Between Mother and Son

Shannon and her teenage son, Joe, share a unique bond that in all likelihood originated more than a half century ago with Shannon’s mother. Shannon and her son share a hereditary disease that has caused havoc in their bodies and nearly cost Shannon her life.

In spring 2003, Shannon began experiencing trouble breathing and a racing heartbeat. Even during normal activity, she would become winded. Then just 39 years old and in great shape, Shannon couldn’t believe her heart was failing. An EKG and a stress test confirmed her heart was healthy, but still she knew something was wrong.

Shannon also was experiencing unexplained hair loss, headaches and blurred vision. She noticed her fingernails were splitting and not growing. Rather than discounting what seemed like random symptoms, the mother of two thought to keep track of them, writing symptoms down as they occurred.

Despite a personal history of colon polyps – over a 10-year period, she’d had about 20 or so removed – as well as having a son with colon polyps, Shannon didn’t suspect a digestive problem. She wasn’t experiencing any trouble with her digestive tract, and her symptoms appeared to be unrelated.

In November 2004, Shannon shared her ever-growing symptom list with her primary care physician, who finally ordered a complete blood count, also known as a CBC blood test. Hours later, she telephoned Shannon at home. With a troubled tone in her voice, she asked, “How quickly can you get to the ER?”

At a hospital near her home in Westerville, Ohio, just north of Columbus, Shannon underwent “every kind of work-up.” Her CBC blood test showed severe anemia; her hemoglobin count was a mere 4.7 gm/dl (normal levels are roughly between 12 and 14 gm/dl in men, and 11 to 13 gm/dl in women). She received four pints of blood within a 24-hour period. The hospital’s medical staff was amazed that she hadn’t gone into cardiac arrest.

Although Shannon’s symptoms and blood test results pointed to severe anemia, the medical staff couldn’t pinpoint the cause. She stayed in the hospital for two days while a myriad of tests were run. The gastroenterologist on call ordered an upper endoscopy and a colonoscopy. The colonoscopy results came back normal, but the results of the upper endoscopy were suspect.

Finally, the results of a biopsy explained the problem: Shannon was slowly bleeding to death as a result of so many polyps in her stomach. There were so many, in fact, the gastroenterologist on call thought it was stomach cancer.

Shannon needed expert medical help right away. Physicians at The Cleveland Clinic successfully had treated her son, Joe; Shannon again turned to the Clinic for help.

To confirm Shannon’s diagnosis, Carol Burke, M.D., director of the Cleveland Clinic’s Center for Colon Polyp and Cancer Prevention, repeated the upper endoscopy. Shannon’s duodenum was clean, but her stomach was carpeted with large, bleeding polyps. “Dr. Burke said we would have to remove my stomach, a total
Between Mother and Son  
continued from page 1

“"I can eat almost anything I like. I can eat cereal, raw fruits or veggies; maybe 80 percent of things I did before,” she says.

Shannon’s son, Joe, experienced intestinal symptoms at a much earlier age than did Shannon. When Joe was just about 3 years old, Shannon noticed blood in his stool. It turned out that Joe had a bleeding polyp in the mid-section of his colon. After the polyp was removed, Joe underwent regular colonoscopies every two to three years, which generally uncovered many, many more polyps.

“The GI specialist ultimately told us that he could continue to ‘be Joe’s plumber,’ but that Joe should see someone more knowledgeable about juvenile polyposis,” says Shannon.

In November 2001, when Joe was about 14, he required major colorectal surgery because the frequency and number of polyps growing in his colon were spiraling out of control. He was referred to The Cleveland Clinic, where he underwent a total abdominal colectomy (removal of the large intestine) with ileorectal anastomosis, which is a procedure to connect the end of the small intestine, or ileum, to the rectum.

About the surgery, Joe admits that he was nervous. "My mom's mom died when my mom was five or six, but I figured everything would be all right," says Joe, now 18. Shannon’s mom did, in fact, die quite young. Only in her early 30s, she died of colorectal cancer.

Based on Shannon and Joe’s personal and family history, physicians suspected a hereditary condition called juvenile polyposis. The syndrome is characterized by polyps in the large intestine, the stomach and, less likely, the small intestine. Usually the colorectal polyps cause the most symptoms like bleeding, diarrhea, abdominal cramps and anemia. People with juvenile polyposis also are at risk for colorectal cancer (lifetime risk of 68 percent) and stomach cancer (lifetime risk of 21 percent).

In spring of 2001, prior to Joe having surgery at The Cleveland Clinic, the family sought genetic counseling and testing at the Arthur G. James Cancer Hospital at Ohio State University in Columbus. Joe’s local physician had recommended genetic testing so that family members could be empowered to make informed health care decisions. For example, those who tested positive could establish a surveillance schedule with their physicians. Those who tested negative could avoid worrying unnecessarily about the unknown.

Juvenile polyposis has been associated with mutations in two genes: SMAD4 on chromosome 18 and BMPR1A on chromosome 10. It has been estimated that SMAD4 and BMPR1A mutations account for 40 percent to 60 percent of juvenile polyposis in families. In about 50 percent of families with juvenile polyposis, the inherited mutation that causes the disease can be found. Usually someone in the family who is affected with the condition undergoes genetic testing. If the genetic mutation is found, other “at-risk” relatives may be offered the blood test.

Because Joe had juvenile polyposis, he underwent testing and the causative mutation was detected. His little brother, Henry, tested negative. Because the disease is hereditary, a parent has a 50 percent chance of passing the gene mutation to each child. In this case, one of Shannon’s children inherited the disease, while the other did not. Of Shannon’s two siblings, one has the gene mutation.

Since her surgery, Shannon is healthy and back to walking the dog three miles a day. Joe also has adjusted well following his surgery. “I’m completely normal,” says Joe, adding that he only gets an upset stomach if he eats greasy foods. He undergoes an annual sigmoidoscopy at the Clinic to check his digestive tract.

Joe will be starting his senior year in high school in the fall. Last summer he spent five weeks at the North Carolina School of the Arts, studying cinematography, sound and special effects; he’ll be attending again this summer. He’s also hoping to attend college there after graduation and is optimistic about the future. “I will be the next Spielberg,” he says.
The most common syndromes of inherited colorectal cancer are Hereditary Non-Polyposis Colon Cancer (HNPCC) and Familial Adenomatous Polyposis (FAP). People diagnosed with HNPCC or FAP carry a mutated gene in their DNA, which, in turn, causes benign and cancerous tumors to develop in the large intestine and in other organs, usually at a young age.

HNPCC and FAP are inherited, or passed on from generation to generation, in an autosomal dominant fashion. The word “autosomal” refers to the 22 chromosomes, different from the “X” and “Y” gender chromosomes. The word “dominant” refers to the pattern of inheritance.

Everyone has two copies of every gene: one from our mother and one from our father. In dominant inheritance, only one copy of the particular gene causing the disease needs to have a mutation for the disease to be transmitted. In a dominantly inherited syndrome, one parent is affected, meaning the parent has one normal and one mutated copy of the gene. The other parent is unaffected. Because each child gets one copy of each parent’s gene, the chance of passing on the mutated gene to a child is 50 percent. Thus, the chance of a child of an affected parent developing a dominantly inherited syndrome is 50 percent.

continued on page 4
MAP is a serious condition, but it can be treated successfully if detected early.

MAP-MYH Associated Polyposis continued from page 3

Recently a new syndrome of inherited colon cancer has been discovered. The syndrome is caused by mutations in the DNA repair gene MYH. Known as MAP (MYH-Associated Polyposis), the condition is inherited in an autosomal recessive fashion.

In recessive inheritance, both copies of a gene need to be mutated for the disease to be transmitted. This means that both mother and father must have at least one mutated gene in their DNA. Although the parents may not necessarily have the disease themselves – for example, if they only have one mutated copy of the gene – they are still “carriers.” MAP is the only known inherited colorectal cancer syndrome with this pattern of inheritance.

When both copies of the mutated genes are passed on – one from each parent – the child inherits the disease. If the parents each carry one mutated and one normal copy of MYH, the chance of this happening is one in four, or 25 percent.

There is some suspicion that even carriers of an MYH mutation are at an increased risk for colon cancer. Therefore, it is necessary to trace each affected parent’s family history, because it is known that each parent must be at least a carrier and that other members of the family also are at risk.

The condition caused by mutations in the MYH gene is similar to a mild form of FAP, which is caused by a mutation on a different gene, called APC. People with FAP develop hundreds to thousands of polyps in the large intestine. If left untreated, one or more of these polyps will turn into a cancer. In addition, some patients with FAP also have extraintestinal manifestations, such as epidermoid cysts, osteomas and dental abnormalities. Because FAP and MAP appear similar, a detailed family history is important to distinguish the two. A dominant family history and the presence of extraintestinal manifestations would support the diagnosis of FAP, whereas a recessive inheritance would support MAP.

When mutations are present in the MYH gene and damaged DNA is not repaired, mutations occur in other growth-controlling genes and an affected person has an increased risk for precancerous polyps and colon cancer. Most people affected with MAP have less than 100 polyps in their large intestine, although there have been some MAP patients reported with more than 400. MAP patients also can develop gastric fundic gland polyps and duodenal adenomas, although the incidence of upper intestinal polyps is not well-defined.

MAP can be identified through a genetic blood test that detects the two common mutations in MYH. Prior to the discovery of the MYH gene, patients with a mild case of polyposis and a family history suggestive of recessive inheritance often tested negative for APC gene mutations. Recent studies have concentrated on the prevalence of MYH gene mutations in these patients.

Results of a recent study by Sieber, et al., showed 30 percent of patients with 15 or more adenomatous polyps had both common mutations in the MYH gene (MAP), and 7.5 percent of patients with more than 100 adenomatous polyps who previously tested negative for mutations in the APC gene were found to have both common mutations on the MYH gene (MAP). Therefore, it would be worthwhile for those APC-negative patients to be retested for mutations in the MYH gene.

Because of the strong similarities between MAP and FAP, blood tests are performed concurrently for mutations in APC and MYH so physicians can make a definitive diagnosis.

Patients diagnosed with MAP need to undergo a colonoscopy. If fewer than 20 polyps are found, they can be removed during the colonoscopy. The patient will then need to be followed with frequent colonoscopy for life, because new polyps can form and turn into a cancer. If the polyps are too numerous or too fast-growing to be removed by colonoscopy, then surgical removal of the entire colon is necessary.

Various risks and implications exist when someone has an inherited colon cancer syndrome. Yes, MAP is a serious condition, but it can be treated successfully if detected early. With prompt treatment, MAP patients live normal, healthy lives. If left untreated, however, MAP can lead to colon cancer.

If you would like more information about MAP or any other colon cancer syndromes, please contact:

The David G. Jagelman Inherited Colon Cancer Registries Department of Colorectal Surgery / A30
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REFERENCE
Study Shows Camera Pill Effective for FAP and PJS Patients

A study performed at The Cleveland Clinic by Carol Burke, M.D., James Church, M.D., and Janice M. Santisi, R.N., found that video capsule endoscopy is a safe and accurate way to diagnose small intestinal polyps in patients with familial adenomatous polyposis (FAP) and Peutz-Jeghers syndrome (PJS).

Video capsule endoscopy, or the pill camera, is an FDA-approved device that visualizes the small intestine for abnormalities. The capsule, the size of a large vitamin, contains the equipment needed to take high quality images of all 22 feet of the small intestine, a feat that cannot be accomplished with traditional endoscope technology.

Once a patient swallows the capsule, it painlessly takes a journey through the small intestine. When the capsule reaches the end of the intestinal tract, it is eliminated from the body.

Approximately 55,000 images of the small intestine are obtained over the six- to eight-hour testing period. The video images are downloaded to a computer workstation and then reviewed by a board-certified gastroenterologist specializing in capsule endoscopy who can detect the cause of intestinal bleeding or other small intestinal disorders.

In the Clinic’s study, published in the July 2005 American Journal of Gastroenterology, small intestinal polyps were found beyond the reach of the upper endoscope in 60 percent of patients with FAP and in 75 percent of patients with PJS. Based upon these study results, capsule endoscopy is recommended every two to three years in place of small bowel X-ray surveillance in people with PJS and in FAP patients with advanced duodenal polyposis (Stage III or IV).

“The frequency of small intestinal polyps in juvenile polyposis is reported to be much rarer than in FAP and PJS, and evidence to support capsule use for surveillance in juvenile polyposis is lacking,” says Dr. Burke.

The pill camera technology is no longer limited to the small bowel. The manufacturer of Pillcam SB (Given Imaging Limited, Israel), recently received FDA approval for its new Pillcam ESO, which examines the esophagus using video capsule technology. Additionally, researchers are investigating the pill camera’s role in inflammatory bowel disease and other disorders of the small intestine.

Medical Concierge Service
Friendly and Caring Assistance

Sue Watson from Grand Rapids, Michigan, says she and her husband, Paul, who is confined to a wheelchair, would probably not have come to The Cleveland Clinic had it not been for the Medical Concierge service.

“We were overwhelmed at the prospect,” says Mrs. Watson. “But everyone was so helpful and really went out of their way to make us feel comfortable.”

Mrs. Watson says patient care representative Mary Ellen Cozad contacted her when the Watsons arrived at the InterContinental Hotel, located on The Cleveland Clinic campus. “The next day, she met us in the hotel lobby and helped us find our way to our first appointment. She stopped back later to see how we were doing and brought us coffee and muffins.

“We were deeply touched by her genuine kindness and compassion,” says Mrs. Watson. Ms. Cozad guided the Watsons to their next appointment, showing them which elevators to use. “I would have been lost without her help.”

The Watsons say they never fail to mention to their friends and family the wonderful service they received from the staff in the Medical Concierge Office. “It was greatly appreciated,” she says.

For more information about the medical concierge service, call 800/223-2273, ext. 55580, weekdays between 8 a.m. and 5 p.m. (EST) or visit: www.clevelandclinic.org/services and click on Medical Concierge in the left-hand column.

www.clevelandclinic.org/services
Going Smoke-Free

In an effort to provide a healthy environment for all employees, patients and visitors and to continue our dedication to health and wellness, The Cleveland Clinic and the Cleveland Clinic Health System became smoke-free on July 4, 2005, Independence Day. To help people quit or reduce their tobacco use, the Clinic is hosting monthly forums on smoking-related topics, offering monthly smoking cessation programs and implementing a smoking-cessation mentoring program.

For more information, call toll-free 877/617-6653, e-mail smashtheash@ccf.org, or visit our “Smash the Ash” Web site at www.clevelandclinic.org/smashtheash.

Current Clinical Trials

We are currently enrolling individuals who have FAP into a study assessing the effectiveness of Celebrex versus Celebrex plus another medicine called Efornithine on colorectal polyp growth. If interested call Carol Burke, M.D. at 216/444-6864 or Hennie Hasson, R.N. at 216/444-6526.

The Cleveland Clinic is in the planning stages of a large national study to analyze the effect of a combination of calcium and vitamin D on the prevention of recurrent colorectal polyps (adenomas) in adults who have had previous colorectal adenomas, and who do not have FAP or HNPCC. Enrollment for the study may begin soon. If you are interested in learning more about this study please call Janine Bauman, B.S.N., at 216/444-6526 or Carol Burke, M.D., at 216/444-6864.