



Inherited Colorectal Cancer Syndromes

Disease	Notes
FAP (familial adenomatous polyposis) which includes typical FAP, Gardner syndrome, attenuated adenomatous polyposis coli and approximately two thirds of Turcot syndrome cases	Autosomal dominant inheritance of hundreds to thousands of colonic adenomatous polyps that appear at an average age of 16 years; colon cancer risk is 100% without colectomy; average age of cancer diagnosis is 39 years. Arises from mutations in the APC (adenomatous polyposis coli) gene; accounts for <0.5% of colon cancer cases; genetic testing available for diagnosis.
HNPCC (hereditary nonpolyposis colorectal cancer) also includes Muir-Torre syndrome and approximately one third of Turcot syndrome cases	Autosomal dominantly inherited colon cancer with an 80% lifetime risk and average age of diagnosis of 44 years; there is a 40%-60% risk of endometrial cancer; a 10%-20% risk of ovarian, gastric, and urinary tract cancer; and a 1%-5% risk of biliary, renal, small bowel and central nervous system cancer Arises from mutations in any 1 of 5 mismatch repair genes; HNPCC accounts for 2%-3% of colon cancer cases; genetic testing available for diagnosis The clinical diagnosis of HNPCC is often based on the Amsterdam Criteria: 1) three relatives must have colon cancer, two of them being first-degree relatives of the third; 2) at least two generations must be affected with colon cancer; and, 3) at least one case of colon cancer must have been diagnosed at age <50. Genetic testing should be done on an index case in families meeting these criteria, but also in families with a strong family history of colon and other relevant cancers.
Peutz-Jeghers syndrome	Perioral melanin pigment spots and frequent histologically characteristic polyps of small bowel, colon, and stomach. Approximately 39% colon cancer risk, usually after age 30. Also significant cancer risk of the pancreas, stomach, small bowel, breast, ovary, uterus, and lung. Arises from mutations of <i>STK11</i> gene; incidence approximately 1 in 200,000; genetic testing available for diagnosis.
Juvenile polyps	Juvenile polyps throughout the bowel, particularly in the colon; benign complications before age 30, but high risk of colon cancer after that age. Arises from mutations of the <i>SMAD4</i> , <i>BMPR1A</i> or <i>PTEN</i> genes; frequency approximately 1 in 100,000; genetic testing available for diagnosis.
Gardner syndrome: FAP associated with osteomas, epidermoid cysts, fibromas, dental abnormalities, and desmoid tumors.	
Turcot's syndrome: FAP or HNPCC and brain tumors (medulloblastomas and gliomas).	
Muir-Torre syndrome: Sebaceous gland tumors with or without keratoacanthomas associated with visceral malignancy.	

Adapted from *Physicians Information and Education Resource (PIER)*, Colorectal Cancer module.