

## From Tragedy to Triumph

In 1967 Mike Tighe, a 19 year old Bucyrus, Ohio, man learned he had familial adenomatous polyposis (FAP). This was the same disease that also affected his mother, maternal grandfather, and his maternal aunt and maternal uncle. All were deceased except his mother and she passed away the same year at age 48 from pancreatic cancer.

At the time, it wasn't widely thought that cancer was hereditary, but his family history prompted renowned Cleveland Clinic colorectal surgeon **Rupert B. Turnbull, MD**, to check Tighe and his six siblings for signs.

Colon polyps were found in his younger brother and sister as well. They all underwent surgery to remove their colons, in hope of a better prognosis.

Despite the early detection and surgery, Tighe didn't think he would live to see his children grow up, graduate or enjoy other milestones. Due to his family history he didn't think he would live past 50.

However, today he is alive and quite well at age 72 — and thankful for it every day.

In 1990, he had a game-changing procedure performed by Cleveland Clinic surgeon **James Church, MD**, after it became clear that Tighe was in danger of getting rectal cancer.

"Instead of giving Mike a permanent ileostomy, we made a J-shaped pouch out of the small intestine," Dr. Church says. "The pouch stores stool so that patients can have reasonable bowel habit. Because pouch surgery is quite complicated, we often give patients a temporary ileostomy to keep stool from entering the pouch until we are sure it has healed well."

That meant a few months of Tighe wearing an external pouch with an opening in his abdomen. Those were some difficult days, but he chose to look on the bright side. The



J-pouch surgery was a success and he has proved a model patient.

"I was 43 in 1990 — close to the age my mom was when she passed — and I count everything since 1990 as a gift from Dr. Church," Tighe says. "Had I not had Dr. Church and had he not done that surgery, my life expectancy would have been maxed out at five or six more years."

The Tighe family is one of 12 four-generation families in Cleveland Clinic's David G. Jagelman Inherited Colon Cancer Registries. He and several family members — including three children and two grandchildren — who have been diagnosed with what is now known as familial adenomatous polyposis, a hereditary colon cancer syndrome.

"FAP is dominantly inherited, which means that 50 percent of the children of an affected parent will inherit the mutation," Dr. Church says.

All the Tighes with FAP have had the initial surgery to remove the colon and are undergoing annual checkups at the Sanford R. Weiss, MD, Center for Hereditary Colorectal Neoplasia in Cleveland Clinic's

Digestive Disease & Surgery Institute

"Each of the last four generations of the Tighe family has faced this disease," Dr. Church says. "They have partnered with us in an exemplary way. We have helped them through surgeries, been there for them when complications occurred and, by and large, kept everyone healthy and able to lead a happy life. They are a great example of family strength overcoming a potentially devastating disease. There have been setbacks for sure, but the overall feeling is one of triumph."

While the 30th anniversary of his J-pouch surgery is coming up in March, Tighe says he doesn't plan to mark it in any special way.

"I tell you, every morning when I get up I celebrate, because it's another day that I've been given," he says. "I'm a Christian and I do believe its God's hand working through Dr. Church that gave me this miracle. And now all of my children and grandchildren can look forward to a full life, not cut short by FAP, but they can look forward to growing with their children and grandchildren like I am."

# Cleveland Clinic FAP patient has healthy child post pre-implantation genetic testing (PGT)

Eric Nichols has had to get a colonoscopy each year since he was 15.

The Brooklyn, New York, resident — now 31 — travels annually to the Sanford R. Weiss, MD, Center for Hereditary Colorectal Neoplasia in Cleveland Clinic's Digestive Disease & Surgery Institute for his condition, familial adenomatous polyposis.

His physician, **Carol Burke, MD**, is internationally renowned for treating FAP, a hereditary colon cancer syndrome often requiring removal of the colon, as well as yearly screening.

Those are among the reasons he and his wife, Rachel Marcy, thought long and hard about starting a family. Nichols was in the third grade when his own father died of a related stomach cancer.

While his condition has yet to come to a colectomy, it is always at the back of his mind.

"I didn't want to pass on this disease because I didn't want to sign up my child for having to deal with what I do," he says.

So, after considering all the options — including taking their chances or using a sperm donor — they chose to obtain a pre-implantation genetic testing and use in vitro fertilization (IVF).

PGT serves to prevent offspring from inheriting certain genetic diseases and disorders.

The couple worked with a fertility clinic in New York and a genomics lab, which took DNA samples from Nichols, his mother and his wife. After the embryos were created, the fertility clinic performed biopsies and looked for the gene mutation that causes FAP.



"They used the DNA sample from Eric's mother to help identify which embryos did not inherit FAP," Marcy says. Twenty-six percent of the embryos were viable and without the gene mutation. "We implanted the embryo that turned into Henry."

Their son was born in April following a normal pregnancy and birth. A genetic

test completed postpartum confirmed he is free of FAP.

"While we did well, it's a complex process and it might not always result favorably," Nichols notes. "It was worth it for us. It's a complex decision for anyone to make."

They acknowledged the ethical debate and the expense of the PGT/IVF process,



which took about a year and wasn't covered by their insurance.

"Given that we were pursuing this because of a known genetic disorder, using a donor seemed like a new gamble," Marcy says. "I think that it is very important for people to understand that PGT can identify mutations that cause specific single-gene disorders, but it does not guarantee that your child will be healthy. Everything else is left up to chance."

"You have a 50 percent chance of passing it on to someone else if you have it, which is a coin flip," Nichols adds. "Do you take the risk? Do you go for it?"

The couple is glad they did.

"It's expensive, but if you count the cost of dealing with FAP, I think this ends up being cheaper," he says.

Marcy expresses relief that their children won't have to worry about passing it on.

"We can stop it in this generation," she says.

## Preimplantation Genetic Testing

*Marissa Coleridge, MG, LGC*

Advances in genetics are changing the landscape of reproductive options and decisions for an increasing number of individuals. Preimplantation Genetic Testing (PGT) is a specialized technique used to identify genetic conditions in embryos created through In Vitro Fertilization (IVF). A few cells are taken from the embryo and can be tested for the genetic mutation that is in the family. The embryos that do not have the mutation can then be implanted into the mother.

PGT- technology is complex. In order to do PGT, the disease causing genetic mutation must be known in the family. In addition, often DNA from other family members is needed to create 'a barcode' around the genetic mutation. This is termed creating a linkage map. Creating a linkage map in this manner is beneficial (and often required) to increase PGT accuracy. PGT is highly accurate but genetic testing is recommended in the prenatal period or postnatally due to risk for a false negative or a rare phenomenon termed mosaicism.

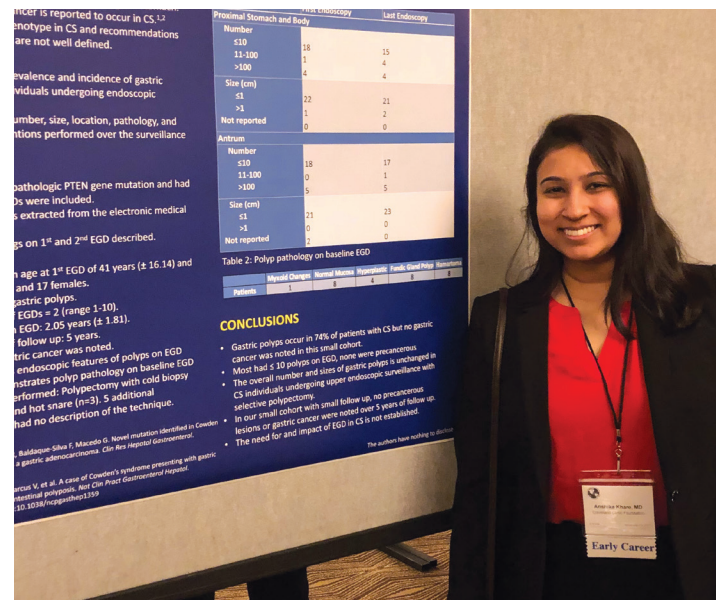
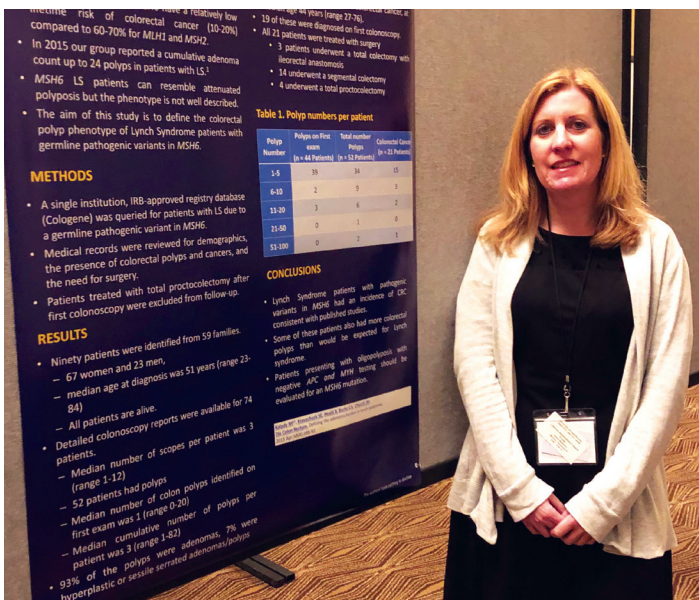
Deciding whether to pursue PGT in the presence or absence of infertility can be a complex decision. Individuals in this situation often face moral and ethical questions regarding the value of a potential life affected by genetic disease. Some parents have voiced concern regarding the lifelong challenges and burden of genetic disease whereas others state the importance of reproductive liberty and decision making for their family. It is important to note that IVF and PGT can be expensive and complicated. Thus, it is important to involve the participation of a genetic counselor knowledgeable about this complex process, conditions and counseling before patients undertake PGT.



# Weiss Center makes significant contribution to the 23rd Annual Meeting of the Collaborative Group of the Americas for Inherited Gastrointestinal Cancer (CGA).

The Collaborative Group of the Americas for Inherited Gastrointestinal Cancer was founded in Cleveland in 1995 to establish a way for American doctors, researchers and genetic counselors to get together and improve the treatment of hereditary colorectal cancer. Each year members of the Group get together to discuss the latest developments in research and the way in which these developments are changing the way we take care of patients. We discuss the difficult challenges that keep coming up and plan for further improvements in care as knowledge increases. This year 330 members of CGA met

in Salt Lake City, including 8 of us from the Weiss Center (see the photo). We presented the results of 13 research studies, contributed to discussions throughout the meeting, led “Meet the Professor” sessions, ran the Challenging Cases session, and were on the panel for “Curbside Consults”. We look forward to continuing involvement and leadership of this group as we work to fulfill the mission of reducing deaths from hereditary colorectal cancer syndromes and maintaining the quality of life of affected patients.



# 2019 Cleveland Undy Run Raises Colorectal Cancer Awareness, Research Funds

For the fifth consecutive year, runners and walkers from Northeast Ohio and beyond gathered in Cleveland with a common purpose: to help end colorectal cancer. On September 28, more than 700 people gathered on the East Bank of the Flats in downtown Cleveland to walk, run, socialize, and remember. In partnership with the national Colon Cancer Alliance, Cleveland Clinic and the Weiss Center led the local event whose main purpose is to raise awareness about colorectal cancer. The message is that colorectal cancer is a disease that can affect both young and older people and that timely screening and evaluation of symptoms can help save lives. "If even one life is saved by what we do here today, this

event will be a success," stated **Matthew Kalady, MD**, the Director of the Weiss Center and local organizer of the Undy Run. There was a special ceremony before the race to remember those who have passed on, and to honor the survivors. Nearly \$90,000 were raised by local sponsors and supporters of the participants.

A portion of the funds will be used to support programs by the Weiss Center and the Taussig Cancer Institute to help provide education, awareness, and screening for colorectal cancer in the community. Please join us next Fall for the 6th annual event, tentatively scheduled for September 2020.



The Weiss Center would like to thank the many patients that have and continue to participate in research at the Cleveland Clinic. Research in patients with rare, hereditary colorectal cancer syndromes enables us to learn more about your condition with hopes of preventing or better controlling of disease.

In May 2019 at the Digestive Disease Week meeting in San Diego, CA, **Carol A. Burke, MD**, presented the results of the “CPP FAP 310” trial. This trial enrolled 171 FAP patients throughout the world including many Weiss Center patients. The study randomized patients to three treatment groups. The treatment groups included eflornithine (750 mg), sulindac (150 mg), or both once daily for up to 48 months. Upper/lower endoscopies were performed every 6 months. The outcome was the time to a first FAP related event (FRE) in the duodenum, colon (if someone did not have surgery yet) or rectum or pouch (if colon surgery had previously done). The overall outcome was polyp progression, need for surgery or snare resection of large polyps or development

of cancer. The good news was that only 37% of patients developed an FRE. Serious side effects from any treatment arm were very low and no different between the treatment arms. While the time to first FRE in the combination treatment (32.3 months) was reduced by 29% versus sulindac (23.5 months) and by 34% versus eflornithine (21.8 months). These differences were not statistically significantly different. However, the combination treatment significantly reduced the risk for an FRE in the colon among patients who still had their colon or those that have had colon surgery and have their rectum or ileal pouch. These results will be submitted for publication in a journal and will be reviewed with the FDA by the sponsor of the trial, Cancer Prevention pharmaceuticals. We are currently studying the role of a novel medication called guselkumab on polyps in FAP.

If you are interested in learning more about the trial, please contact the study coordinator, **Deanne Nash, RN**, at 216.445.0953.

## Carol A. Burke, MD, appointed to the National Comprehensive Cancer Network® (NCCN®) panel.

Carol A. Burke, MD, in recognition of her expertise in caring for patients with hereditary gastrointestinal cancer, was appointed as a member to the National Comprehensive Cancer Network® (NCCN®) panel which creates practice guidelines for patients with a genetic predisposition to colorectal cancer. The panel consists of national experts chosen from an alliance of 28 leading cancer centers in the United States who are devoted to patient care, research, and education.

The clinical practice guidelines are created for use by patients, clinicians, and other health care decision-makers around the world. Patients can access the NCCN guidelines and many other resources after creating an online account at [nccn.org](http://nccn.org)

The information about diagnosis and management of patient with high risk of colorectal cancer is in the guideline entitled : *Genetic/Familial High-Risk Assessment: Colorectal*.

The screenshot shows the NCCN website interface. At the top, there is a navigation bar with the NCCN logo and the text 'National Comprehensive Cancer Network'. Below this is a search bar and social media links. The main content area is divided into several sections:

- NCCN Guidelines® & Clinical Resources**: This section includes a sub-section for 'Development and Update of the NCCN Guidelines®' with an 'Introduction' and 'NCCN Guidelines Panel Composition and Roles'.
- Quick Links**: A sidebar on the right contains a dropdown menu for 'Clinicians' and a list of links including 'NCCN Guidelines® - FREE', 'NCCN Compendium®', 'NCCN Biomarkers Compendium®', 'NCCN Imaging AUC™', 'NCCN Radiation Therapy Compendium™', 'NCCN Templates®', 'Educational Events', 'CME/CE Programs', and 'NCCN Guidelines for Patients®'.
- Navigation Menu**: A horizontal menu at the top of the content area includes links for 'NCCN Guidelines®', 'NCCN Compendia', 'NCCN Templates®', 'Educational Events & Programs', 'Subscriptions & Products', 'Clinical & Business Resources', 'NCCN Global', 'NCCN Oncology Research Program', and 'Patient Resources'.

The 'Introduction' text states: 'The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are comprised of recommendations for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® currently apply to more than 97% of cancers affecting patients in the United States. The NCCN Guidelines® incorporate real-time updates in keeping with the rapid advancements in the field of cancer research and management. Specific NCCN Guidelines have also been developed for cancer screening and prevention, supportive care issues, and specific populations. The NCCN Guidelines are intended to assist all individuals who impact decision-making in cancer care including physicians, nurses, pharmacists, payers, patients and their families, and many others. The development of the NCCN Guidelines is an ongoing and iterative process based on a critical review of the best available evidence and derivation of recommendations by a multidisciplinary panel of experts in the field of cancer.'

## ASK THE TEAM

*Gautam Mankaney and David Liska*  
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**Patient: “I am planning my pregnancy, is it okay to do my procedures at that time?”**

**MD:** Great question. The procedures we do for your hereditary cancer syndrome are mostly for surveillance. Our hope is to inspect your upper and lower gut to remove polyps that can turn into cancer, or cancers before they have progressed to more advanced stages. The timing for this varies, but generally ranges from 6 months to several years, depending on what cancer syndrome you have, your family history, and what we have found on your previous exams. Given this broad interval, we recommend having your procedures done either before or after delivery of your baby. As a rule of thumb, we save endoscopy during pregnancy for emergent or absolutely necessary situations. This minimizes the possibility of any complications from sedation (to both mother and baby), bleeding, or the pressure of the scope on the uterus/ blood supply to the uterus. Other testing such as ultrasounds, blood work, or other non-invasive screening tests are safe during pregnancy.

**Patient: “My baby is 6 months old and I am still breast feeding. I had an EGD today with conscious sedation. When can I breast feed again?”**

**MD:** This is an important question that you bring up. Our recommendation on when to resume breast feeding has changed over the last several years. Initially, we recommended waiting at least 24 hours. This then changed into pump-and-dump, or pumping after your procedure and dumping the breast milk, just once. Now, the recommendation is that as long as you are awake enough to hold and interact with your baby following the procedure, it is okay to breast feed.

**Patient: “What if I had general anesthesia?”**

**MD:** The same principle applies.

**Patient: I had a J pouch done for FAP when I was 19. Now I am married and my husband and I want to start a family. However my mother also had FAP and developed a desmoid tumor in her abdomen when she was 27. My doctor tells me that getting pregnant can make me more likely to get a desmoid tumor and that these tumors can grow really fast. Should we try to get pregnant?**

**MD:** Desmoid tumors are overgrowths of fibrous or scar tissue that occur in about 1/3 patients with FAP. They tend to develop within 4 or 5 years of abdominal surgery and a small percentage can indeed grow quickly and cause major problems. They do seem to be hormone sensitive tumors because they are twice as common in women as in men, and are most common in young women. In fact sometime we use anti-estrogen drugs to treat them. Pregnancy, with its major changes in female hormone levels, is therefore

a concern. You are particularly at risk for developing desmoid tumors because of your family history of desmoids, and because you are a woman. Other risk factors include having osteomas (benign bony tumors), epidermoid cysts or dental abnormalities. In our very extensive experience we have not found that pregnancy makes desmoid tumors develop or grow faster. Therefore we don't discourage patients at risk for desmoid disease from having a family. We do encourage a thorough discussion of the risks and possible issues that might occur should desmoid tumors develop during or after pregnancy so that you and your husband can make informed decisions. Because of your risk level we may suggest an abdominal MRI to see if you already have desmoid tumors that are currently asymptomatic.

**Patient: “I am 9 months pregnant and have an Ileal pouch-anal anastomosis (J-pouch) what is the recommended delivery method in women with IPAA’s**

**MD:** The question whether vaginal delivery or cesarean section is the preferred method of delivery following ileal pouch-anal anastomosis (IPAA) is somewhat controversial. Most of our experience regarding the effects of vaginal delivery in women with IPAA stems from patients who had surgery for inflammatory bowel disease. While these patients are different from polyposis patients, functional implications of vaginal delivery are likely similar. In our experience here at the Cleveland Clinic, women who had vaginal deliveries following IPAA had a higher incidence of anal sphincter injury and worse sphincter function than women who had cesarean sections. We therefore generally recommend cesarean section as the preferred method of delivery in patients with IPAA. We also advise our patients to discuss with their obstetrician having an experienced colorectal surgeon available at the time of cesarean section in case intestinal adhesions are encountered. This is especially important in patients with multiple prior abdominal surgeries or known desmoid disease.



## 2019 Publications from the Weiss Center

**Gene Expression Changes Accompanying the Duodenal Adenoma-Carcinoma Sequence in Familial Adenomatous Polyposis.** Sushrut S. Thiruvengadam, MD1, Margaret O'Malley, BS2, Lisa LaGuardia, BSN2, Rocio Lopez, MS3, Zhen Wang, MD, PhD4, Bonnie L. Shadrach, BS4, Yanwen Chen, PhD5, Chunbiao Li, BS5, Martina L. Veigl, PhD5, Jill S. Barnholtz-Sloan, PhD5, Rish K. Pai, MD, PhD4, James M. Church, MD2,6, Matthew Kalady, MD2,6, R. Matthew Walsh2,7 and Carol A. Burke, MD2. *Clin Transl Gastroenterol.* 2019 Jun;10(6):e00053.

**Colonic Surgery in Patients With Familial Adenomatous Polyposis.** Bolshinsky V1. *Dis Colon Rectum.* 2019 Jul;62(7):781-785.

**Superior Mesenteric Artery Pseudoaneurysms in Patients With Familial Adenomatous Polyposis-Associated Intra-abdominal Desmoids: Case Series.** Bolshinsky V1, Xhaja X, Halleran DR, Church J. *Dis Colon Rectum.* 2019 Jun;62(6):721-726.

**Combined endoscopic and surgical management of small-bowel polyposis in a patient with Peutz-Jeghers syndrome.** Li F1, Mehta N1, Liska D2, Dionigi B2, Kalady MF2, Burke CA1, Bhatt A1. *Endoscopy.* 2019 Sep 27.

**Mental Health Symptoms in Patients With Familial Adenomatous Polyposis: An Observational Study.** Wood E1, Church J, O'Malley M, LaGuardia L, Heald B, Burke C, Kalady M. *Dis Colon Rectum.* 2019 Oct;62(10):1204-1211.

**Methylated SEPTIN9 plasma test for colorectal cancer detection may be applicable to Lynch syndrome.** Hitchins MP1, Vogelaar IP2, Brennan K2, Haraldsdottir S2, Zhou N2, Martin B2, Alvarez R1, Yuan X3, Kim S4, Guindi M3, Hendifar AE5, Kalady MF6, DeVecchio J7, Church JM6, de la Chapelle A8, Hampel H8, Pearlman R8, Christensen M9, Snyder C9, Lanspa SJ9, Haile RW#10, Lynch HT#9. *BMJ Open Gastroenterol.* 2019 May 28;6(1):e000299.

**Expert Commentary on the Diagnosis and Management of Lynch Syndrome.** Kalady MF1. *Dis Colon Rectum.* 2019 Apr;62(4):406-407.

**Mismatch repair-signature mutations activate gene enhancers across human colorectal cancer epigenomes.** Hung S1, Saiakhova A1, Faber ZJ1, Bartels CF1, Neu D1, Bayles I1, Ojo E2, Hong ES1, Pontius WD3, Morton AR1, Liu R2, Kalady MF3,4,5, Wald DN2,6, Markowitz S1,6,7, Scacheri PC1,6. *Elife.* 2019 Feb 13;8: pii: e40760.

**Endoscopic and histologic features associated with gastric cancer in familial adenomatous polyposis.** Leone PJ1, Mankaney G2, Sarvapelli S1, Abushamma S1, Lopez R3, Cruise M4, LaGuardia L5, O'Malley M5, Church JM5, Kalady MF5, Burke CA6. *Gastrointest Endosc.* 2019 May;89(5):961-968.

**Web-Based Model for Predicting Time to Surgery in Young Patients with Familial Adenomatous Polyposis: An Internally Validated Study.** Sarvepalli S1, Burke CA1,1,1, Monachese M1, Lopez R1,1, Leach BH1,1, Laguardia L1, O'Malley M1, Kalady MF1,1, Church JM1,1. *Am J Gastroenterol.* 2018 Dec;113(12):1881-1890.

**Spigelman stage IV duodenal polyposis does not precede most duodenal cancer cases in patients with familial adenomatous polyposis.** Thiruvengadam SS1, Lopez R2, O'Malley M3, LaGuardia L3, Church JM4, Kalady M4, Walsh RM5, Burke CA6. *Gastrointest Endosc.* 2019 Feb;89(2):345-354.e2.

**Outcome of thyroid ultrasound screening in FAP patients with a normal baseline exam.** Monachese M1, Mankaney G2, Lopez R3, O'Malley M4,5, Laguardia L4,5, Kalady MF4,5, Church J4,5, Shin J5,6, Burke CA7,8,9. *Fam Cancer.* 2019 Jan;18(1):75-82.

**Comparison of pancreas-sparing duodenectomy (PSD) and pancreatoduodenectomy (PD) for the management of duodenal polyposis syndromes.** Walsh RM1, Augustin T2, Aleassa EM2, Simon R2, El-Hayek KM2, Moslim MA2, Burke CA2, Church JM2, Morris-Stiff G2. *Surgery.* 2019 Oct;166(4):496-502.

**Expert Commentary on Colonic Surgery in Patients With Familial Adenomatous Polyposis.** Church JM1. *Dis Colon Rectum.* 2019 Jul;62(7):785.

**Clinical implications of the genetics of sporadic colorectal cancer.** Fischer J1, Walker LC2, Robinson BA3,4, Frizelle FA1,5, Church JM6, Eglinton TW1,5. *ANZ J Surg.* 2019 Oct;89(10):1224-1229.

**Patients in Whom to Consider Genetic Evaluation and Testing for Hereditary Colorectal Cancer Syndromes.** Kupfer SS1, Burke CA2. *Am J Gastroenterol.* 2019 Oct 11.

**Refining Risk Factors for Gastric Cancer in Patients With Lynch Syndrome to Optimize Surveillance Esophagogastroduodenoscopy.** Mankaney G1, Macaron C2, Burke CA3. *Clin Gastroenterol Hepatol.* 2019 Oct 10. pii: S1542-3565(19)31101-2. **Enhancing the efficacy of colonoscopy in Lynch syndrome: the search for the holy grail continues.** Mankaney G1, Burke CA1. *Gastrointest Endosc.* 2019 Oct;90(4):633-635.

**Serrated Polyposis Syndrome.** Mankaney G1, Roupheal C2, Burke CA3. *Clin Gastroenterol Hepatol.* 2019 Sep 11. pii: S1542-3565(19)30989-9.



# *In Memoriam, 2019*

This year the community of those working to defeat hereditary colorectal cancer has suffered two significant losses.

Tom Weber, MD, a surgeon from New York, and Professor Henry Lynch, MD, the famous oncologist for whom Lynch Syndrome was named, passed away. Here we remember these two friends, and pay tribute to their contributions.

**Tom Weber, MD**



Tom Weber, MD, was a surgeon, a scientist, a fundraiser and a leader in the battle against colorectal cancer. Dr. Weber died in September this year at the untimely age of 64 years. With his death we at the Weiss Center lost a good friend, and humanity lost an inspirational leader who's aim was to create a world without colorectal cancer. At the time of his passing, he was Director of Surgical Oncology for Northwell Health in Westchester, NY, and had a career dedicated to achieving a World Without Colorectal Cancer. He created the Colon Cancer Foundation in 2003 which stages a Charity Run in Central Park each year and funds research into Colorectal Cancer. He has more recently devoted time to young age of onset colorectal cancer and has organized an international conference in New York for the last 3 years aimed at figuring out the reason this problem is increasing. Dr. Weber was also the Chair of the National Colorectal Cancer Roundtable and Chairman of the International Society for Gastrointestinal Hereditary Tumors. He had a passion for the diagnosis and care of patients with hereditary colorectal cancer. In particular he was determined to increase the awareness of Lynch syndrome and to make sure that all affected people were diagnosed. Above all these accomplishments and in addition to all his leadership, Dr. Weber was a genuinely nice person, a loving husband and father, and a charming friend. His loss is deeply felt.

**Henry Lynch, MD**



Henry Lynch, MD, passed away on June 2 this year at the age of 91. His passing ends the era of clinical discovery of genetic diseases, where the qualities of astute observation and logical thinking produce insights into disease that affect hundreds or thousands of patients. Lynch syndrome, named after Henry Lynch, MD, is a dominantly inherited syndrome of colorectal and other cancers caused by a mutation in the one of four genes controlling an important aspect of DNA repair. A family affected by Lynch Syndrome will have many relatives developing cancer; some in the colon and rectum, some in the uterus, and some in the stomach. These cancers often occur early in life. Back in the days before genetic testing was available and well before we knew the genes to test, Dr. Lynch noticed these "cancer families". He deduced that there would be an inherited genetic factor underlying the cancers and set out to find it. For years he was turned down for grants and found very little support. However, he persisted, and finally, in the 1990s, the field of genetics caught up with Henry's ideas. Finally, testing technology was able to identify the genes that, when mutated, caused the cancers in Lynch's families. Henry was vindicated and a new era in colorectal cancer research and management had arrived. Here at the Weiss Center we have over 500 patients with Lynch Syndrome. This seems like a lot but it is estimated that in the USA 1 in 280 people is affected. Diagnosis and treatment of patients with Lynch Syndrome is a top priority for us, and we save patients from developing or dying from cancer, while at the same time preserving a good quality of life. We all owe a great debt of gratitude to Dr. Lynch. To those of us that knew him he was a big man with a cheerful disposition, an enquiring mind and a strong sense of caring for his patients, his colleagues, and his fellow human beings. He is missed.

# Let's Talk Hereditary

In the era of social media and dissemination of information, It was necessary to start thinking about ways to connect more with the patients and the medical community. "When thinking of the complexity of care of patients with hereditary colorectal cancer syndromes its necessary in my mind to educate providers but also to educate patients as well who are at any given point in time the judge of their own health," stated Dr. James Church, regarding the reason for starting such a program.

"Let's Talk Hereditary" is an interactive show that includes members of the Sanford R. Weiss, MD Center for Hereditary

Neoplasia discussing what they do best and answering questions about the disease process, genetic testing, medical and surgical care of patients with hereditary syndromes.

The program is being put together by our current Hereditary Fellow, Dr. Abbas, as one of his projects to improve education.

The goal is to increase the viewers' knowledge and understanding of these conditions away from complex medical terms and papers. The initial episodes will be available in early 2020. Communication will be following about how to access these.



**Cleveland Clinic**  
Digestive Disease & Surgery Institute

## Let's Talk Hereditary

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# When should I or my family member have genetic testing?

As most of the polyp syndromes we treat at the Weiss center are inherited and carry a 50% risk of passing it on to a child, an inevitable and common, recurring question is “When should my child be tested”. The answer to this question can elicit a number of emotions and distress around the testing. Generally, families fall into two categories, those who want to know the answer from the start and those that do not want to know until they need to. Neither are wrong but it is what you do with that information that should drive the decision on testing. We draw our recommendations from both research, professional medical group recommendations, and our own patient experience as a group.

When deciding on testing of a child the first piece of information to gather is at what age does child need testing that would align with the first recommendations to screen for a particular lesion or cancer. For patients with Familial Adenomatous Polyposis (FAP), the first colonoscopy is typically at 10 to 12 years of age while patients with Peutz-Jeghers Syndrome (PJS) may develop polyps in the small bowel at 8 to 10 years of age, potentially a 4 year difference in the age to perform genetic screening and should be accounted for. For those who are considering testing early, a

positive diagnosis may result in a significant amount of caregiver anxiety far before recommended screening due to the fear of the unknown. At the same time, disclosure of a diagnosis earlier in life may also lead to unnecessary testing because of the increased awareness of what may arise later in life even though a young child may not yet be at any risk. We also counsel that the disease course for the parent may not be the same for the child, and we do not find worsening disease generation to generation.

We also realize the comfort in a negative diagnosis which is also a driver in the decision to test early. Research has shown a significant reduction in anxiety and uncertainty in a family after negative testing of a child. However, when there are multiple children at risk, there may be a significant impact on the parent to child relationship as well as the sibling to sibling relationship in the event one or all children are positive. In addition, there is added anxiety over the future health and well-being after a positive diagnosis. While this hurdle may be inevitable, and our group strives to help the family navigate these difficult discussions, we typically do not recommend genetic testing until it is needed.

Polyp Syndromes	Age for Genetic Testing (unless symptoms arise earlier)
<b>Familial Adenomatous Polyposis (FAP)</b>	10-12 years
<b>Juvenile Polyposis Syndrome</b> *SMAD4 mutations	12-15 years *Prenatal or perinatal testing, screening for vascular lesions starts in infancy
<b>Peutz-Jeghers Syndrome</b>	8 years
<b>PTEN Hamartoma Tumor Syndrome/Cowden Syndrome/Bannayan-Riley-Ruvalcaba Syndrome</b>	Early childhood/infancy (earlier if signs of autism or macrocephaly)
<b>Lynch Syndrome (non-polyposis syndrome)</b>	18 years or older

## Weiss Center Members to lead International Hereditary Colorectal Cancer Group

Weiss Center Director, Dr. Matthew Kalady, has recently been elected as Chairman of the Executive Council of the International Society of Inherited Gastrointestinal Tumors (InSiGHT) which is based in London, England. Brandie Leach, Section Head of Genetics within the Weiss Center was also recently appointed to InSiGHT Council. InSiGHT is a broadly reaching scientific organization with representation from around the globe. The aim of the group is to improve the quality of care of patients and families with hereditary conditions resulting in gastrointestinal

tumors. One of the major activities of InSiGHT is to create a scientific program every other year with lectures and updates from international leaders in the field. Surgeons, gastroenterologist, oncologists, geneticists, genetic counselors, and scientists provide a truly multidisciplinary approach to the best ways to care for patient. Dr. Kalady and Ms. Leach have been honored with the opportunity to lead the next program which will be held in New York City in May, 2021.

**Family Matters**

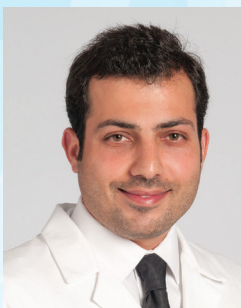
Cleveland Clinic Foundation  
9500 Euclid Avenue / A30  
Cleveland, OH 44195

**SAVE THE DATES**

**Hereditary Health  
Promotion Day**  
March 6, 2020

**6th Annual Cleveland  
Undy RunWalk**  
September 29, 2020

## Introducing New Team Members



*Mohammad Ali Abbass, MD*

**Mohammad Ali Abbass, MD**

My name is Mohammad Ali Abbass and I am the Inaugural James Church and Sheetz Family Hereditary Colorectal Cancer Syndromes Fellow. I finished my training in General surgery followed by a fellowship in colorectal surgery at Cleveland Clinic Foundation. During this time, I had the chance to interact with multiple patients with FAP and Lynch syndrome. Throughout this interaction I came to learn the complexity of such patients and how providing exceptional care can only be done after a thorough knowledge of the disease process has been acquired.

The James Church and Sheetz family hereditary colorectal syndromes fellowship provides an interested candidate with the armamentarium to establish a center that can care for such patients and provide excellent care to fulfil two main objectives: 1) Prevent mortality from cancer 2) Improve the quality of life of the affected patients

Outside work, I enjoy working out and spending time with my two toddlers and family. I also am interested in the science of success on a personal and leadership level and enjoy reading books like: *Start with Why*, *The Infinite Game*, *Gritt*, *The Culture Code* and *Better Together*.