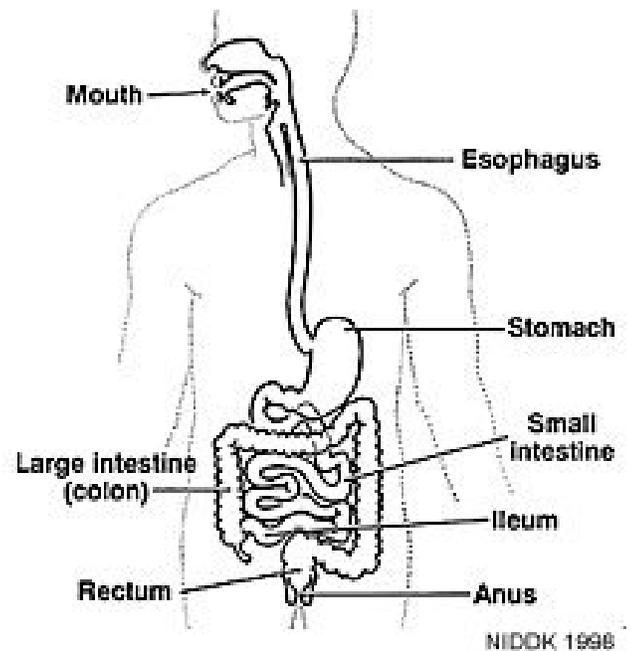


Familial Adenomatous Polyposis (FAP)

What is familial adenomatous polyposis (FAP)?

Familial adenomatous polyposis (FAP) is a genetic condition where affected individuals will develop hundreds to thousands of polyps (abnormal, mushroom-like growths) throughout their gastrointestinal (GI) tract beginning at a young age (usually as a teenager or young adult). These polyps are usually found in the large intestine (colon and rectum), but they can develop in the stomach and small intestine as well. The polyps that form in the large intestine are known as adenomas. Adenomas are considered to be precancerous. In addition, individuals with FAP may also develop other features outside of the gastrointestinal tract.

Attenuated FAP (AFAP) is a milder form of FAP. People with AFAP also develop precancerous polyps throughout the GI tract; however, the polyps in the colon tend to be fewer in number, usually less than 100.



Gastrointestinal Tract

Since people with FAP or AFAP develop many precancerous polyps in the colon and rectum, they have an increased chance that one or more of the polyps may develop into cancer of the large intestine (also known as colon cancer, colorectal cancer, or rectal cancer).

What causes FAP?

FAP is caused by an inherited gene change (mutation) in the Adenomatous Polyposis Coli (APC) gene. Genes are the biologic unit of heredity that give us our hair and eye color, the shape of our nose, our blood type, and the number of fingers and toes we have. If the APC gene carries the correct biologic information, it helps protect the colon from developing polyps and cancer. If a mutation occurs in the APC gene, precancerous polyps will develop because the APC gene is no longer functioning properly and the colon is not protected.

Most of the time, FAP is passed on to a child from the parent who has the condition. If the APC gene mutation is passed on to a child, he or she will inherit FAP. It is important to remember that parents do not have control over which genes are passed on to their children, and that

passing on the APC gene mutation occurs by chance. In about one-third (33%) of all cases, people develop FAP even though their parents do not have FAP. When this occurs, it is due to a new gene alteration, or mutation, and it occurs by chance.

What are my chances of inheriting FAP?

If a parent has FAP, each child has a 50% (or, 1 in 2) chance of inheriting FAP. Each child also has a 50% chance of not inheriting FAP. FAP does not skip generations. Both males and females are equally likely to be affected. Therefore, if you have FAP, your children each have a 1 in 2 chance of having FAP.

What are the signs and symptoms of polyps?

Signs and symptoms are rare with the early development of polyps. However, as polyps grow, multiply, and become cancerous over time, the following may occur:

- Bright red blood in the stool
- Thin stools
- Diarrhea and/or constipation that cannot be explained by diet or illness
- Abdominal pain, cramping, or bloating
- Continued weight loss
- Continued lack of energy
- Anemia

If a parent has FAP or AFAP, it **is not** safe to wait for symptoms to occur in their children before having them checked for FAP by a doctor. Parents who have FAP should first have their children checked when they are between 10 and 12 years old. Children of parents with AFAP should typically begin checking for polyps at age 18, although they may begin earlier depending on when other family members were diagnosed with polyps or colorectal cancer. For families with AFAP, it is important to talk with a healthcare provider familiar with AFAP to determine when screening should begin. It is extremely important that parents with FAP or AFAP have their children checked early, because polyps can occur at a young age. Genetic testing is an ideal way to find out if a child has FAP. Genetic testing is explained in the “Are there other ways of diagnosing FAP?” section of this document.

Are there other signs or features of FAP?

Individuals with FAP and AFAP may develop polyps in other parts of the GI tract. Almost all individuals with FAP and many individuals with AFAP will develop polyps in the stomach called fundic gland polyps. The chance that a fundic gland polyp will develop into stomach cancer is very low, but it is important to have your stomach checked regularly to monitor the fundic gland polyps.

Additionally, individuals with FAP and AFAP can develop polyps in the small intestine, particularly in the duodenum (the first part of the small intestine). Sometimes the polyps can

occur on the ampulla of Vater, which is an opening in the duodenum where bile and pancreatic juices enter to help in the digestion of food. These polyps are called adenomas and are considered to be precancerous because they have a small chance (about 4-12%) to develop into cancer. It is very important that individuals with FAP and AFAP have their duodenum checked regularly to monitor for polyps.

In addition to polyps in the GI tract, people with FAP may have other signs of FAP. These include lumps or bumps on the skull and jaw (osteomas); cysts on the skin (epidermoid cysts); dental changes (extra teeth); non-cancerous tumors most often found in the abdomen (desmoid tumors); and freckle-like spots on the inside of the eye (CHRPE). Previously, individuals with FAP who had these other features were considered to have Gardner's syndrome. We now know that Gardner's syndrome and FAP are the same condition.

Individuals with FAP do have an increased chance of developing certain other cancers. These include thyroid cancer, brain cancer (called medulloblastoma), and liver cancer in children (known as hepatoblastoma). However, most of these cancers are rare even in FAP and most people with FAP will not develop them. These other signs of FAP vary considerably among individuals both between and within families.

How is FAP diagnosed?

There are several tests that can be used to diagnose FAP. These tests include genetic testing, flexible sigmoidoscopy and colonoscopy. With each test, the nurse or doctor will instruct the patient about what to do to prepare for the test. Individuals with a family history of FAP should begin annual colon evaluation at 10-12 years of age. People with a family history of AFAP should begin colon evaluation by 18 years of age, or earlier based on family history. The following options should be discussed with a physician.

Genetic testing can be used to help diagnose FAP. With genetic testing, a small blood sample is taken from the individual with FAP and is sent to a special laboratory that studies the APC gene. About 80% of the time a change (also called an alteration or mutation) in the APC gene that leads to FAP is found. Genetic testing is useful in confirming a diagnosis of FAP in those rare cases where there is some doubt about the diagnosis. Once an individual is confirmed to have an APC gene mutation, genetic testing can help identify whether or not family members have FAP. Family members who do not have the APC gene mutation, did not inherit FAP. Therefore, they do not need to undergo screening procedures recommended for individuals with FAP. Genetic testing is recommended beginning at 10-12 years of age in families with FAP, which is also the age when screening for FAP should start. In families with AFAP, genetic testing is recommended beginning at 18 years of age, or earlier based on family history, which is also the age when screening for AFAP should start. Most people find it helpful to meet with a genetic counselor to talk about genetic testing.

A **flexible sigmoidoscopy** is an examination of the rectum and the lower colon through a sigmoidoscope. The sigmoidoscope is a small flexible tube with a light on one end, which allows the doctor to examine the inner lining of the lower part of the colon and rectum after inserting it

through the anus. Prior to the exam, a sedative may be given to help the patient relax. During the exam, the doctor may take a small amount of tissue (biopsy) from the polyps for examination under a microscope.

A **colonoscopy** is a test in which the doctor looks at the inner lining of the large intestine (colon and rectum). This is done using an instrument called a colonoscope. A colonoscope is similar to the flexible sigmoidoscope, but longer. Prior to the colonoscopy, a sedative will be given to help the patient relax. Most people sleep through this procedure and feel little or no discomfort during this test. During the colonoscopy, the doctor may take a biopsy from the polyps for examination under a microscope. This is the recommended method of screening for families with AFAP.

Both the flexible sigmoidoscopy and colonoscopy require that the colon be cleaned out ahead of time. The patient cleans out the colon by drinking a large volume of liquid laxative. The liquid laxative causes a temporary, overnight diarrhea.

Why is early diagnosis important?

Early diagnosis of FAP is important for early detection and prevention of cancer. Cancer in FAP develops when cells in a polyp begin to grow out of control. People who are diagnosed with FAP are at risk for developing colon cancer. When multiple precancerous polyps are detected, it is treated by removing the colon before cancer occurs.

How is FAP managed?

If you are diagnosed with FAP, your doctor will discuss medical management options with you. Medical management options include regular examination of the colon and rectum for polyps, medication, and surgery.

Surveillance

Colon Polyps and Colorectal Cancer

A surveillance examination at regular intervals is very important. Beginning at age 10-12 years a flexible sigmoidoscopy is recommended every year for individuals with FAP. Once colon polyps are found, or by age 20-25 years, colonoscopy with chromoendoscopy (dye spray) should be completed every year. Individuals with AFAP are recommended to undergo a colonoscopy beginning at age 18 years, or earlier based on family history, and repeated every year. If present, precancerous polyps are removed during the colonoscopy **before** they develop into cancer, unless they are too numerous or too large to remove.

Upper Intestinal Polyps and Cancer

Surveillance of the upper GI tract is also very important for people with FAP or AFAP. Upper endoscopy exam (also called an EGD) should be performed every 1-3 years for monitoring of fundic gland (stomach) polyps and duodenal (first part of the small intestine) adenomas. A side-viewing scope is also recommended for viewing of the ampulla of Vater,

which is a common location for polyps in the duodenum. Most individuals are recommended to start having EGD at age 20-25 years, or just prior to colorectal surgery.

Additional Surveillance for FAP

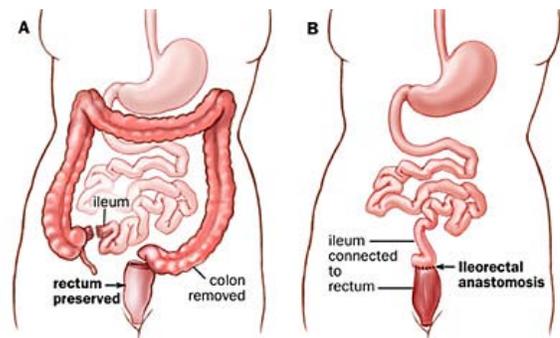
- Annual complete physical exam to monitor for extra-intestinal features of FAP.
- Annual thyroid examination, including thyroid palpation.
- Some families may also consider screening of young children, from birth to age 5 years, for hepatoblastoma (liver cancer) which includes annual physical exam and/or abdominal ultrasound exam and measurement of AFP.
- An abdominal ultrasound or CT scan is recommended prior to abdominal surgery to evaluate for desmoid tumors.

Surgery

Since individuals with FAP develop too many precancerous colon polyps to remove them one by one, colon surgery is recommended to help prevent the development of cancer. The timing of surgery can vary among family members who have FAP or AFAP. Once surgery is recommended for you, it means that removing the colon is the only way to prevent the development of colon cancer. If colon surgery is not performed, studies indicate all patients with FAP will develop colorectal cancer. Because the colon and rectum are affected, most people having colon surgery will have most of the colon and/or rectum removed rather than only part of the colon or rectum, to reduce the risk of developing a colorectal cancer. The three most common types of colon surgery are described below. The choice of procedure depends on various factors including, but not limited to: the number of rectal polyps, presence or absence of colorectal cancer, age of the patient, history of desmoids tumors, and patient preference.

Colectomy with Ileorectostomy (Ileorectal Anastomosis)

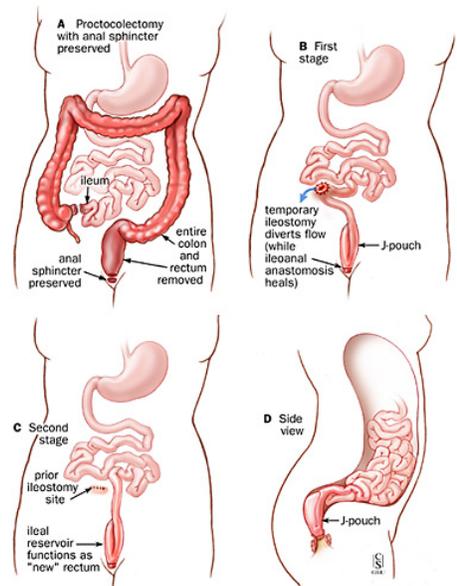
In this procedure, the colon is removed, but all or most of the rectum is left in place. The small intestine is attached to the upper portion of the rectum. The advantage of this procedure is that it is the least complicated operation. Most patients maintain very good bowel function, though anti-diarrhea medications are sometimes needed. This procedure is typically recommended when there are very few polyps in the rectum.



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Restorative Proctocolectomy (Ileal Pouch Anal Anastomosis)

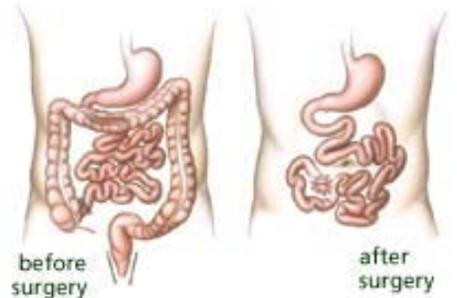
This operation involves removing the entire colon and most of the rectum. A new rectum, or reservoir for stool, called a pouch, is made out of the lower end of the small intestine (ileum). The pouch is joined to the anus so bowel movements can flow in the normal way. A temporary ileostomy, or a stoma where the waste empties into a bag through the abdominal wall, is usually needed to help heal this delicate connection. The temporary ileostomy is then removed during a second less involved surgery about 8-10 weeks after the first surgery. This surgery is typically recommended when there are many polyps in the rectum.



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Total Proctocolectomy With Ileostomy

This operation involves removing the entire colon and rectum. The end of the small bowel (ileum) is brought to the surface of the abdomen, where it is permanently stitched into place. This is called an end ileostomy. Because the rectum is removed, it is not possible to control bowel functions in the normal way. Liquid stool will come out of the ileostomy into a bag that is securely attached onto the skin of the abdomen. People go on to live normal lives after this type of surgery. An ileostomy should not be viewed as a handicap. Fortunately, few people need to have this kind of operation today.



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All three operations involve removing all or most of the colon. After a detailed discussion of these operations, the patient and doctor can decide which one is best.

After Surgery

After the first surgery for FAP, the following check-ups are recommended:

- Complete physical exam **yearly**.
- Flexible sigmoidoscopy:
 - **Every 6-12 months** for a patient whose rectum has not been removed for the first few years. If the rectum remains relatively free of polyps, patients may be recommended to come back every 1-2 years.
 - **Every 1-2 years** for patients with an ileoanal pouch, and patients whose polyps do not return.

- Ileostomy surveillance:
 - **Every 1-3 years** for patients with an ileostomy. It is important that the stoma (the opening in the abdominal wall) be looked at closely.
- Upper endoscopy (EGD) with side-viewing scope **every 1-3 years**.

Are there other ways of treating FAP?

After surgery, polyps can occur in the remaining portion of the rectum. To treat these polyps, patients will have regular endoscopic examinations of the rectum or the ileal pouch and may receive a prescription for medications that will help reduce the risk of polyps returning. These anti-inflammatory medications, or nonsteroidal anti-inflammatory drugs (NSAIDs), include Sulindac (Clinoril[®]) or Celecoxib (Celebrex[®]). However, treatment with these medications will not replace endoscopy or surgery if it is needed.

Researchers are working to find medications that reduce the size and number of polyps, as well as prevent polyps from occurring. The ultimate goal is to treat FAP with medication(s) rather than surgery. Several studies, including some studies done at MD Anderson Cancer Center, have already been completed and have found that NSAIDs decrease the formation of polyps. Medications such as Celecoxib are approved by the Food and Drug Administration (FDA) for treatment of polyps, but are not a substitute for endoscopy or surgery. However, clinical trials and further research still need to be done in this area. Chemoprevention is one of the main focuses of the researchers at MD Anderson Cancer Center. There are several clinical trials open for recruitment. These clinical trials are described below:

What are clinical trials?

Clinical trials are carefully designed and controlled human research studies that test new ways to treat or prevent specific diseases. They often involve the evaluation of a new drug or a new combination of existing drugs. Some clinical trials compare the best known standard therapy with a newer therapy to see if one produces a better outcome or causes fewer side effects than the other therapy.

What research studies are available at MD Anderson Cancer Center?

Adult Clinical Trial

MD Anderson Cancer Center is currently enrolling participants in the “Familial Adenomatous Polyposis Prevention Trial.” This is a clinical trial for individuals diagnosed with FAP. The goal is to see if two medications used together, versus one medication used alone, will have a better chance of reducing the size and number of polyps. In the trial, Celecoxib, an anti-inflammatory drug, will be used by participants in combination with a drug called DFMO (difluoromethylornithine). Other participants will take Celecoxib with a placebo (sugar pill). The clinical trial researchers will then compare the size and number of polyps in these two groups of participants before and after they receive 6 months of treatment with these medications.

Adult Clinical Trial Contact Information

Phone: 713-563-4390 or 1-888-502-8446

Fax: 713-563-9740

E-mail: FAPteam@mdanderson.org

Pediatric Clinical Trial

MD Anderson Cancer Center is enrolling patients in the “Pediatric Adenomatous Polyposis Chemoprevention Trial.” This is a clinical trial for children between the ages of 10-17 years diagnosed with FAP. The goal is to study the effectiveness of Celecoxib in preventing or reducing the number of polyps in children. In the trial, one group of children will receive Celecoxib and a second group of children will receive a placebo (sugar pill) for up to 5 years. Children in both groups will undergo a colonoscopy each year that they are on the study and clinical researchers will compare the size and number of polyps in these two groups of children.

Pediatric Clinical Trial Contact Information

Phone: 713-563-4390 or 1-888-502-8446

Fax: 713-563-9740

E-mail: FAPteam@mdanderson.org

MyFAP - A Web-based Intervention Study for Teens and Young Adults with FAP

MD Anderson is recruiting teens and young adults age 13 to 24 years old for MyFAP, a study to develop and evaluate a Web-based intervention for young persons facing FAP. The goal of this study is to develop and evaluate an interactive, multimedia Web site, MyFAP, that will provide information and support to young persons with FAP. Study participants will review and provide feedback regarding the content, usability and overall design of the Web site.

MyFAP Contact Information

Rebecca Yzquierdo, BS

Phone: 713-792-0215 or 1-800-472-4376

E-mail: ryzquier@mdanderson.org

What is the FAP Registry?

Researchers at MD Anderson have created a registry for individuals and families affected by FAP. Joining the registry involves completing a family history questionnaire, providing personal health information, and giving permission to be contacted yearly. The registry coordinator will contact individuals yearly, to update this information. All information submitted to the registry will remain confidential. When joining this registry, you agree to be contacted about new clinical trials.

If you would like more information about the FAP registry or clinic services available for FAP at MD Anderson Cancer Center, please contact:

FAP Registry Contact Information

Phone: 1-888-502-8446

Fax: (713) 563-9740

E-mail: FAPteam@mdanderson.org

Where can I find information about FAP?

The University of Texas MD Anderson Cancer Center Clinical Cancer Genetics Program

<http://www.mdanderson.org/departments/ccg/>

The Clinical Cancer Genetics Program at MD Anderson Cancer Center is dedicated to providing hereditary cancer risk assessment and consultation services. Click on the links for “Hereditary Cancer Predisposition Syndromes and Resources & Links” to learn more about FAP and general information on cancer genetics.

Cancer.net

<http://www.plwc.org/>

Oncologist-approved cancer information from the American Society of Clinical Oncology. Click on the link in the center of the page “For Patients, Families, and Friends.” Then, on the left hand side of the page, click on the link for “Learning About Cancer,” then click on the link for “Genetics” to learn more about the Genetics of Colorectal Cancer and FAP.

Desmoid Tumor Research Foundation

<http://www.dtrf.org/>

The Desmoid Tumor Research Foundation seeks to advance the science related to desmoid tumors by: funding research related to the diagnosis and treatment of desmoid tumors, providing informational support for desmoid tumor patients and their families and friends, and heightening awareness of desmoid tumor diagnosis and treatment.

Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA)

<http://www.cgaicc.com/>

The CGA focuses on families with rare forms of colorectal cancer, including FAP.

National Cancer Institute (NCI)

Genetics of Colorectal Cancer

<http://www.cancer.gov/cancertopics/pdq/genetics/colorectal/healthprofessional>

1-800- 4-CANCER or 1-800-422-6237

Click on the link on the left hand side of the page to access more information on FAP.

Support Groups for Individuals and Families

Title: Yahoo! Groups FAP/Gardners Syndrome
URL: <http://groups.yahoo.com/group/gardnerssyndrome/>
Description: Yahoo! Groups runs an online support group for people with FAP.

Title: IMPACC (Intestinal Multiple Polyposis and Colorectal Cancer)
Address: P.O. Box 11
Conyngham, Pennsylvania 18219
Telephone: 570-788-1818 or 570-788-3712
Fax: 570-788-4046
Email: impacc@epix.net
Description: IMPACC is a support group for families with FAP and/or hereditary colon cancer.

Title: UOA (United Ostomy Association)
URL: <http://uoa.org>
Address: National Headquarters
19772 MacArthur Blvd., Suite 200
Irvine, California 92612-2405
Telephone: 1-800-826-0826
Email: info@uoa.org
Description: The UOA is a national volunteer-based organization. More than 500 chapters are made up of people with ostomies whose goal is to provide mutual aid, moral support, and education to those who have had colostomy or ileostomy surgery. Check the telephone directory for your local chapter.