Clinical features

Familial adenomatous polyposis (FAP) is a cancer predisposition syndrome and includes a milder, attenuated form (AFAP) of the disease. Individuals with FAP develop hundreds to thousands of adenomatous polyps in their colon, sometimes beginning in childhood. Without surgical intervention, they have nearly a 100% risk of developing colorectal cancer by age 45. Individuals who have AFAP generally develop 100 or fewer polyps in their lifetime. They have a lower risk of colorectal cancer (approximately 70%) than individuals who have classic FAP.

Individuals with FAP/AFAP also have an increased risk for other cancers, including upper gastrointestinal tract tumors, pancreatic, thyroid, central nervous system, and liver (hepatoblastoma in children under age 5) cancer. Non-cancer features include congenital hypertrophy of the retinal pigment epithelium (CHRPE), desmoid tumors, osteomas, dental abnormalities, gastric fundic gland polyps, and gastric and duodenal adenomas.

Lifetime cancer risks associated with FAP

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>FAP Risk</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>up to 100%</td>
<td>5%</td>
</tr>
<tr>
<td>Duodenum</td>
<td>5-12%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.7%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Hepatoblastoma</td>
<td>1.6%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

Prevalence of FAP

FAP is a rare condition affecting approximately 1 in 5,000 to 10,000 individuals. FAP accounts for about 0.5% of colorectal cancer cases.

Diagnosis

An individual should meet clinical criteria or have a mutation that is identified by molecular genetic testing of the APC gene.

Clinical criteria

A clinical diagnosis of FAP can be made if an individual has 100 or more adenomatous colon polyps diagnosed before age 40.

There are no clinical diagnostic criteria for AFAP. Generally, a clinical diagnosis is suspected when an individual has between 10 and 99 adenomatous colon polyps, or more than 100 polyps diagnosed at an older age than that expected for FAP (age 35–40 or older).

Genetics & inheritance

FAP/AFAP is an autosomal dominant condition caused by a mutation in APC. First-degree relatives of an APC mutation carrier have a 50% chance of also carrying the mutation. Men and women are equally likely to inherit, and pass on, a mutation. Seventy percent of cases are familial or inherited and 30% of cases are de novo, or sporadic, mutations.

Clinical testing

Clinical testing includes gene sequencing and deletion/duplication analysis of APC. Gene sequencing will identify up to 90% of individuals with FAP/AFAP, and deletion/duplication testing an addition 8-12%.
Management

Colectomy is recommended for individuals with advanced polyposis. Until then, or if the individual declines colectomy, increased colorectal and gastrointestinal surveillance (colonoscopy and esophagogastroduodenoscopy) are recommended. Screening should also include evaluation for extra-intestinal manifestations. Published guidelines with age-specific management recommendations are available (see below).

Other genes that contribute to polyposis

There are other hereditary cancer syndromes that increase the risk for polyps and colorectal cancer, including MUYTH-associated polyposis (MAP), juvenile polyposis syndrome, Peutz-Jeghers syndrome, and Cowden syndrome. The presentation of these syndromes in a family may overlap with that of FAP/AFAP, but can sometimes be distinguished based on characteristic features, such as physical exam findings and polyp pathology. In addition, a number of common genetic susceptibility variants are thought to increase polyp and colorectal cancer risk beyond APC. There are likely other genes that contribute to polyp development which have not yet been identified. See GeneReviews for more information about the genetic differential diagnosis for FAP.

Select guidelines & resources

Resources
GeneReviews (2014): APC-Associated Polyposis Conditions
American Society of Clinical Oncology (2014): Familial Adenomatous Polyposis and Attenuated Familial Adenomatous Polyposis
National Cancer Institute (2015): Genetics of Colorectal Cancer PDQ – Major Genetic Syndromes

Guidelines