

FEATURED ARTICLE

New Developments in Endoscopy _____ p.04



Digest This

DIGESTIVE DISEASE INSTITUTE | FALL | 2014

STAMPEDE
Update

p.03



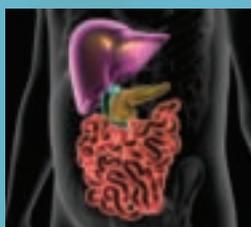
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Complex Visceral
Transplant

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Cleveland Clinic No. 2 in the U.S. – Gastroenterology & GI Surgery





Dear Colleagues,

We all know that Japan has disproportionate rates of gastric dysplasia. So it is not surprising that Japanese specialists are at the forefront of developing refinements in endoscopic surgery. Digestive Disease Institute members have trained in Japan and now offer these endoscopic procedures as part of our ongoing efforts to provide patients with the newest minimally invasive offerings. These physicians, part of our new Developmental Endoscopy Group, are featured in the cover story in this issue of *Digest This*.



You'll also be able to read an interview with a true pioneer of endoscopic surgery, Jeffrey Ponsky, MD, who has returned to Cleveland Clinic as a senior staff surgeon. Another interview introduces you to Emina Huang, MD, and her groundbreaking research into the pathogenesis of inflammatory-associated colorectal cancer.

The nationally recognized STAMPEDE trial demonstrated that bariatric surgery is a highly effective and durable treatment for type 2 diabetes in obese patients. But what are the implications for gastroenterologists? DDI's Ibrahim Hanouneh, MD, answers that question in a special report on p. 3.

Finally, we urge you to study the face of young Khaled Malamid, whose multivisceral transplant led by Kareem Abu-Elmagd, MD, PhD, Director of our Transplant Center, is described on p. 10. His joy is a vivid reminder of how much our patients gain from renewed health and restored digestive function.

Sincerely,

R. Matthew Walsh, MD

Chairman | General Surgery

John Vargo, MD, MPH

Chairman | Gastroenterology and Hepatology

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CME Calendar

CLEVELAND, OHIO

Oct. 2-3

9th Annual Obesity Summit: Science and Practice of Obesity Management

Oct. 17-18

International Symposium: Prevention and Management of Complications in Bariatric Surgery

Nov. 6-7

50th Annual Gastroenterology Update

Nov. 14-15

1st Beta Cell Therapy Symposium: Advances in Management of Diabetes

FORT LAUDERDALE, FLA.

Feb. 10-15, 2015

26th Jagelman/36th Turnbull Annual International Colorectal Disease Symposium

Feb. 12-14

Gastroenterology & Hepatology Symposium

CORAL GABLES, FLA.

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14th Annual Surgery of the Foregut Symposium

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STAMPEDE: An Update for GIs About Bariatric Surgery for Type 2 Diabetes

Potential Implications for Our Practices | By Ibrahim Hanouneh, MD

Type 2 diabetes impacts almost every organ system in the body, including the gastrointestinal (GI) system. Obesity and diabetes increase patients' risks for developing nonalcoholic fatty liver disease, gastroparesis, esophageal dysmotility, gastroesophageal reflux disease and glycogenic hepatopathy.

But now, data from an ongoing study by a group of researchers at Cleveland Clinic offer new hope for obese patients with type 2 diabetes — which may also help resolve many of these common GI complications. The study, known as STAMPEDE (Surgical Therapy and Medications Potentially Eradicate Diabetes Efficiently), indicates that bariatric surgery is a highly effective and durable treatment for type 2 diabetes in obese patients.

The trial was headed by lead investigator Philip Schauer, MD, Director of Cleveland Clinic's Bariatric and Metabolic Institute, located within our Digestive Disease Institute. It involved 150 patients (ages 20 to 60 years) with type 2 diabetes and with a body mass index of 27 to 43.

“As gastroenterologists, we will also be keeping our eye on any upcoming data regarding the effect bariatric surgery may have on reversing GI complications of obesity and diabetes.”

The study compared glycemic control with advanced medical therapy versus medical therapy plus one of two types of bariatric surgery (Roux-en-Y or sleeve gastrectomy). Nearly all surgical patients were able to discontinue insulin and other diabetic medications within three years after surgery. Additionally, there was

a significant reduction in the need for blood pressure and cholesterol medications following bariatric surgery. Patients who underwent bariatric surgery also experienced an improvement in quality of life compared with those receiving medical therapy.

This is the first randomized controlled clinical trial that compares surgery with intensive medical therapy head-to-head for obese patients with type-2 diabetes. The results of the study were presented at the American College of Cardiology's annual conference in Washington, D.C., and published in the *New England Journal of Medicine*.

The next major goals of the study, which will continue for at least five years of follow-up, are to determine the effects of bariatric surgery on reduction of microvascular and macrovascular complications.

As gastroenterologists, we will also be keeping our eye on any upcoming data regarding the effect bariatric surgery may have on reversing GI complications of obesity and diabetes. For instance, recent research presented at Digestive Disease Week 2014 shows that bariatric surgery improves liver histology in severely obese patients and is associated with resolution of fatty liver disease in the majority of patients.

These results are exciting, as they suggest bariatric surgery should be considered as a treatment for nonalcoholic steatohepatitis in severely obese patients — and potentially for an even wider patient population with other GI complications of obesity and diabetes in the future.

Dr. Hanouneh's specialty interests include liver transplantation, alcoholic and nonalcoholic fatty liver disease, and chronic hepatitis C virus infection. ■



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Help for

GI

Tract Diseases



Today, many GI tract diseases that once required surgery can now be treated without incisions. At Cleveland Clinic, a new Developmental Endoscopy Group can help your patients with conditions ranging from motility disorders — such as achalasia — to esophageal, gastric and colorectal cancer.

POEM and ESD Among New Group's Minimally Invasive Offerings

"This new effort combines laparoscopy and endoscopy, which have traditionally been separate groups," explains Matthew D. Kroh, MD, Director of Surgical Endoscopy in Cleveland Clinic's Digestive Disease Institute. "Now we have a core group of interventional endoscopists who are embarking on these procedures — functionally operating through the endoscope."

The Developmental Endoscopy Group, a fusion of gastroenterology, general surgery and colorectal surgery experts, is headed by both Dr. Kroh as Surgical Director and Mansour Parsi, MD, MPH, as Medical Director. The main focuses to date are peroral endoscopic myotomy and endoscopic submucosal dissection. Here is a closer look at each:

POEM FOR ACHALASIA

Peroral endoscopic myotomy (POEM) is an entirely endoscopic procedure to treat achalasia. The technique originated in Japan and has been performed in the U.S. for approximately two years.

"Through the esophagus, we make a small incision in the mucosa and make a tunnel underneath it," Dr. Kroh

explains. "Then, we cut the muscles in the esophagus — mainly at the lower esophageal sphincter — which are too tight in achalasia. It's an effective way to release this tension and restore the ability of food to pass through the esophagus and into the stomach."

The Developmental Endoscopy Group has successfully completed its first series of POEM patients. Advantages include requiring no incisions and patients returning home the following day. Early data for POEM are compelling, Dr. Kroh says. "It results in dramatic relief of achalasia symptoms — as good as a surgical (Heller) myotomy, without the potential morbidity associated with the incisions on the abdominal wall," he says.

Cleveland Clinic advanced endoscopist Madhu Sanaka, MD, underwent POEM training in Japan under Haroue Inoue, MD, who pioneered the POEM procedure. Dr. Sanaka performs POEM procedures along with Cleveland Clinic thoracic surgeon Siva Raja, MD, who specializes in esophageal surgeries. Dr. Sanaka says, "Gastroenterologists and surgeons bring different skill sets to the table, which translates into the best possible care for the patient."



General surgeons Dr. Jeffrey Ponsky (left) and Dr. Matthew Kroh.

OUR TEAM



Matthew D. Kroh, MD
Surgical Director



Mansour Parsi, MD, MPH
Medical Director



Amit Bhatt, MD
Gastroenterology & Hepatology



I. Emre Gorgun, MD
Colorectal Surgery



Jeffrey Ponsky, MD
General Surgery



Siva Raja, MD
Thoracic Surgery



Madhu Sanaka, MD
Gastroenterology & Hepatology



John Vargo, MD, MPH
Gastroenterology & Hepatology



What's New in Advanced Endoscopy at Cleveland Clinic Florida

Advanced endoscopists **Luis F. Lara, MD**, and **Tolga Erim, DO**, performed the Digestive Disease Center's first flexible endoscopic Zenker's diverticulotomy at Cleveland Clinic Florida in March.

This less-invasive technique than open surgical diverticulotomies takes about 20 minutes. It is done by placing a flexible endoscope in the throat of a sedated patient and then carefully cutting the cricopharyngeal muscle and the pocket that can fill with food and water in Zenker's diverticulum.

Most patients are discharged the same day and a regular diet is generally resumed within 48 hours. Although some patients may require multiple procedures, the ultimate success rate is more than 85 percent.



GI Dr. Amit Bhatt (left) and Dr. Matthew Kroh.

ESD FOR GI CANCERS

Endoscopic submucosal dissection (ESD) allows for the removal of early esophageal, gastric and colorectal cancers through an endoscope while avoiding more invasive surgery. This technique was developed in Japan where early gastric cancer is common.

At Cleveland Clinic, gastroenterologist Amit Bhatt, MD, underwent intensive ESD training in Japan thanks to grants from the American College of Gastroenterology and the American Society of Gastrointestinal Endoscopy.

Dr. Bhatt says ESD is valuable in the treatment of early gastric and esophageal cancer. It allows for a complete one-piece resection of cancers allowing pathologists to verify curative resection similar to a surgically removed tumor — an opportunity that is missed with other endoscopic ablation techniques.

The goal of ESD is to be curative. But, Dr. Kroh adds, if it is not possible to remove the cancer with negative margins and avoid an operation, ESD gives the team a better idea of how advanced the disease is prior to surgical intervention: "For instance, when a surgeon and a gastroenterologist do a gastric case together, the beauty of it is that even if it doesn't come out endoscopically, the patient can still get the next less invasive technique."

Dr. Bhatt emphasizes that the collaboration between gastroenterologists and general surgeons is a remarkable benefit to patients who now have another

option to avoid a traditional intervention. "Having an advanced endoscopist and a surgeon work side by side allows us to combine our expertise, ideas and innovations to develop novel approaches to problems," Dr. Bhatt explains.

Dr. Sanaka, who also performs ESD procedures for neoplastic lesions in the GI tract, adds that ESD is less invasive compared with surgery but has similar outcomes.

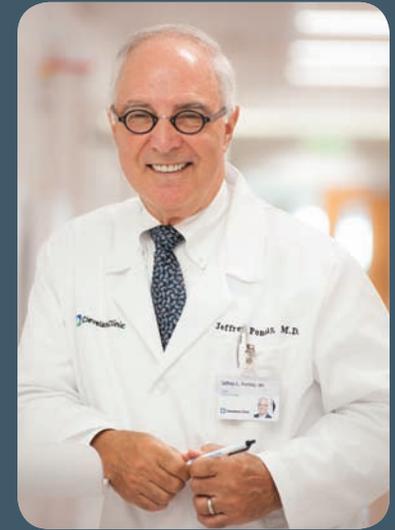
The Developmental Endoscopy Group has effectively used ESD for both gastric and colorectal cancers over the past six months.

ESD FOR COLORECTAL LESIONS

In the U.S., only a few centers are using ESD to remove large colonic polyps. At the Digestive Disease Institute, Emre Gorgun, MD, has been using the technique for removing such polyps — especially flat colonic lesions — for the past three years.

Dr. Gorgun, who received his ESD training in Japan, was one of the first U.S. colorectal surgeons to successfully remove intraluminal lesions en bloc through the anus using ESD. Overall, he says, ESD is safe and useful in carefully selected patients.

"ESD is helping us provide better healthcare and avoid bowel resection," Dr. Gorgun says. He hopes that ESD will become more widely utilized, citing data he presented at the last American Society of Colon



Endoscopy, Laparoscopy Pioneer Dr. Jeffrey Ponsky Rejoins Cleveland Clinic

After a 9.5-year hiatus from Cleveland Clinic during which **Jeffery Ponsky, MD**, served in various clinical and administrative leadership roles, he has returned here — to a newly created role focused on his passion for hands-on clinical innovation. *Digest This* asked Dr. Ponsky to share his thoughts on his new role and what he hopes to accomplish.

ON WHY HIS NEW ROLE APPEALED TO HIM:

“I’m going to be holding senior staff surgeon positions in both GI and general surgery. At the point I’m at in my career, I really wanted to focus on what I enjoy most: developmental surgical endoscopy and pioneering new, minimally invasive surgical (MIS) procedures.

The future holds more and more replacement of traditional procedures by endoscopy and MIS approaches, and we’re on the cutting edge here at Cleveland Clinic. I’ll be collaborating with surgeons and GI specialists to develop new techniques and advance existing ones.

In addition, I have a half-time appointment in the Office of Patient Experience, which is directed by Chief Experience Officer James Merlino, MD. I’ll be working closely with referring doctors throughout the region and country to provide both consultation and education. I’m really looking forward to the outreach and collaboration involved in that role.”

ON THE DRIVING FORCE BEHIND HIS CONTINUAL FOCUS ON INNOVATION IN THE FIELD:

“That’s easy: It’s the desire to help patients. My contributions in developing advanced endoscopic techniques and new approaches to minimally invasive laparoscopic surgery have always focused on making patients’ lives better by minimizing or eliminating surgical operations.”

Selected career highlights

- Pioneered the percutaneous endoscopy gastrostomy procedure in 1979
- Served as the Director of Endoscopic Surgery and the first-ever Executive Director of the Minimally Invasive Surgery Center at Cleveland Clinic from 1997 to 2005
- Has won numerous prestigious medical society awards

ON THE ADVANCES SINCE BEING ONE OF THE FIRST TO PERFORM FLEXIBLE GI ENDOSCOPY — AND WHAT THE FUTURE HOLDS:

“Since then, I’ve been very involved in the ongoing development of minimally invasive laparoscopic surgery and helping to expand advanced endoscopic techniques such as endoscopic retrograde cholangiopancreatography.

We’ve ushered in the era of natural orifice transluminal endoscopic surgery, with some of the first work in the laboratory and surgically having been done here in Cleveland. We’re currently performing POEM, a novel advanced endoscopic therapy for achalasia. There’s been much more — and more to come — but those are some of the highlights.”

and Rectal Surgeons meeting that only 9 percent of polyps removed over a five-year period were actually cancerous.

“So basically 91 percent of the time, these benign lesions were overtreated with colectomy,” he explains. “If you could remove these lesions with a procedure such as ESD, the patient would be perfectly treated and the colon would be saved.”

For difficult colonic lesions, Dr. Gorgun also utilizes laparoscopic mobilization of the colon performed with combined intraoperative CO₂ colonoscopy. Called combined endoscopic-laparoscopic surgery (CELS), this new approach allows removal of difficult colonic lesions via a dual technique avoiding formal bowel resection. CELS is safely offered to selected patients with benign polyps or early colonic neoplasms that could not purely be removed via colonoscopy. This combined approach is successfully performed at Cleveland Clinic by Dr. Gorgun with good outcomes.

To refer a patient to our Developmental Endoscopy Group, call 855.REFER.123.

PROFILE

Emina Huang, MD

When colorectal surgeon and researcher Emina Huang, MD, joined Cleveland Clinic's staff in August 2013, she brought along two five-year NIH R01 grants with remaining funding totaling \$1.5 million. The monies support her groundbreaking research into the pathogenesis of inflammatory-associated colorectal cancer.



Q What is the premise behind your work?

A The relationship between chronic inflammation and cancer development is well-known, but the cellular and molecular mechanisms underlying this relationship are not well-understood. We suspect that increased levels of the inflammation-causing protein interleukin-8 (IL-8) may be partly to blame for increased rates of colon cancer in patients with ulcerative colitis. Our long-term goal is to clarify the link between inflammation and cancer in general, and to prevent colitis-associated cancer (CAC) in particular.

Q Discuss the role of colonic stem cell niche in oncogenesis

A In this project, we are examining the contribution of the microenvironment to inflammatory-associated cancer. Our immediate objective is to determine the roles of genetic defects, cancer stem cells and stromal fibroblasts in the generation of colon cancer-initiating cells. Our central hypothesis is that these three factors are key to CAC development. Proving this hypothesis will facilitate the development of novel strategies to prevent CAC and substantially improve our ability to predict which patients will progress to malignancy.

Q Explain your work with IL-8 in colitis-associated tumor initiation

A Up to 18 percent of patients with chronic ulcerative colitis develop colorectal cancer. This project focuses on why epithelial cells make IL-8, and what effect the protein has on the development of cancer. Is it creating the angiogenic switch by making VEGF downstream and usurping the local vessels to feed itself? If IL-8 is the culprit in cancer formation, we can focus on finding ways to regulate its function to prevent inflammation-associated cancer, and specifically, colorectal cancer. Our approach is innovative, because we have unique tools, including colitis-derived colon cancer-initiating cells (CCICs), and are using CCICs from sporadic colorectal cancer for comparison. Our central hypothesis is that IL-8 signaling is required for the colitis-to-cancer transition. Once we understand the contribution and mechanism by which IL-8 promotes tumor initiation, we will be able to develop ways to interfere with the progression from benign colitis to malignant cancer.

Q Are you working with any other researchers at Cleveland Clinic?

A Several of my colleagues are studying colitis-associated cancer, but from different angles. Others are studying inflammatory bowel disease or colorectal cancer. We will be discussing ways to dovetail our research in order to more quickly gain an understanding of the mechanisms that promote the development of colorectal cancer and develop novel ways to prevent this devastating disease.

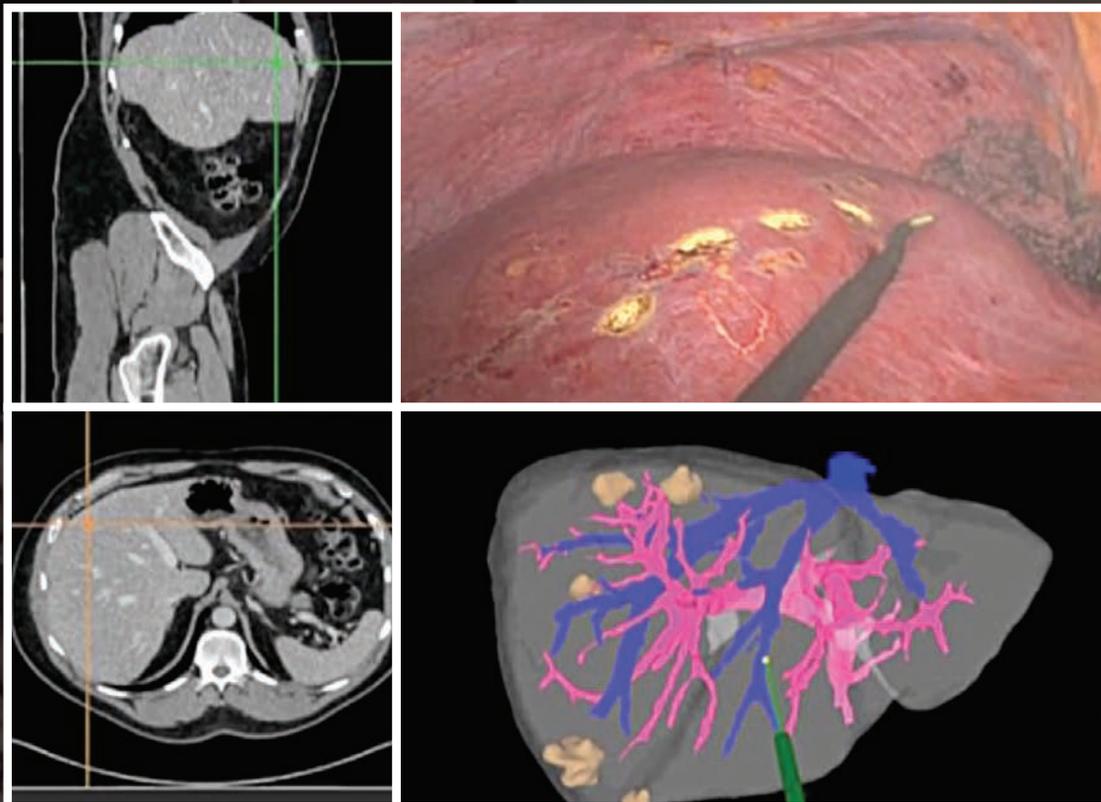
Dr. Huang can be reached at 216.445.4631 or huange2@ccf.org.

Image *of the* Issue

A novel laparoscopic right hepatectomy was recently performed using intraoperative navigation guidance. This 3-D reconstruction of the liver, vascular-biliary structures and tumors was created (right two images, displayed next to patient's preoperative CT scans) to help Cleveland Clinic general surgeons plan and accurately perform the successful resection. ■



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CASE STUDY

Complex Visceral Transplant Rewrites the Book on a Rare Syndrome

A 4-year-old boy with a rare genetic disorder was recently transplanted with a new liver, intestine, pancreas and duodenum by a team led by Kareem Abu-Elmagd, MD, PhD, Surgical Director of the Center for Gut Rehabilitation and Transplantation (CGRT) and Director of Cleveland Clinic's Transplant Center. It was the first pediatric complex visceral transplant to be performed at Cleveland Clinic, and the patient was the first in the world to survive beyond the first year after birth and be transplanted for Martinez-Frias/Mitchell-Riley syndrome. Medical care was provided by a pediatric gastroenterology team from Cleveland Clinic Children's.



DEFYING EARLY EXPECTATIONS

As a result of the syndrome, Khaled Malamid had a host of life-threatening complications, including neonatal diabetes, enterocyte failure and iron overload with end-stage cholestatic liver disease.

Since birth, Khaled required intravenous feeding and multiple daily doses of insulin. After he turned 2, his doctors in his home country in the Middle East suggested that his parents explore options for a transplant abroad.

They eventually connected with Dr. Abu-Elmagd, the leading member of a pioneering team that developed multivisceral transplantation in the early 1990s. He proposed a complex transplant procedure to provide Khaled with a new intestine, duodenum, liver and pancreas.

“The fact that Khaled had survived longer than any other patient with Martinez-Frias syndrome suggested he might fare well,” says Dr. Abu-Elmagd. “It prompted us to try to give him a second chance through transplantation.”

ENDURING THE WAIT WITH COMPREHENSIVE CARE

Khaled and his parents came to Cleveland Clinic in August 2012 to wait for suitable organs. Thus began more than a year of intricate inpatient therapy to manage Khaled's TPN, fluid balance and diabetes. Then, the good news arrived and it was time to act.

TRANSPLANT AND TRANSFORMATION

In September 2013, Khaled underwent the 15-hour, five-surgeon transplant procedure. It was a success, with all three organs and the duodenum grafting well.

Khaled was discharged less than two months later on an unrestricted oral diet and with his diabetes cured. At seven months after transplant, he was faring well, with no need for insulin and enjoying his favorite foods: mussels, octopus and lobster.

“I'm certain he won't have recurring disease with the new organs,” Dr. Abu-Elmagd says. “I want to see the boy healthy, to have a normal life and to go back home to enjoy his family and siblings.”

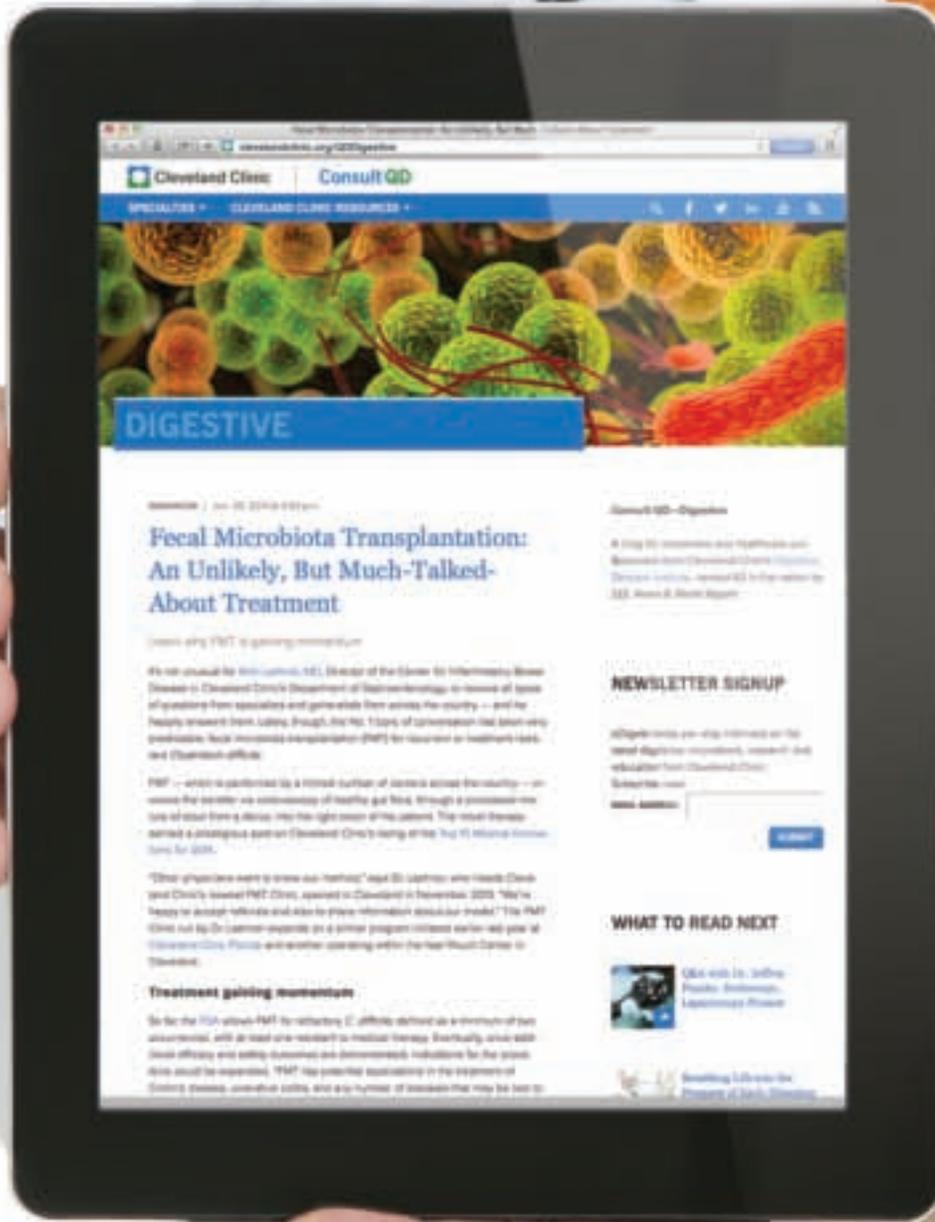
Dr. Abu-Elmagd and his team will monitor Khaled to study what happens to someone with Martinez-Frias syndrome as he ages and grows — something that had never been possible before.

The CGRT is among the world's few centers that offer both intestinal and multivisceral transplantation. It closely collaborates with experts at Cleveland Clinic Florida's transplant program, headed by Andreas Tzakis, MD, PhD, which recently received approval from the Centers for Medicare & Medicaid Services.

Contact Dr. Abu-Elmagd at 216.445.8876. | For CGRT 24-hour referrals, call 216.312.0308.

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Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,000 physicians and researchers represent 120 medical specialties and subspecialties. We are a nonprofit academic medical center with a main campus, eight community hospitals, more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City and Cleveland Clinic Abu Dhabi.

In 2014, Cleveland Clinic was ranked one of America's top hospitals in *U.S. News & World Report's* annual "Best Hospitals" survey. The survey ranks Cleveland Clinic among the nation's top 10 hospitals in 13 specialty areas, and the top hospital in heart care (for the 20th consecutive year) and urologic care.



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