • Annual abdominal palpation is recommended. • If there are symptomatic desmoids in the family, consider abdominal MRI with and without contrast or CT with contrast within 1-3 years post-colectomy and then every 5-10 years. • Suggestive abdominal symptoms should prompt immediate imaging.

Other possible findings associated with classic FAP include congenital hypertrophy of retinal pigment epithelium (CHRPE), osteomas, supernumerary teeth, odontomas, and epidermoid cysts.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *APC* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- *APC* genetic testing should be performed in children by age 10, when colon cancer screening would be initiated. However, if there is intent to do hepatoblastoma screening, *APC* genetic testing should be considered in infancy.

- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

References

1. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal (v3.2019). 2019.
2. Achatz MI, Porter CC, Brugieres L, et al. (20170. Cancer Screening Recommendations and Clinical Management of Inherited Gastrointestinal Cancer Syndromes in Childhood. Clin Cancer Res: 23(13): e107-e14.
3. Jasperson, K., Patel, S.G. & Ahnen, A.J. (2017). APC Associated Polyposis Conditions. GeneReviews. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1345/