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ADVANCES IN GASTROENTEROLOGY AND GI SURGERY

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INSIDE THIS ISSUE

Dr. David E. Cohen Named Chief of Gastroenterology and Hepatology at Weill Cornell

David E. Cohen, MD, PhD, an internationally renowned physician-scientist who combines clinical care as a hepatologist with research focused on obesity-related liver disease, has been named Chief of the Division of Gastroenterology and Hepatology at NewYork-Presbyterian/Weill Cornell Medical Center.


Dr. David E. Cohen

Dr. Cohen oversees a division that has more than doubled in size over the past five years resulting in an expansion in a number of areas of expertise, including major programs in invasive endoscopy, transplant hepatology, as well as leading-edge clinical and basic research on a variety of gastrointestinal and liver conditions. In his new role, Dr. Cohen will build upon that momentum by further strengthening the Division's mission to provide excellence in clinical care, education, and research; growing its research, and in particular, translational collaborations; and fostering the mentoring and training of junior faculty and fellows.

Dr. Cohen was previously Director of Hepatology at Brigham and Women's Hospital, the Robert H. Ebert Professor of Medicine at Harvard Medical School, and Director of the Harvard-Massachusetts Institute of Technology Division of Health Sciences. An expert in obesity-related gastrointestinal disorders, Dr. Cohen is particularly interested in nonalcoholic fatty liver disease, which affects as much as 20 percent of the population.

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Multiple Specialties COMMiT to Managing Obesity

"Obesity is a chronic disease with many health consequences of which diabetes, cancer, liver and kidney disease, and sleep apnea are but a few examples," says **Marc Bessler, MD**, Chief of the Division of Minimal Access/Bariatric Surgery and the Director of the Center for Metabolic and Weight Loss Surgery at NewYork-Presbyterian/Columbia University Medical Center. "Its incidence is startling. More than one-third of the American adult population is obese. One in 20 adults are considered extremely obese."

To address this multifaceted public health issue, Dr. Bessler and his colleagues in GI surgery and interventional endoscopy, endocrinology, psychology, nursing, and nutrition have come together to create COMMiT – Comprehensive Obesity and Metabolism Management and Treatment – to offer patients a range of expertise related to obesity under one umbrella of care and to integrate the newest medical, endoscopic, and surgical treatments that can help them achieve their weight loss goals.

"There are almost as many reasons why people become overweight as there are people who are overweight," says Dr. Bessler. "The COMMiT team understands the social, emotional, and behavioral factors in an individual's life and environment that can affect their weight and their health. We work with patients to develop safe and effective strategies on a number of fronts. In addition to promoting healthier nutrition and lifestyle choices, we are able to recommend the latest medications, nonsurgical procedures, or minimally invasive surgery."

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> — Dr. Marc Bessler

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Multiple Specialties COMMiT to Managing Obesity *(continued from page 1)*

Dr. Tamas A. Gonda, Dr. Tirissa J. Reid, Dr. Judith Korner, Dr. Marc Bessler, and Dr. Abraham Krikhely

The Endocrine Connection

"People describe obesity as though it is a single disease, but it isn't," says **Judith Korner, MD, PhD**, an endocrinologist in the Division of Endocrinology and Metabolism and Director of the Weight Control Center at NewYork-Presbyterian/Columbia. "If we can identify factors that contribute to an individual's obesity, we can then target the right therapy for them."

Dr. Korner's research – both NIH and industry funded – is focused on the neurohormonal regulation of body weight, appetite, and glucose homeostasis with forms of weight reduction, including diet and bariatric surgery. "Some individuals can eat a slice of pizza and feel full, and some individuals need a whole pizza to feel full. This is not just a matter of willpower," says Dr. Korner. "It may be due to a deficiency in the individual's reward center or in the hypothalamus. Researchers now realize that the gastrointestinal tract is comparable to a huge endocrine organ, with dozens of different hormones secreted from the stomach, the small intestine, and the large intestine. They not only help in terms of processing food that is consumed, but hormones also regulate the brain to control hunger, satiety, metabolism, and how the body manages insulin."

Dr. Korner explains, for example, that the ghrelin hormone in the stomach increases hunger. In the large intestine, the hormones GLP-1 and PYY signal fullness. Some of the hormones have multiple roles, so in addition to signaling fullness or hunger, they may also be related to insulin secretion and insulin sensitivity, creating an overlap between weight control and glucose control. One of the avenues of research that Dr. Korner is therefore pursuing is the relationship of bariatric surgery to metabolic benefit and, in particular, type 2 diabetes. The question she seeks to answer is: Does weight loss alone produce metabolic improvement or does the particular surgery change the types and the quantity of hormones that control blood sugar?

"Individuals can have the same surgery and the same surgeon, and some of them will lose a lot of weight and some will not," notes Dr. Korner. "Likewise diabetes will go into remission with normal glucose control for some patients, while others are more resistant. Results are very individualized. So to try to identify the response of one person, either to a particular medication or to a particular type of surgery, is very important. Our goal is to develop a hormone profile based on the outcomes of these surgeries to be able to triage patients to the surgery that is best suited for their metabolic condition."

Dr. Korner also serves as the principal investigator of two major clinical trials: an NIH-funded trial to study the effects of leptin administration after gastric bypass surgery on body weight and neuroendocrine function and a multicenter randomized trial of medical management versus gastric bypass surgery for the treatment of diabetes.

The Current State of Bariatric Surgery

"Although choosing to undergo bariatric surgery is a major decision, these operations have proven to be the best long-term treatments for significant weight loss," says Dr. Bessler. "Some of these procedures have been used for over 30 years and have been shown to resolve diabetes, high blood pressure, sleep apnea, and many other medical ailments."

More than 60 years have passed since the introduction of the first effective surgery for obesity in the United States. Since then, many different surgical approaches, including gastric bypass in the 1960s, have advanced the field and that trend continues today. "Since the advent of bariatric surgery, the field has seen two major transitions," says Dr. Bessler. "One is the more broad recognition of obesity requiring treatment as a chronic disease. The second is that while appreciating that surgery is still the most effective approach for permanent weight loss, there are less invasive options that can provide considerable benefit to patients."

According to Dr. Bessler, laparoscopic banding – which became available 15 years ago – had been a major offering in bariatric surgery practices but has since fallen by the wayside. "Interestingly over the past five years, of the many procedures that have come and gone, only gastric bypass and biliopancreatic diversion have stood the test of time in terms of effectiveness – both for weight loss and sugar control," says Dr. Bessler. "But gastric bypass has its drawbacks, including post-surgical predilection to ulcers and intestinal obstructions. It also affects absorption of B12, iron, and calcium, resulting in the need for patients to take supplements for the long haul."

A newer surgical option, sleeve gastrectomy, which is a part of the biliopancreatic diversion, is becoming more commonplace. Today, sleeve gastrectomy represents more than 50 percent of obesity and weight loss surgery volume. "When we remove the portion of the stomach that produces ghrelin, hunger is significantly reduced," explains Dr. Bessler. "The surgery is very effective in helping control hunger and limiting portion sizes. It has been shown to be within 10 percent of the effectiveness of gastric bypass, but without some of its side effects. The only disadvantage of a sleeve gastrectomy is that it can cause reflux in a percentage of patients." To address this concern, Dr. Bessler and his colleagues are now studying Stretta® and LINX therapies for the treatment of reflux in patients after sleeve gastrectomy.

Biliopancreatic diversion and a modification of that operation called single anastomosis duodenoileostomy, or SADI, are also offered

to patients. "SADI is a simplified version of the biliopancreatic diversion with duodenal switch," says Dr. Bessler. "We do a sleeve gastrectomy and also short circuit the intestine slightly by taking the duodenum and hooking it to the ileum. This is the most effective weight loss operation with about 40 percent of starting weight loss and 80 percent of excess weight loss, and it is the most effective operation we have for diabetes resolution."

Moving Toward the Minimally Invasive Arena

"The role of the gastroenterologist in bariatrics is evolving with new and exciting endoscopic weight loss procedures," says **Tamas A. Gonda, MD**, a gastroenterologist at NewYork-Presbyterian/Columbia with particular expertise in therapeutic endoscopy.

Dr. Gonda notes that in the last two years several procedures – all of which are available at Columbia – have received FDA approval. "We currently offer the intragastric balloon procedure, aspiration therapy, and endoscopic sleeve gastroplasty," he says. "By working together with the surgeons and the medical weight loss team, we can tailor therapy to shift from an endoscopic procedure to a surgical procedure, as well as add medications or nutritional counseling."

The FDA has approved intragastric balloons, some that are placed endoscopically and others that are swallowed and removed endoscopically. Both of these are offered by the COMMiT program. This incisionless, non-surgical procedure is recommended for adults with a BMI of 30 to 40, with or without a weight-related comorbidity, who have tried alternative weight loss methods without durable success. "The balloon is placed in a simple, outpatient procedure that takes less than an hour and does not require general anesthesia," says Dr. Gonda. "Patients lose about 15 percent of their starting weight, over 30 pounds on average, over a period of six months. After adapting to the balloon, more than 96 percent of patients tolerate it well and the weight loss success rate is over 98 percent."

According to Dr. Gonda, the balloon procedure has been performed on thousands of patients. "The balloon is in place for six months and then is completely removed," says Dr. Gonda. "However, that has its advantages and disadvantages. There can be significant weight gain afterwards if the person returns to their previous eating habits. The other procedures, which have been performed in smaller clinical trials in several hundred patients, are either permanent, like the gastroplasty, or have a longer duration.

"The aspiration device is a recently FDA approved option and it has a wider BMI range," continues Dr. Gonda. "In general, today's endoscopic procedures are meant and approved for those at the lower end of the obesity spectrum. This may change as these procedures evolve and we begin to understand the benefit of repeated procedures to manage this chronic condition."

Dr. Gonda and his colleagues also treat patients with complications from prior bariatric interventions or surgeries. "Endoscopic management of bariatric surgical complications offers an incredible advantage over reoperations and other much more morbid interventions," he says. "These are patients who've had difficult surgical situations. Repeating their surgery is not easy. But our team has the medical knowledge and the endoscopic and surgical expertise to manage any complications."

"The trend, in general," Dr. Bessler says, "has been toward less invasive therapy for obesity as patients often do not want surgery. In response, we have seen the growth of many alternative options. These include non-surgical gastric balloons and other incisionless procedures, and numerous FDA-approved medications that target a different aspect of cravings and satiation. In the past five years, the FDA has approved five new drugs for obesity and some drug combinations for weight loss."

The COMMiT team continues to look at less invasive or non-surgical devices on the FDA docket for approval in the next year or so. "There are other balloons that may be able to stay in longer than six months and a balloon that is embedded in a pill that can be swallowed and then inflates inside the stomach that does not require endoscopic placement," says Dr. Bessler. "I think every 18 months for the next few years, we are potentially going to be seeing new devices approved by the FDA or coming in front of the FDA for approval."

With a plethora of choices for patients, Dr. Bessler notes that it is indeed an exciting time in the field. "So much so," he says, "that we need an organized focus on how to marshal all of these resources to meet the community's needs and those of the individual patient grappling with complex choices. Obesity management used to be simply guiding people on losing weight, and they were able to or not. But now with the focus on obesity as a chronic disease, we recognize that we have to keep working at finding better ways of managing the condition and its consequences. That's the fundamental principle of COMMiT."

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Clinical Trial Update: The LESS GERD Trial for Adults Living with Severe Reflux Disease

Gastroesophageal reflux disease (GERD) affects nearly 65 million people in the United States. Most individuals with GERD are successfully treated with acid blocking medications such as proton pump inhibitors (PPI). However, nearly 30 percent of individuals on PPI medication continue to suffer symptoms, including bothersome regurgitation. Earlier studies conducted outside the U.S. have shown the elimination of pathological reflux in 70 percent of patients. This study is open to individuals between the ages of 22 and 75 who suffer from chronic reflux, take PPI medication, and continue to suffer from reflux symptoms. The LESS GERD Trial will examine the effects of the EndoStim® Lower Esophageal Sphincter Stimulation System, a new minimally invasive approach to severe reflux treatment, on GERD outcomes, such as esophageal pH, GERD symptoms, and the effect of GERD on overall quality of life.

The LESS GERD Trial is open to male and female patients who meet the following requirements:

- 22-75 years of age and diagnosed with GERD
- No prior surgery involving the esophagus
- Taking PPI medication (maximal dose)
- GERD symptoms are not completely resolved by PPI or intolerant to the PPI

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Dr. David E. Cohen Named Chief of Gastroenterology and Hepatology at Weill Cornell *(continued from page 1)*

Patients with nonalcoholic fatty liver disease are at high risk for plaque to accumulate in cardiac arteries, and may also face cirrhosis, as well as liver cancer. Dr. Cohen aims to better understand the metabolic basis of the condition to improve its management.

His research has been supported by several grants from the National Institute of Diabetes and Digestive and Kidney Diseases. In 2012, he received a MERIT (Method to Extend Research in Time) award from the National Diabetes and Digestive and Kidney Diseases Advisory Council to study regulation of lipid and glucose metabolism in the liver by the StarD2 protein.

"David is an esteemed physician, scientist, and leader whose contributions to understanding and treating obesity-related fatty liver disease exemplifies his commitment to providing the very best in patient care," says **Augustine M.K. Choi, MD**, Interim Dean, Weill Cornell Medicine, and Chairman of the Department of Medicine at NewYork-Presbyterian/Weill Cornell.

Dr. Cohen oversees a number of clinical programs, including the Jay Monahan Center for Gastrointestinal Health, the Jill Roberts Center for Inflammatory Bowel Disease, and the Joan and Sanford I. Weill Center for Metabolic Health, as well as general gastroenterology, invasive endoscopy, and hepatology and transplant hepatology.

Dr. Cohen received his medical degree from Harvard Medical School and his doctorate from the Graduate School of Arts and Sciences at Harvard University. He completed clinical and research fellowships in gastroenterology and hepatology at Brigham and Women's Hospital, serving as a faculty member of Harvard's graduate program in biological and biomedical sciences. Previously, he served as an associate professor of medicine and of biochemistry in the Marion Bessin Liver Research Center at the Albert Einstein College of Medicine.

Dr. Cohen has received numerous awards, including the American Liver Foundation Research Prize, an American Liver Foundation Liver Scholar Award, an International HDL Research Award, and a Hirschl Career Scientist Award. He was also named an Established Investigator of the American Heart Association. He is a fellow of the American College of Physicians, the American Association for the Study of Liver Diseases, and the American Gastroenterological Association, as well as a member of the American Society for Clinical Investigation, American Society for Biochemistry and Molecular Biology, and the Interurban Clinical Club.

Dr. Cohen's research has been published in *Science Signaling*, *Nature Structural Biology*, *Proceedings of the National Academy of Sciences*, *American Journal of Physiology*, *Journal of Lipid Research*, *Journal of Biological Chemistry*, *Hepatology*, *Gene*, *FASEB Journal*, *FEBS Letters*, *Biochemical Journal*, and *Biochemistry*. He is also the author of numerous book chapters. In July 2016, Dr. Cohen was named Editor-in-Chief of *Hepatology*, published by the American Association for the Study of Liver Diseases.

"NewYork-Presbyterian's intense focus on investing in both infrastructure and in people to strengthen the clinical and research enterprises was a major reason why I decided to move back to New York," says Dr. Cohen. "My goal is to further establish the Division of Gastroenterology and Hepatology as a model for how investments in basic and clinical research can translate into better care for patients."

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Endoscopic Sleeve Gastroplasty: A Newer Option for Weight Loss

Of the 98 million individuals in the United States who are obese and who would benefit from weight loss surgery, a scant 2 percent ultimately pursue it. "There are a number of reasons for this, including a fear of surgery and the potential side effects or perceived complications," says **Reem Z. Sharaiha, MD, MSc**, Director of Bariatric Endoscopy in the Division of Gastroenterology and Hepatology at NewYork-Presbyterian/Weill Cornell Medical Center. "Furthermore, there are an additional 86 million with a BMI of 30 to 40 for whom diet and exercise have not worked, and medication would only help achieve a 5 percent weight drop. People want something more sustainable without surgery and that's where endoscopic weight loss procedures are coming more into play."

Dr. Reem Z. Sharaiha

More than three years ago, Dr. Sharaiha and her colleagues began offering endoscopic sleeve gastroplasty, a minimally invasive, safe, and cost-effective alternative to surgery. "Patients can expect to lose between 17 and 20 percent of their body weight on average by six months to a year. This is an ideal option for select patients," says Dr. Sharaiha. "And it's a repeatable procedure."

Endoscopic sleeve gastroplasty mimics the traditional surgical sleeve. In a procedure performed under general anesthesia in an outpatient endoscopy unit, the physician inserts an endoscope with a suturing device down the patient's throat into the stomach, making about six to eight sutures to transform the stomach into a tube-shaped structure one third of its original size. "The way I bring the stomach together is similar to a corset or an accordion, where you just pleat the stomach on itself," says Dr. Sharaiha. "Patients generally spend two to three hours in recovery before going home the same day."

Dr. Sharaiha believes that research results coming in five to 10 years will more clearly validate the procedure's efficacy. "However, what we do know from our two-year and three-year data is that the people who follow up with their dietician and nutritionist continue to have good weight loss," says Dr. Sharaiha, who also notes that the effects of the procedure extends to improvements in blood sugar levels, cholesterol, and blood pressure based on data they recently submitted for publication.

Dr. Sharaiha continues to explore the full potential of the procedure. "We know the patient can achieve weight loss, but we want to know if it's sustainable, if it improves a patient's health, and down the line, if it improves mortality. Those are harder endpoints," she says. "If we can determine these points, we can begin to change the paradigm of this disease.

"The reason why endoscopic sleeve gastroplasty has become so successful is that it's very acceptable to a lot of patients, and I think that's the key," adds Dr. Sharaiha. "With obesity, you want something that patients are willing to do and take that leap of faith to start making a change."

According to Dr. Sharaiha, the increasing prevalence of obesity further necessitates close collaborations between surgeons, gastroenterologists, and endocrinologists. "We're starting to treat obesity more as a chronic condition," she says. "The patient may need more treatments throughout their lifetime, more surgery perhaps, endoscopy, medication, or all three."

Dr. Sharaiha emphasizes that no single approach will help a patient achieve all of their weight loss goals. "Over time, patients need a program that includes behavioral changes, diet, exercise, and nutrition counseling," says Dr. Sharaiha, who together with **Louis J. Aronne, MD**, Director of the Center for Weight Management and Metabolic Clinical Research, and **Alfons Pomp, MD**, Chief of Laparoscopy and Bariatric Surgery at NewYork-Presbyterian/Weill Cornell, has established the Weight Management Center to offer comprehensive, individualized treatment plans for each of their patients.

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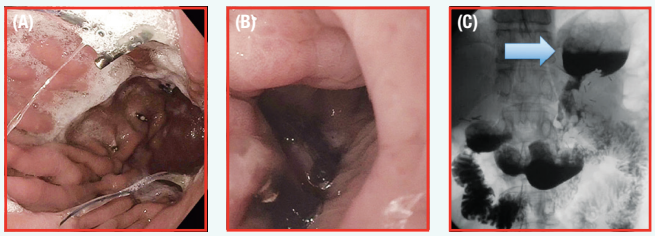
Endoscopic Sleeve Gastroplasty: A Case Study

A 60-year-old woman, weighing 214 pounds with a body mass index of 33.5 kg/m2, underwent successful endoscopic sleeve gastroplasty (ESG). One year post-ESG, she weighed 169 pounds (45 pounds weight loss, 21 percent total body weight loss, with BMI 26.5). However, her weight reached a plateau and she reported a diminishing change in satiety. A preliminary study showed ESG-induced decrease in caloric consumption and slowing of gastric emptying. Endoscopy revealed prior gastroplasty with loosened sutures. An endoscopic suturing system was used to place running stitches. The stitches were cinched to approximate opposing gastric walls. Two layers of sutures were placed to narrow the gastric lumen. Three months after this procedure, patient weighed 156 pounds (an additional 13-pound weight loss and 8 percent total body weight loss). From her initial ESG, the patient lost 58 pounds and 27 percent total body weight loss, with an improved BMI of 24.4. This case highlights the efficacy and repeatability of endoscopic sleeve gastroplasty for further weight loss.



(A) Endoscopic sleeve gastroplasty after one year with loosening of prior sutures (B) Gastric body after tightening of gastric sleeve (C) Upper GI series after tightening demonstrating narrow gastric body with fundal reservoir (blue arrow)

Source: Kumta NA, Doshi R, Aronne LJ, Sharaiha RZ. Trimming the fat: endoscopic suturing for tightening of prior endoscopic sleeve gastroplasty. *Gastrointestinal Endoscopy.* 2016 Sep 10. [Epub ahead of print]

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