Familial Adenomatous Polyposis (FAP)

Familial adenomatous polyposis (FAP) is a genetic condition that causes hundreds to thousands of polyps (abnormal, mushroom-like growths) to develop in the gastrointestinal (GI) tract. See Figure 1. In people who have FAP, the polyps begin developing 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.

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).

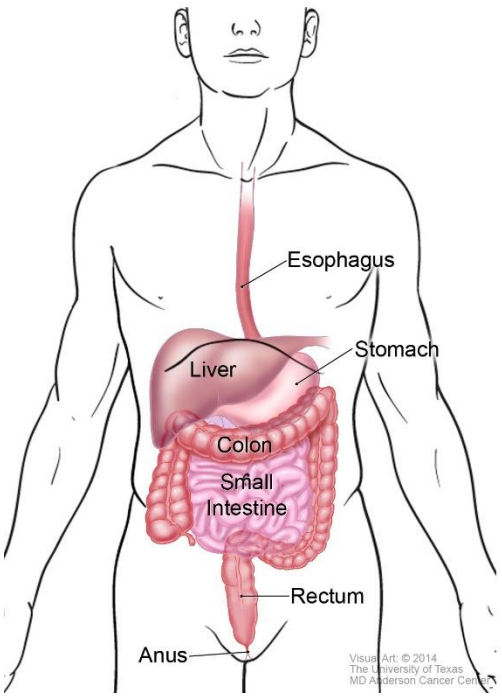

Figure 1
Organs in the Gastrointestinal Tract

What causes FAP?

FAP is caused by an inherited gene change (mutation) in the *APC* gene. Genes are the set of instructions that tell all of the cells in our bodies what to do. Genes determine our hair and eye color, the shape of our nose and our blood type. When the *APC* gene is working properly, it helps protect the colon from developing polyps and cancer. A mutation in the *APC* gene can cause the gene to stop working properly. In the case of FAP, precancerous polyps will develop because the *APC* gene is no longer functioning correctly 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. Passing on the *APC* gene mutation occurs by chance. In about one-quarter (25%) of all cases, people develop FAP even though their parents do not have FAP. When this occurs, it is due to a new gene mutation happening 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. Checking for FAP is done usually by genetic testing for the *APC* mutation in the family. Parents who have FAP should first have their children checked between ages 10 and 12. 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 on page 3.

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 these polyps.

Individuals with FAP and AFAP also 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)
- 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. People with FAP 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. People with a family history of FAP should begin annual colon evaluation at age 10-12. People with a family history of AFAP should begin colon evaluation by age 18 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 person with FAP and is sent to a special laboratory that studies the *APC* gene. A mutation in the *APC* gene that leads to FAP is found in about 90% or more of cases 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 age 10-12 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 age 18, 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 exam 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. Before the exam, a sedative may be given to help relax the patient. During the exam, the doctor may take a small amount of tissue (biopsy) from the polyps to view 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. Before 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 the colonoscopy, the doctor may take a biopsy from the polyps for to view under a microscope. This is the recommended method of screening for families with AFAP.

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 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. These options include medicine, surgery and regular exams of the colon and rectum for polyps,

Surveillance

The fundamental purpose of surveillance is preventing cancer through the detection and removal of polyps and polyp formation. Surveillance exams at regular intervals are very important for FAP.

Colon Polyps and Colorectal Cancer

Beginning at age 10-12 a flexible sigmoidoscopy is recommended yearly for people with FAP. Once colon polyps are found, or by age 20-25, a special colonoscopy should be completed every year. People with AFAP should consider having a yearly colonoscopy beginning at age 18, or earlier based on family history. 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 to monitor for fundic gland (stomach) polyps and duodenal (first part of the small intestine) adenomas. A side-viewing scope is also recommended for viewing the ampulla of Vater, which is a common location for polyps in the duodenum. Doctors often recommended having an EGD at age 20-25 or just prior to colorectal surgery.

Additional Surveillance for FAP

- Annual complete physical exam to monitor for extra-intestinal features of FAP
- Annual complete thyroid exam
- Some families may also consider screening of young children, from birth to age 5, for hepatoblastoma (liver cancer) which includes annual physical exam and/or abdominal ultrasound exam and measurement of AFP.

- An abdominal ultrasound or computerized tomography (CT) scan is recommended prior to abdominal surgery to check for desmoid tumors

Surgery

Since people with FAP develop too many precancerous colon polyps to remove one by one, colon surgery is recommended to help prevent cancer. The timing of surgery can vary among family members who have FAP or AFAP. When doctors recommend surgery, it means that removing the colon is the only way to prevent 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 those below.

- The number of rectal polyps
- Presence or absence of colorectal cancer
- Age of the patient
- History of desmoids tumors
- 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. See Figure 2. 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.

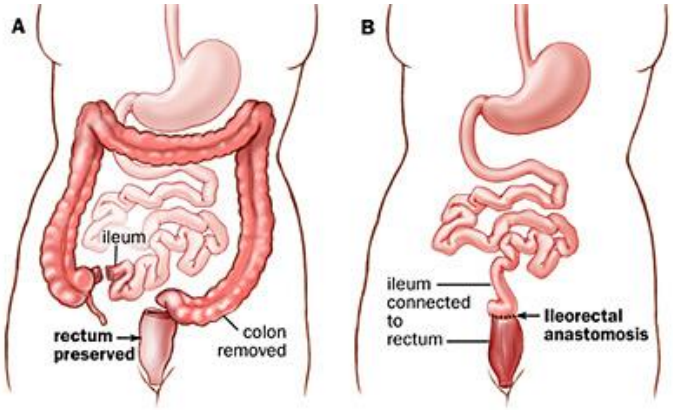

Figure 2

Figures 2 and 3
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Restorative Proctocolectomy (Ileal Pouch Anal Anastomosis)
This operation involves removing the entire colon and most of the rectum. See Figure 3. 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.

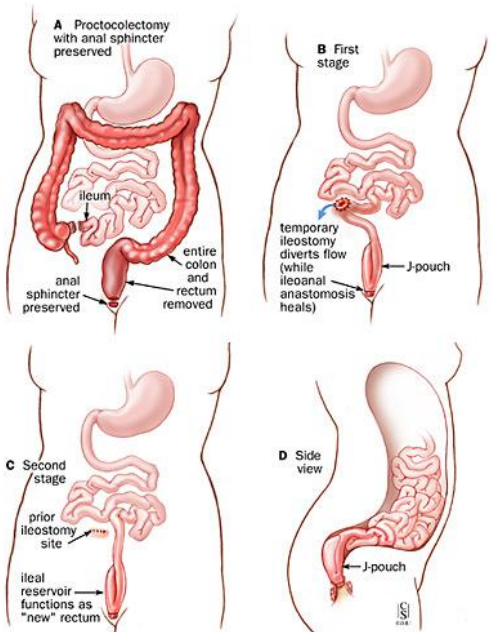

Figure 3

Total Proctocolectomy With Ileostomy
This operation involves removing the entire colon and rectum. See Figure 4. 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.

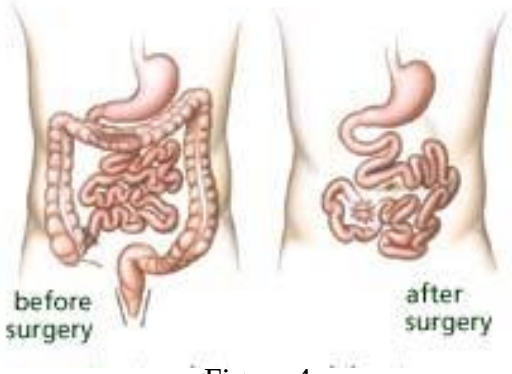

Figure 4
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All three operations involve removing all or most of the colon. After a detailed discussion, the patient and doctor can decide which surgery is best.

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 exams of the rectum or the ileal pouch and may receive a prescription medicines that will help reduce the risk of polyps returning. These anti-inflammatory medicines, or nonsteroidal anti-inflammatory drugs (NSAIDs), include Sulindac (Clinoril®) or Celecoxib (Celebrex®). However, treatment with these medicines will not replace endoscopy or surgery if it is needed.

Researchers are working to find medicines that reduce the size and number of polyps, as well as prevent polyps from occurring. The ultimate goal is to treat FAP with medicine rather than surgery. Several studies, including some done at MD Anderson, have found that NSAIDs decrease polyp formation. Medicines such 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.

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. MD Anderson has hosted many clinical trials for FAP in the past. Ask your doctor or genetic counselor for information about current clinical trials at MD Anderson.

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 provides 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/
This website of the American Society of Clinical Oncology provides cancer information.

Desmoid Tumor Research Foundation
http://www.dtrf.org/
The Desmoid Tumor Research Foundation seeks to advance the science related to desmoid tumors.

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
800-4-CANCER or 800-422-6237
Click on the link on the left hand side of the page to access more information on FAP.