Cancer and Genes

*Genes* are pieces of DNA code that direct cell growth and reproduction. A *mutation* is a change or error that may occur in a gene, causing it to malfunction. When certain cell growth genes become mutated, the cell can grow and develop into cancer. Some genes work to repair common errors that occur in other genes. If these *repair genes* do not work these errors are not corrected, and the cell can develop into a cancer.

Most of these gene mutations are *random* events that occur more frequently as we age, however up to 15% of all cancers are due to *inherited* gene changes that are passed from parent to child. People with these inherited gene mutations have a higher risk of cancer.

Hereditary Colon Cancer

The most common types of inherited colon cancer include:

- Familial Adenomatous Polyposis (FAP)
- MutYH-associated polyposis (MAP)
- Serrated polyposis syndrome (SPS), and
- Nonpolyposis Colorectal Cancer (HNPCC), also known as Lynch syndrome.

**Familial Adenomatous Polyposis (FAP)**

- FAP is caused by an inherited mutation in the adenomatous polyposis coli (APC) gene. The healthy, unchanged APC gene protects the colon from developing polyps (mushroom-like growths) that can develop into cancer.
- Inheritance is *autosomal dominant* meaning if one gene of the two normally present is mutated, the disease will develop. Therefore, 50% of children of a single parent with FAP will be affected.
- Individuals with FAP develop hundreds to thousands of polyps throughout the digestive tract usually starting in their teens. Most of these polyps are in the colon and rectum and the duodenum (upper small intestine).
- These polyps arise from the cells that line the intestine (mucosa); they are called adenomas. Adenomas are precancerous, meaning that they have a high risk of becoming cancer if they are not removed.
- Because people with FAP have so many adenomas in the colon and rectum, they have a high risk that one or more of the adenomas will develop into cancer. Most patients with FAP develop cancer by the age of 40.
Attenuated FAP is a form of FAP with slightly different changes in the APC gene. People with this mutation form between 10 and 100 colonic polyps.

MutYH-associated polyposis (MAP)
- MAP is caused by an inherited mutation in the MutYH gene, another DNA repair gene.
- Inheritance is autosomal recessive meaning both of the two copies of the gene must be mutated before the disease develops. Therefore, both parents must carry the mutation, and 25% of their children will develop the disease.
- MAP is often confused with attenuated FAP because of the number of polyps (10-30).
- Polyps are found in people in their 40s-50s.
- 50% of those affected will have colorectal cancer when diagnosed.
- Most people will develop colon cancer by 65.

Serrated Polyposis Syndrome (SPS)
- This is a rare and only recently described form of inherited colon cancer.
- Patients typically present with large polyps and/or colon cancer in the right colon.
- Serrated Polyposis is defined as
  - more than 20 serrated polyps anywhere in the colon,
  - greater than 5 serrated polyps with 2 or more larger than 1 cm, or
  - any number of serrated polyps in a person with a primary relative with SPS.
- There is an increased risk of developing cancer by age 55, but the rate is not known.
- Family members are at increased risk but the rate is not known.
- The inheritance pattern is not yet clear.

Nonpolyposis Colorectal Cancer (HNPCC) or Lynch syndrome
- Nonpolyposis Colorectal Cancer (HNPCC), also known as Lynch syndrome, is caused by an inherited change in one of several mismatch repair genes including the MLH1, MSH2, MSH6, PSM2, and EPCAM genes.
- People with Lynch syndrome have a 60-80% lifetime risk of colon cancer, often before the age of 50.
- Women with Lynch syndrome have a 40-60% lifetime risk of endometrial (uterine) cancer.
- Ovarian, stomach, urinary tract, liver and bile duct, small intestine, skin, and brain cancers may also occur as part of Lynch syndrome.
- HNPCC may be suspected in a person with more than one colorectal or related cancer, a first-degree relative with colon cancer who is less than 50 years old, or more than one first-degree or second-degree relatives with colon or related cancers, regardless of age.

Diagnosing Hereditary Colon Cancer

Symptoms
Early polyps rarely cause symptoms. Colon cancer may produce bright red blood in the stool, thin stools, prolonged diarrhea or constipation, abdominal pain, cramping, bloating, urge to have a bowel movement when there is no need, and unexplained weight loss.

Genetic Testing
People who have a personal or family history of early-onset colon cancer or other related cancers may benefit from genetic testing. A genetics professional can help determine whether you should be tested.
Genetic testing is performed by taking a small blood sample which is analyzed for gene mutations. Genetic counseling is provided as needed.

Screening and Management of Hereditary Colon Cancer

Genetic testing is important for people who may have inherited colon cancer syndromes because life-saving intervention is available when timely applied.

**Familial Adenomatous Polyposis (FAP)**
- Yearly flexible sigmoidoscopy at age 10-12
- If polyps are found, or by age 20-25:
  - Yearly colonoscopy to remove polyps
  - Many polyps - surgery to remove the colon
  - Upper endoscopy every 1-3 years

**Attenuated FAP (aFAP)**
- Colonoscopy at age 20-30 or 10 years earlier than first polyp diagnosis in the family
- Yearly colonoscopy to remove polyps
- Consider surgery to remove the colon if too many polyps

**MutYH-associated polyposis (MAP)**
- Colonoscopy at age 20-30 or 10 years earlier than first family diagnosis
- Yearly colonoscopy to remove polyps
- Upper endoscopy to look for polyps

**Serrated Polyposis syndrome (SPS)**
- Colonoscopy at age 40 or 10 years earlier than first polyp diagnosis in the family
- Colonoscopy every 5 years; more frequently if polyps are found
- Consider surgery to remove the colon if too many polyps

**Lynch syndrome/HNPCC**
- Beginning at age 20-25 years:
  - Colonoscopy every 1 – 2 years
- Consider surgery to remove the part or all of the colon if too many polyps
- Beginning at age 30-35 years:
  - Upper endoscopy every 2 – 3 years
  - Women - yearly endometrial biopsy and vaginal ultrasound
- Consider preventive removal of the uterus, ovaries, and fallopian tubes in women who have completed childbearing.

Patient information materials developed in the Section of Colon and Rectal Surgery at Rush University Medical Center. The information contained in this brochure is believed to be accurate; however, questions about your individual health should be referred to your physician.

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