Irritable bowel syndrome (IBS) is the most common gastrointestinal disorder in the United States, affecting 20% of adults, about two-thirds of them women. It costs the country more than $30 billion per year in direct and indirect expenses. Yet IBS has historically been the neglected stepchild of GI research. Few treatment options are available.

NewYork-Presbyterian Hospital and Weill Medical College of Cornell University, however, are at the forefront of efforts to change that, leading major research efforts on IBS and its treatment.

“In the past, there has been a lack of insight and effective treatments, but in the last few years we have been involved in the investigation of several novel and exciting compounds,” said Christine L. Frissora, MD. “The basis of IBS is now thought to be an abnormal communication between the central nervous system in the brain and the enteric nervous system in the intestine (illustrated above). The work of Christine L. Frissora, MD, at NewYork-Presbyterian/Weill Cornell has centered around breaking that connection to make patients more comfortable.

Advances in stent-graft technology, developed by researchers at NewYork-Presbyterian Hospital and Columbia University College of Physicians & Surgeons, have improved the patency and thus the effective life of transjugular intrahepatic portosystemic shunts (TIPS) in patients with portal hypertension.

Ziv Haskal, MD, has spent years investigating various coatings, materials, and strategies to prolong the primary patency of TIPS; he has successfully demonstrated that combining the device with polytetrafluoroethylene can “potentially improve the patency of the TIPS almost indefinitely.”

A large, randomized, multicenter trial based at NewYork-Presbyterian/Columbia compared the existing FDA-approved Wallstent with the new stent-graft device (Viatorr) in more than 250 patients with TIPS. “This is the largest trial of its kind in the world. We are analyzing the data,” said Dr. Haskal, the lead investigator. “It will hopefully lead to FDA approval of this particular device.”

While Dr. Haskal was unable to provide specific findings prior to FDA review, which is scheduled for the early part of this year, he was enthusiastic about the results so far. “I was just at the FDA, presenting data from the entire cohort,” he said. “There are clear and dramatic improvements in patency in the stent-graft.”
Allen Pavilion at the Forefront of Gallstone Surgery and Research

Spencer E. Amory, MD, believes the Allen Pavilion offers “the best of both worlds,” combining “the expertise of a major university medical center and the ambience of a community hospital.”

More than 10 years ago, the Department of Surgery at Columbia University College of Physicians & Surgeons chose to focus the clinical and research efforts at its northern Manhattan location on gallstone disease. In the past 2 years alone, the general surgical group, which includes Dr. Amory—as well as Peter Geller, MD, Zachary Gleit, MD, and Michael Treat, MD—has performed 750 laparoscopic gallbladder removals with 0% mortality and 0% common bile duct injury. Average length of hospital stay is less than 24 hours. The team’s overall conversion rate—the number of patients in whom the laparoscopic procedure has to be converted to open surgery—is only 6 in 750 cases, or less than 1%.

These outcomes, which are among the best nationally, have occurred despite the high number of complex cases treated at the Allen Pavilion. In the past 2 years, for example, acute cholecystitis was encountered in 34% of patients, compared to a national average of less than 10%, according to Dr. Amory.

Many patients with acute gallbladder disease are first seen in the emergency rooms at either the Allen Pavilion or at NewYork-Presbyterian/Columbia. The majority of these patients have urgent surgery performed at the Allen Pavilion by the General Surgery Group.

Nonetheless, the majority of gallbladder procedures at the Allen Pavilion campus are elective, with many of the patients referred by physicians from other hospitals, who are aware of the outstanding reputation of the attending surgeons at the Allen Pavilion.

“We recognized at the outset the potential for bile duct injuries during laparoscopic cholecystectomy. Our large volume of challenging patients spurred us to develop techniques for preventing those injuries. Our techniques… have been widely disseminated and adopted. As our outcomes would suggest, we have continued to develop and refine those techniques.”

—Spencer E. Amory, MD

“We recognized at the outset the potential for bile duct injuries during laparoscopic cholecystectomy,” said Dr. Amory. “Our large volume of challenging patients spurred us to develop techniques for preventing those injuries. Our techniques, which were published in the early 1990s, have been widely disseminated and adopted. As our outcomes would suggest, we have continued to develop and refine those techniques.”

Dr. Amory is currently leading a research project at the Allen Pavilion, focusing on predictors of surgery for patients with gallstones. “I hope we can find a way of predicting which of the 25 million Americans with gallstones will need surgery, because we could intervene earlier and lower the number of patients who develop secondary pancreatic inflammation or who require more hazardous emergency surgery,” he explained. “Currently, we are gathering clinical data that hopefully will help us to answer this and other unsolved questions in the management of gallstone disease.”

In the meantime, Dr. Amory and his surgical colleagues will continue to produce outstanding surgical results with a cohort of gallbladder disease patients that is often the most difficult to treat. “The way I would sum up what we do here,” he said, “is a large volume of gallbladder surgery on a complicated group of patients. We do it successfully and we do it safely.”

Spencer E. Amory, MD, is Chief of the General Surgery Group Section, NewYork-Presbyterian Hospital at the Allen Pavilion, and Assistant Professor of Surgery at Columbia University College of Physicians & Surgeons. E-mail: sea99@columbia.edu.
New Physician Appointments 2003

NewYork-Presbyterian Hospital has recruited the following physicians to its Digestive Diseases Service Line:

William Barlow Inabnet, III, MD, FACS, was named Chief of Endocrine Surgery at NewYork-Presbyterian Hospital/Columbia University Medical Center, and Assistant Professor of Surgery at Columbia University College of Physicians & Surgeons. His interests include minimally invasive thyroid, parathyroid, adrenal, and pancreatic surgery, as well as laparoscopic bariatric surgery.

E-mail: wbi2102@columbia.edu.

Tracey D. Arnell, MD, was named Assistant Professor of Surgery in the Division of General Surgery at NewYork-Presbyterian Hospital/Columbia University Medical Center. She is also Assistant Professor of Surgery at Columbia University College of Physicians & Surgeons. Her interests include inflammatory bowel disease, colorectal cancer, and evidence-based medicine.

E-mail: ta2107@columbia.edu.

John D. Allendorf, MD, was named Assistant Attending Surgeon at NewYork-Presbyterian Hospital/Columbia University Medical Center, and Instructor of Clinical Surgery at Columbia University College of Physicians & Surgeons. He completed his fellowship in liver transplantation and hepatobiliary surgery in July 2002.

E-mail: jda13@columbia.edu.

Michel Gagner, MD, was named Director of the Bariatric Surgery Program at NewYork-Presbyterian Hospital/Weill Cornell Medical Center. He is also Assistant Professor of Surgery at Weill Medical College of Cornell University. His interests include studying the surgical treatment of morbid obesity.

E-mail: mrig2016@med.cornell.edu.

Gerond V. Lake-Bakaar, MD, was named Assistant Attending Physician at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and Associate Professor of Clinical Medicine at Weill Medical College of Cornell University. His laboratory is currently focused on viral infection of intestinal epithelial cells.

NewYork-Presbyterian Digestive Diseases is a publication of the Digestive Diseases Center of NewYork-Presbyterian Hospital. The Digestive Diseases Center is at the forefront of research and practice in the areas of gastroenterology; GI surgery; and liver, bile duct, and pancreatic disorders. NewYork-Presbyterian Hospital/Columbia University Medical Center and NewYork-Presbyterian Hospital/Weill Cornell Medical Center are respectively affiliated with Columbia University College of Physicians & Surgeons and the Weill Medical College of Cornell University.

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www.nypdigestive.org
Clinical Trials Update

The following is a partial list of current clinical trials:

**Title:** Randomized evaluation of the safety, efficacy, and outcomes of laparoscopic adjustable gastric banding (LARG) versus laparoscopic gastric bypass (LGB) in patients with morbid obesity

**Principal Investigator:** Marc Bessler, MD

**Contact:** Amna Daud, ad731@columbia.edu

**Title:** A phase II trial of oral thalidomide as an adjuvant agent following metastectomy in patients with recurrent colorectal cancer

**Primary Investigator:** John Chabot, MD

**Contact:** Steven K. Libutti, MD, steven_libutti@nih.gov

**Title:** An open-label, multicenter, dose-escalation study to assess the safety, tolerability, and activity of ISIS 14803 in chronic hepatitis C patients undergoing pegylated interferon alfa-2b and ribavirin treatment who have not achieved an early virologic response

**Primary Investigator:** Ira M. Jacobson, MD

**Contact:** Nova Y. West, nyw2002@med.cornell.edu

**Title:** An open-label phase I study to evaluate the safety and tolerability of Panvac-VF in combination with GM-CSF in patients with unresectable adenocarcinoma of the pancreas

**Primary Investigator:** Howard L. Kaufman, MD

**Contact:** Josie Mitcham, jm2124@columbia.edu

**Title:** A prospective, randomized, open-label study evaluating the viral kinetics and pharmacokinetics of pegassus plus copegus and peg–intron plus rebetol in interferon-naïve patients with chronic hepatitis

**Primary Investigator:** Gerond Lake-Bakaar, MD

**Contact:** Nova Y. West, nyw2002@med.cornell.edu

**Title:** A phase III, randomized, controlled study comparing the survival of patients with unresectable hepatocellular carcinoma (HCC) treated with thymitaq to patients treated with doxorubicin

**Primary Investigator:** Kyriakos Peter Papadopoulos, MD

**Contact:** Cara DeRosa, derosa@cancercenter.columbia.edu

**Title:** Percutaneous treatment of liver tumors with acetic acid

**Primary Investigator:** John H. Rundback, MD

**Contact:** Leslie Schmidt, ls72@columbia.edu

**Title:** A multicenter, randomized, double-blind, placebo-controlled trial of rifaximin in patients with pouchitis with prior abdominal colectomy and ileal pouch–anal anastomosis for ulcerative colitis followed by 4 weeks of dosing with open-label rifaximin

**Primary Investigator:** Ellen Scherl, MD

**Contact:** Debbie Golden, dlg2006@med.cornell.edu

**Title:** International cooperative pancreatic cyst (CPC) investigation

**Primary Investigator:** Peter Stevens, MD

**Contact:** Peter Stevens, MD, pds5@columbia.edu

**Title:** A randomized clinical trial comparing 2 management strategies for the treatment of neutropenia and anemia associated with pegylated interferon and ribavirin treatment of compensated chronic hepatitis C in adult subjects infected with HIV

**Primary Investigator:** Andrew H. Talal, MD

**Contact:** Andrew H. Talal, MD, aht2002@med.cornell.edu

**Title:** Phase III randomized, controlled study comparing the survival of patients with unresectable hepatocellular carcinoma treated with thymitaq to patients treated with doxorubicin

**Primary Investigator:** Scott Wadler, MD

**Contact:** Shannon Holloway, 212-746-3224

For information on more clinical trials in Digestive Diseases, visit: www.nypdigestive.org.

Appointments

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dynamics of hepatitis C and the rapid early evolution of the virus, which allows it to “escape” interferon antiviral therapy.

E-mail: gvl2002@med.cornell.edu.

**Alfons Pomp, MD,** was named Assistant Attending Physician at NewYork-Presbyterian Hospital/Weill Cornell Medical Center and Assistant Professor of Surgery at Weill Medical College of Cornell University. His primary clinical research interest is laparoscopic bariatric surgery.

E-mail: alp2014@med.cornell.edu.

**Sang Lee, MD,** Assistant Attending Surgeon at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, was appointed Assistant Professor of Surgery at Weill Medical College of Cornell University. His interests include laparoscopic colon and rectal surgery.

E-mail: sal2013@med.cornell.edu.
**Monahan Center Incorporates Gastrointestinal Cancer Research and Treatment**

The Jay Monahan Center for Gastrointestinal Health, a collaboration of NewYork-Presbyterian Hospital and Weill Medical College of Cornell University, provides seamless, multidisciplinary care through a core team made up of gastroenterologists, surgeons, oncologists, and a nurse coordinator. Patients will also have access to genetic counselors, social workers, psychologists, nutritionists, and home care services.

“This place is going to be unique,” said Mark Pochapin, MD. “It’s not going to be a place where patients just get shuttled in and out of rooms.”

The Monahan Center is named for Jay Monahan—the late husband of NBC Today show co-anchor Katie Couric. Monahan was diagnosed with advanced colon cancer at the age of 41. He and his family were troubled by the exhausting effort needed to collect information and identify treatment options. Monahan battled the disease for several months. He died in 1998.

In 2000, Couric brought attention to the need for further research in the area of gastrointestinal cancers with a 5-part series of broadcasts entitled, “Confronting Colon Cancer,” during which she underwent a televised colonoscopy performed by Kenneth Forde, MD, at NewYork-Presbyterian Hospital and Columbia University College of Physicians & Surgeons. Dr. Pochapin, who was Monahan’s gastroenterologist, took part in the series. A year later, a follow-up series won the prestigious Peabody Award for broadcast journalism.

“After that segment aired, investigators looked at the rates of colonoscopy, and they had jumped by almost 20%,” said Dr. Pochapin. This phenomenon, dubbed the “Couric Effect” by researchers at the University of Michigan and the University of Iowa, was the subject of an article in Archives of Internal Medicine last year (2003 Jul 14;163(13):1601-1605).

After Monahan’s death, his family pledged to find a better way to treat GI cancers. With the support of the Entertainment Industry Foundation’s National Colorectal Cancer Research Alliance, the Center was established. Physicians at the Center will have the resources to evaluate and offer new approaches to prevention and treatment of gastrointestinal cancers, from the latest diagnostic equipment to alternative and holistic options.

The Center will also provide a universal referral service for information on clinical outcomes, research protocols, prevention, and treatment. Research will focus on the most promising clinical trials, ensuring the latest and most effective patient care options.

Mark Pochapin, MD, is Director, Jay Monahan Center for Gastrointestinal Health, and Director, GI Endoscopy, Division of Gastroenterology and Hepatology at NewYork-Presbyterian/Weill Cornell. He is also Associate Professor of Clinical Medicine at Weill Medical College of Cornell University.

E-mail: mbpocha@mail.med.cornell.edu.

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At the Monahan Center, GI cancer patients will have access to genetic counselors, social workers, psychologists, nutritionists, and home care services.
David A. Brenner, MD: New Chair of Medicine Sees Breakthroughs in GI Research
Hopes to Bring New Research Focus to GI Division

David A. Brenner, MD, says his primary goal as the new Director of Medical Service at NewYork-Presbyterian Hospital/Columbia University Medical Center and Chairman of the Department of Medicine at Columbia University College of Physicians & Surgeons is to “bridge the gap between the terrific basic research and devoted patient care” through translational research.

“This is one of the unique roles of academic medical centers,” explained Dr. Brenner. “Basic science can be done in many places. But translating those seminal observations into asking clinically relevant questions can really only be done at academic medical centers. That’s going to be one of our unique niches in the next 20 years.”

Dr. Brenner is editor-in-chief of Gastroenterology, the field’s premier journal. He arrived at NewYork-Presbyterian/Columbia from the University of North Carolina, where he served as the university’s Chief of the Division of Digestive Diseases and Nutrition.

He received his medical degree from Yale University. After serving as a resident at Yale, he worked at the National Institutes of Health, then joined the Department of Medicine at the University of California, San Diego. In 1992, he was appointed the Nina and John Sessions Distinguished Professor of Digestive Diseases at the University of North Carolina, where he also held a professorship in biochemistry and biophysics.

Having moved his laboratory to NewYork-Presbyterian/Columbia, Dr. Brenner is continuing his fundamental research in liver fibrosis and intracellular signaling. In his first 6 months on the job, his primary observation is that “the students, the residents, and the faculty here are all just outstanding, the best I’ve ever had the honor of working with.”

In GI research, he foresees exciting new advances. “Irritable bowel disease is an area where there are incredible breakthroughs in biologics and new therapies,” he said. “The opportunities to offer improved patient care and new diagnostic tests are going to be enormous over the next 10 years.”

The study of obesity and nonalcoholic fatty liver disease offers another opportunity for making important observations, according to Dr. Brenner. “It’s become an area of particularly intense research because of the large number of patients undergoing surgery for obesity,” he said. “This is an opportunity to not only provide better clinical care, but also to learn more about the disease and its treatment. There will be clinical trials to assess what the effect of gastric surgery is on obesity and on the liver disease associated with it.”

In research on Barrett’s esophagus, he predicted, researchers at NewYork-Presbyterian Hospital/Columbia will “clarify what the benefits are of screening for adenocarcinoma in Barrett’s patients.” And to increase access to colon cancer screening, he said, “virtual colonoscopy done by CT scans—as well as new tests in the blood and stool for cancer cells and cancer markers—will make for much more efficient screening. Only those patients who have positive findings will get a colonoscopy.”

To lead the GI division, Dr. Brenner is in the process of recruiting a new division chief, whose primary focus will be on basic research.

“I want someone to be a leader in the molecular pathophysiology of GI diseases, someone who does fundamental research,” he said. “We hope to reinvigorate that field.”

David A. Brenner, MD, is Director, Medical Service at NewYork-Presbyterian/Columbia, and Chairman, Department of Medicine at Columbia University College of Physicians & Surgeons. E-mail: dab2106@columbia.edu.
group, with far fewer interventions and better uninterrupted maintenance of portosystemic decompression.”

Most patients with TIPS require the procedure because worsening liver disease and resultant portal hypertension lead to recurrent variceal bleeding or refractory ascites. But Dr. Haskal’s team of interventional radiologists uses TIPS in other, more unusual ways, in patients whose portal hypertension is not caused by liver disease. They work closely with transplant specialists Robert Brown, MD, and Jean C. Emond, MD, to employ a multidisciplinary approach for patients with portal hypertension and other liver-related conditions.

“Our approach is to look at the portal pressure and blood flow, as well as the underlying condition,” said Dr. Brown.

One example is Budd-Chiari syndrome. This occurs in patients whose livers may be healthy but, because of a variety of hypercoagulation disorders, their blood tends to clot, causing blockages in veins flowing out of the liver. “These patients have an essentially normal liver with an outflow problem,” Dr. Haskal said. “The liver becomes swollen, congested, and painful. The patients develop ascites. These are patients in whom pressure-lowering procedures like TIPS can actually prevent development of liver disease.”

Dr. Haskal and his team recently looked at a series of patients with Budd-Chiari syndrome, who were treated with TIPS. Over a follow-up period of more than 2 years, “we have seen that every patient has had improvement or regression of their hepatic congestion, improvement of liver function, and resolution of their ascites,” he reported.

“We’re looking at a treatment that will have a 20- to 50-year horizon, unlike the other patients with chronic liver disease. I practice very aggressive follow-up by doing transjugular biopsies in these patients to demonstrate that there is no further stimulus to ongoing cirrhosis or scarring because the congestion has been treated by bypass. In 10 years of treating such patients with TIPS, I’ve seen only 1 require liver transplantation.”

The interventional radiology team has explored other unusual conditions to leverage the advantage of TIPS patients with acute or chronic mesenteric portal and splenic vein thrombosis, for example. “They are generally healthy patients with a hypercoagulation syndrome, who come in with abdominal pain and whose symptoms worsen despite anticoagulation,” he said. “And we have used catheter-directed techniques, including thrombolysis, mechanical thrombectomy, and TIPS together in the same patient to restore patency. These patients are seen potentially by a cohort of physicians across specialties. If they come to see me directly, I involve the liver team and vice versa.”

Ziv Haskal, MD, is Director of the Division of Vascular and Interventional Radiology, NewYork-Presbyterian/Columbia, and Professor of Radiology and Professor of Surgery, Columbia University College of Physicians & Surgeons. E-mail: zh50@columbia.edu.

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### IBS

*continued from page 1*

system in the brain and the enteric nervous system in the intestine. By breaking the brain–gut connection, we can make patients more comfortable and less visceralized—less focused on their intestine and more focused on their life.”

According to Dr. Frissora, approximately 96% of serotonin is located in the GI tract, compared to just 2% in the central nervous system. The serotonin receptors most important in the GI tract in general and IBS in particular, she says, are the 5-HT3 and 5-HT4 receptors. Dr. Frissora was involved in the work that led to the FDA’s approval in July 2002 of the newest drug for IBS in women: tegaserod, a 5-HT4 partial agonist that increases intestinal motility. It remains the first and only agent shown to relieve all 3 of the so-called ABCs of IBS: abdominal pain, bloating, and constipation.

Currently, Dr. Frissora is recruiting patients for a 12-week, double-blind, placebo-controlled Phase II trial of dextofisopam in men and women with IBS that is either diarrhea-predominant or characterized by alternating diarrhea and constipation. “The greatest efficacy for the drug is expected in these groups,” she said, although it may eventually prove effective for other types of IBS, she added. “Dextofisopam is a novel compound for which there is no equivalent drug in the United States,” Dr. Frissora continued. “The main appeal is that it is a nonnarcotic, nonad- see IBS, page 8
Important news from the Digestive Diseases Services Center of NewYork-Presbyterian Hospital, leading the way in treatment and research in gastrointestinal, liver and bile duct, pancreatic, and nutritional disorders.