



Pitt

Digest

Spring 2009



Inside This Issue

Page Two

**Pancreatic Problems
after Gastric Bypass**

Page Three

Division Highlights

Pages Four and Five

GI Grand Rounds

Page Six

Faculty Update

Page Seven

**Advances in Research and
Endoscopic Therapy**

Page Eight

• **What Is This?**

• **PancreasFest 2009**

CENTERS OF EXCELLENCE:

- PANCREAS & BILIARY DISEASES
- INFLAMMATORY BOWEL DISEASE
- LIVER DISEASES
- NEUROGASTROENTEROLOGY AND MOTILITY DISEASES
- INTESTINAL HEALTH & NUTRITION SUPPORT
- GASTROINTESTINAL CANCER PREVENTION & TREATMENT
- WOMEN'S DIGESTIVE HEALTH

Pitt Digest

is a publication of the
*University of Pittsburgh
Division of Gastroenterology,
Hepatology and Nutrition*

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Shadyside Gastroenterology Group at UPMC

by **Randall E. Brand, MD**

The Division of Gastroenterology, Hepatology and Nutrition's new group located at UPMC Shadyside illustrates a triumphant union between private practice and academic medicine. Building upon the successful private gastroenterology practice of Drs. Howard Dubner and Lee Weinberg, our group has expanded to five gastroenterologists with the additions of Drs. Andres Gelrud, Scott Cooper and myself. Amid this expansion, the team has maintained a commitment to the general gastroenterology service at UPMC Shadyside, Hillman Cancer Center and the surrounding community, while simultaneously offering the clinical expertise and resources of a major, academic institution.

The Division of Gastroenterology, Hepatology and Nutrition recruited Dr. Gelrud from the University of Cincinnati to serve as the director of Therapeutic Endoscopy at UPMC Shadyside. Dr. Gelrud provides tertiary therapeutic endoscopic support including ERCP, single balloon enteroscopy and stent placement. More information about



Division of Gastroenterology, Hepatology and Nutrition at UPMC Shadyside (L to R, starting with back row): Lee Weinberg, MD; Heather Hathy, PA-C; Andres Gelrud, MD; Randall Brand, MD; Scott Cooper, MD; Howard Dubner, MD.

Dr. Gelrud's research may be found on page 7 of this issue. Dr. Cooper graduated from the University of Pittsburgh GI Fellowship Program in July 2008. Currently an

instructor of medicine, he is an advanced EUS and ERCP trainee and will join the practice on a full-time basis in June 2009. As you may know,

continued on page 6

Malnutrition and Pancreatic Problems After Gastric Bypass Surgery for Morbid Obesity

After gastric bypass surgery for morbid obesity (BMI > 40kg/m²), stomach volume is reduced and the duodenum and proximal jejunum is bypassed, resulting in malabsorption and weight loss. While most patients tolerate surgery well with weight loss plateauing near ideal body weight, some patients continue to lose weight, becoming so malnourished that a reversal of the surgery is considered. Until now, no studies have investigated pancreatic function in obese patients following bypass surgery. It is likely that the pancreas atrophies due to bypass of pancreatic stimulation paired with perpetual stimulation of the inhibitory ileal break.

This current research examines pancreatic secretion and food absorption in patients who have lost >100 lbs. in the first year following bypass surgery. Collaborators include the



Division of Gastroenterology, Hepatology and Nutrition, Clinical & Translational Science Institute (CTSI) and Magee Bariatric Surgery with support from Solvay Pharmaceuticals. Patients with excessive, continued weight loss after bariatric surgery will be screened for fat absorption and loss of pancreatic secretion. Those with >20% fat malabsorption will be treated with pancreatic enzyme supplements for a three-month period to assess weight stabilization or gain. After three months, fat absorption and a pancreatic stimulation test will be repeated to determine if fat digestion and absorption are improved after enzyme supplementation.

More subjects are needed for this study. Gastric bypass patients with uncontrolled weight loss may be referred to **Dr. Tina Rakitt** – pager: (412) 571-4038 – or **Dr. Stephen O’Keefe** (412) 648-7217 for study information.

Division’s Expansion to Serve Patients Better

by **Chad J. Scott, MA, MPM**

Despite the outstanding services available to GI and liver patients in the Division of Gastroenterology, Hepatology and Nutrition’s main UPMC Presbyterian location, Oakland is not an easy destination for some – especially for those already nervous about a colonoscopy!

Over the past few years, our Division expanded clinical and procedure service locations to optimize patient convenience. Highly specialized patient services are still performed in the Division’s primary Oakland location. Consults and most procedures are now done “off campus” as well. Extensive outpatient clinics and procedure services have been added

at UPMC Shadyside, as Dr. Brand discussed in this issue’s cover story. Also, both male and female patients are cared for at the Magee-Womens Hospital of UPMC.

More recently, our faculty physicians have started seeing more patients in the east, north and south suburbs. Procedure clinics now operate at the Monroeville Surgery Center, South Side Surgical Center, McKeesport Hospital and the Bethel Surgical Center. Additionally, the Monroeville Image Center hosts a gastroenterology outpatient clinic, and UPMC Passavant has a liver consult clinic.

We plan to offer even more services in the South Hills of Pittsburgh within the coming year, as well as in a new North Hills location. Of course, we will

enhance services in Monroeville to complement UPMC’s new Monroeville hospital, scheduled to open in 2011.

Referrals for interested patients are easy. Simply call the main UPMC Presbyterian Digestive Disorders Center number at **(412) 647-8666** or, toll-free, **1-866-4GASTRO (1-866-442-7876)**, and the receptionist can refer you to the preferred service location for your patient.



Mr. Scott is the chief administrator for the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition.

DIVISION HIGHLIGHTS

The University of Pittsburgh Medical Center (UPMC) is a network of over 20 health care facilities in Western Pennsylvania with two flagship hospitals: UPMC Presbyterian, linked to a world famous transplant center, and UPMC Shadyside, linked to the Hillman Cancer Center. The clinical, research and education mission of the Division of Gastroenterology, Hepatology and Nutrition is thriving at both facilities and in other specialty and outreach locations. Expansion to UPMC Shadyside began several years ago with the recruitment of **Drs. Howard Dubner** and **Lee Weinberg**, representing one of our region's top consultative groups and members of our Division's training faculty. The UPMC Shadyside group has rapidly expanded with the recruitment of **Drs. Randall Brand, Andres Gelrud, Scott Copper** and **Marc Schwartz** (starting July 2009). This extraordinary team is featured in this issue of *Digest*.

Amidst this expansion, our Division continues to attend to the discovery of new knowledge about complex inflammatory diseases of the digestive systems and to treat related complications of these diseases. Complex disorders, by definition, are syndromes which occur through the interaction of multiple variables (genetic, metabolic, and environmental) that may not be independently pathologic but can combine in various permutations to alter disease severity and progression in the same underlying disease. Being able to characterize and quantify the individual and synergistic contributions of these factors could result in accurate, predictive tools to provide the *right* treatment to the *right* patient at the *right* dose at the *right* time – i.e. personalized medicine.



The Division's 2009 **GI Division Research Retreat** focused on personalized medicine, particularly for diseases of the liver and pancreas as well as IBD and functional pain syndromes. Clinical faculty met with scientists from the University of Pittsburgh, Carnegie Mellon University and other institutions, on March 7–8, 2009. Physicians discussed unpredictable outcomes and features of inflammatory disorders with scientists specializing in immunology, tissue repair & regeneration, neuroscience,

DNA repair and oncogenesis, psychology, epidemiology, genetics and biomarkers. Bonding started during the Pitt–UConn basketball game, while research collaborations developed during the poster sessions and subsequent meetings.



Anticipated retreat outcomes include the development of more than a dozen NIH Challenge Grant applications, plans for collaborative RO1s and related discussions. Stay tuned for details. I hope that you continue to enjoy reading about Division happenings and discoveries in this publication. We look forward to close interactions in the future.



In good health,

A handwritten signature in black ink, appearing to read "D. Whitcomb".

David C. Whitcomb, MD, PhD

*Giant Eagle Foundation Professor
of Cancer Genetics*

*Professor of Medicine, Cell Biology
& Physiology and Human Genetics*

*Chief, Division of Gastroenterology,
Hepatology and Nutrition*

A Perplexing Patient with Refractory Ascites



by **Behar Madani, MD**
Hepatology Fellow

Case Presentation

A 39-year-old Saudi woman returned to Pittsburgh after a 17-year absence due to worsening ascites. She underwent a liver transplant at UPMC in 1991 secondary to autoimmune hepatitis. In 2003, she developed HCV and was treated with standard interferon (IFN) for one year with no response. In 2006, she developed ascites secondary to tuberculous peritonitis and was treated with isoniazid, ethambutol and rifampin. Initially yellow, the ascitic fluid became milky six months prior to current presentation. Though initially responsive to diuretics, the ascites became refractory requiring large volume paracenteses every two weeks. Concurrent with the refractory ascites, she developed



Figure 1: Kidney biopsy with membranoproliferative form of glomerulonephritis. The glomerulus (arrow) has accentuated lobularity and a more solid appearance. Adjacent to the glomerulus is an area of interstitial fibrosis and tubular atrophy.

acute renal injury and was told she may require hemodialysis. An August 2007 liver biopsy revealed grade I hepatitis C activity index and stage II/IV fibrosis.

Past medical history is significant for diabetes and hypertension, and medications include tacrolimus, spironolactone, furosemide, amlodipine and insulin. Married and living with her husband, she had no children and denied any tobacco, alcohol or illicit

drug use. She worked as an office manager prior to her return to Pittsburgh.

Examination was notable for cachexia. Her abdomen was severely distended, diffusely tender with a peritoneal catheter *in situ* draining milky fluid.

Labs were notable for mild hyponatremia; creatinine 1.3 mg/dl; normal platelets; hemoglobin 10.7 mg/dl; hypoalbuminemia 1.8 mg/dl; and mild transaminases (ALT 30;

AST 58). HCV RNA was 2200 copies/ml, Genotype 4; ANA was 1:80; and serum complements, C3 41, C4<10. There was hematuria (RBC 15/hpf) and proteinuria (6.5gm/24hr). The ascites was chylous with elevated triglycerides (261 mg/dl), a SAAG < 1.1 g/dl; gram stain and cultures for bacteria and acid fast organisms were negative. A CT scan of the abdomen revealed splenomegaly, large ascites, patent hepatic vessels and no evidence of cirrhosis or portal hypertension. Liver biopsy showed mild fibrosis and peritoneal biopsy was negative for TB and lymphoma. A kidney biopsy was performed showing changes consistent with membranoproliferative glomerulonephritis (MPGN) associated with cryoglobulinemia (CG), and blood work was positive for cryoprecipitate, type III, polyclonal (IgG, IgM, IgA) confirming the diagnosis.

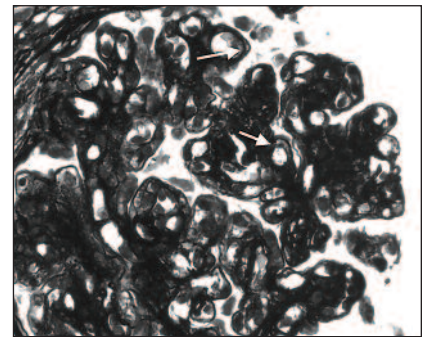


Figure 2: Glomerulus with "tram track" which results from basement membrane splitting and reduplication (white arrows).

Cryoglobulinemia (CG) is defined by the presence of CG in serum and immune complex deposits in small to medium vessels and presents typically with a classical triad of purpura, weakness and arthralgia. Type II and III are mixed polyclonal (IgM and IgG) and can be seen with viral infections such as hepatitis C. MPGN associated with type II CG is the predominant type of HCV-related glomerulonephritis (GN) and presents with nephritic syndrome or acute nephritis with rapid deterioration in renal function. MPGN and CG are late presentations in the natural course of HCV infection and are often clinically unsuspected.

The treatment of HCV-CG includes symptomatic therapy, anti-HCV therapy and immunosuppressives. Recommended screening for HCV patients should include assessment of renal function and serum cryoglobulin, complements and rheumatoid factor.

Our patient was started on antiviral therapy with pegylated IFN and ribavirin, and her HCV-RNA became undetectable at four weeks.

Epistaxis and a Bloody Liver



by **Joseph Rodemann, MD**
Gastroenterology Fellow

Case Presentation

A 32-year-old female with recurrent epistaxis was admitted to Magee Women's Hospital of UPMC at 29 weeks gestation with a three-week history of sharp, intermittent RUQ pain and nausea. She had no other past medical or surgical history. Her family history was only significant for epistaxis in her father.

The patient's labs were consistent with gallstone pancreatitis. Ultrasound displayed cholelithiasis with findings of acute cholecystitis. Labor was induced one week later due to the patient's deteriorating clinical status, and normal vaginal delivery occurred. Following ERCP with sphincterotomy and stone extraction, her symptoms and labs improved, and she was sent home.

Four weeks later, the patient was admitted to UPMC for interval cholecystectomy. At that time, she presented with abnormal LFTs and abdominal pain. Hepatology was consulted prior to surgery.

examination revealed an obese female in no overt distress with normal vital signs. Sclera were anicteric. Abdomen was distended with moderate RUQ tenderness and hepatomegaly. There were no stigmata of chronic liver disease, and neurologic exam was normal.

Notable labs including albumin of 2.2, total bilirubin 2.2, direct bilirubin of 1.4, AST 87, ALT 53, AP 652, lipase 245, and INR of 2.2 indicated a mixed hepatocellular and cholestatic liver injury pattern with synthetic dysfunction. Testing for viral, autoimmune, and metabolic causes of liver disease was unremarkable. Abdominal CT scan displayed numerous telangiectasia in liver parenchyma, numerous arteriovenous fistuli with early filling and enlargement

of hepatic veins with mild ascites in a non-cirrhotic liver. Abdominal ultrasound showed a combination of fatty infiltration and hereditary hemorrhagic telangiectasia and patent major hepatic vessels. After undergoing an uneventful cholecystectomy, the patient was discharged home.

One month later, she was admitted with recurrent abdominal pain, acute renal failure, leukocytosis, and abnormal LFTs including a total bilirubin of 4.1 and an INR of 2.4. During this hospital course, the patient became acutely ill with mental status changes and was transferred to the ICU for blood pressure support and mechanical ventilation.

She was diagnosed with *Enterococcal* bacteremia of unknown etiology without signs of endocarditis on TEE. The patient was listed status 1 for liver transplant and received a liver, but she died intraoperatively.

Pathology of the native liver revealed multiple abnormal venous channels, shunts and arteriovenous malformations consistent with hereditary hemorrhagic telangiectasia (HHT). Notable were central vein sclerosis and focal hepatic venous obliteration with marked congestion and hemorrhage, severe ischemic cholangiopathy with widespread bile duct necrosis and tissue necrosis containing gram positive coccoid bacteria, and moderately severe steatohepatitis.

HHT, also known as Osler-Weber-Rendu syndrome, was first recognized in the 19th century as a familial disorder with abnormal vascular structures causing bleeding from the nose and gastrointestinal tract. Common symptoms are epis-

taxis, gastrointestinal bleeding and iron deficiency anemia, and incidence is 1:20,000 in retrospective U.S. studies. The Curaçao Criteria, used to diagnose HHT, includes epistaxis, telangiectasias, visceral lesions and family history.

Hepatic involvement occurs in 30 to 80 percent of cases of HHT with common complications including portal hypertension, high-output cardiac failure and biliary disease. Treatment options include hepatic artery embolization, liver transplant and antibodies targeting vascular endothelial growth factor receptor.

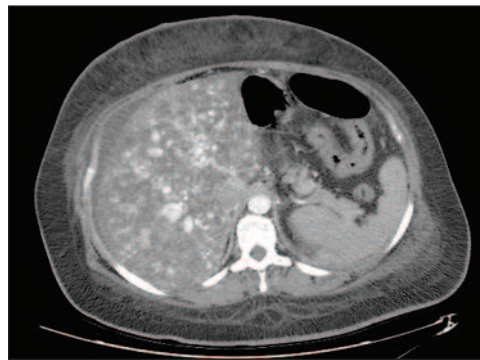


Figure 1: CT scan showing numerous telangiectasia seen within the liver parenchyma. Numerous arteriovenous fistulas with early filling and enlargement of the hepatic veins.

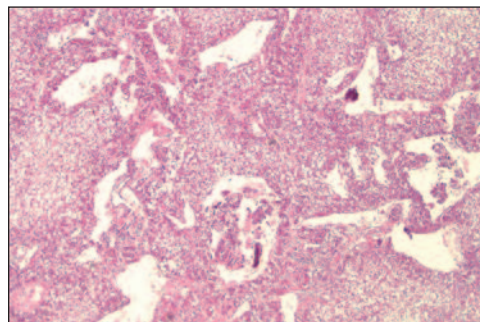


Figure 2: Pathology demonstrates tortuous thin-to-thick-walled abnormal vessels.



Robert E. Schoen, MD, MPH, professor of medicine and epidemiology with the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition, has initiated testing on a vaccine that could prevent colon cancer in people at high risk. In a novel approach to cancer prevention, his study will explore an abnormal variant of a self-made cell protein called MUC1, which is altered and produced in excess in advanced adenomas and cancer. If shown to be effective, Dr. Schoen's research may spare patients the risk and inconvenience of repeated invasive surveillance tests.

Pitt's colon cancer vaccine research is sponsored by the National Cancer Institute and The Nathan S. Arenson Fund. Dr. Schoen's co-investigator is **Olivera Finn, PhD**, professor and chair in the Department of Immunology.



Adam Slivka, MD, PhD will be honored with the National Pancreas Foundation's 2009 Courage Award recognizing his distinguished achievements and dedication to patients with pancreas diseases. Dr. Slivka will receive this award at NPF's annual gala on Friday evening, June 26, 2009 at the Circuit Center on Pittsburgh's South Side.

Dr. Slivka is a professor of medicine with the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition, where he serves as the Division's associate chief for clinical services. Dr. Slivka's research interests include clinical applications of gastrointestinal endoscopy for diagnosis and therapy, including the development and testing of new instrumentation and therapy to improve endoscopic outcomes in pancreaticobiliary disease.

For more information on NPF's gala, visit www.pancreasfoundation.org or call, toll free, 1-866-726-2737.



Miguel Regueiro, MD and colleagues have found that infliximab prevents Crohn's disease recurrence after surgery. (Regueiro M., et. al. *Gastroenterology* 2009; 136:441-50). One year after resective intestinal surgery only nine percent of patients receiving infliximab had endoscopic recurrence compared to 85 percent of patients on placebo ($p=0.0006$).

Dr. Regueiro is an associate professor of medicine with the Division of Gastroenterology, Hepatology and Nutrition. He serves as the associate chief for education and as the program director for the University of Pittsburgh's Gastroenterology Fellowship Program. Dr. Regueiro co-directs the UPMC Inflammatory Bowel Disease Center and heads IBD clinical services.

Gastroenterology Group at UPMC Shadyside *continued from page 1*

I hail from Evanston Northwestern University and am an established EUS specialist and also perform stent placements in the gastrointestinal tract. Drs. Dubner and Weinberg are outstanding gastroenterologists with interests in IBD, and their leadership and collegiality have made our Division expansion possible. Finally, we are welcoming **Marc Schwartz, MD** from the University of Chicago to further strengthen the Division's IBD program.

State-of-the-art renovation of the UPMC Shadyside GI Laboratory reflects the administration's commitment to program success. Construction will be complete this summer and will provide a technologically advanced

procedural environment with a dedicated emphasis on patient comfort.

The primary intention of the GI Division at UPMC Shadyside is to provide continuity of care for the general GI needs of UPMC Shadyside complemented by solid expertise in advanced GI procedures and specialized care for GI oncology patients served by the Shadyside and Hillman facilities. For example, my research on the early detection of pancreatic cancer and high risk pancreatic cancer families, will hopefully translate to better care for these at-risk individuals. In collaboration with genetics counselor **Sally Hollister, MS**, we are also available to assist in the management of hereditary GI diseases including cancer syndromes and pancreatic disorders.

Information about Division of Gastroenterology, Hepatology and Nutrition services at UPMC Shadyside campus may be found at <http://www.dom.pitt.edu/gi>. Physician referrals may be made by calling **1-800-544-2500**.



Dr. Brand is a visiting professor of medicine with the Division of Gastroenterology, Hepatology and Nutrition and serves as the academic director of the GI Division, UPMC Shadyside. He also directs the GI Malignancy Early Detection, Diagnosis and Prevention Program for the University of Pittsburgh Department of Medicine.

Advances in Research and Endoscopic Therapy at UPMC Shadyside

Since early in my training, I have been intrigued by genetic influence in the development of recurrent acute and chronic pancreatitis. My initial research focused on the impact of cystic fibrosis gene mutations on the development of pancreatitis in patients with pancreas divisum. I now study other genes which also predispose to pancreatitis as well as novel medical and endoscopic therapies.



Pancreas divisum is an anatomic variant resulting from failure of the fusion of the embryonic dorsal and ventral pancreatic buds and their ductal systems. Most of the pancreatic secretions drain through the smaller accessory pancreatic duct via the minor papilla, rather than through the main pancreatic duct and

major papilla as in most individuals. In a subset of patients, this anatomical variant leads to recurrent episodes of pancreatitis. Although most subjects with pancreas divisum remain asymptomatic, approximately five percent develop recurrent episodes of acute pancreatitis, for reasons which remain unknown. Current treatment involves endoscopic or surgical minor sphincterotomy and has a high success rate.

Cystic fibrosis (CF) is the most common autosomal recessive disorder. More than 1,200 gene mutations have been reported, and up to five percent of CF patients will develop pancreatitis. During research with other colleagues, we learned that phenotypic expression of CFTR by direct measurement of the chloride channel utilizing nasal transmembrane potential difference measurements (NTPD) was examined in patients with pancreas divisum who failed to respond to treatment. We found that the majority of patients had an abnormal or borderline test result.

Prior to moving to Pittsburgh, I was the principal investigator (PI) for the North American Pancreatic Study

Group II (NAPS-2) study group at the University of Cincinnati. NAPS-2 is a multicenter group collaborating on clinical and translational research for patients with recurrent acute and chronic pancreatitis. Dr. David Whitcomb is the PI for this NIH-sponsored study at UPMC, and I continue my active commitment to this project.

Current faculty colleagues Randall Brand, MD and Yang Liu, PhD and I are addressing early detection of pancreatic cancer through light scattering spectroscopy in duodenal mucosa. Preliminary data of this novel approach appears to be very promising. More information about this research may be found on page three of the Summer 2008 issue of *Pitt Digest* www.dom.pitt.edu/gi/gastrointestinal.

Clinically, I am exploring minimally invasive endoscopic techniques for the treatment of pancreatitis complications, such as which symptomatic patients with walled-off pancreatic necrosis require surgery. I am working to change this paradigm using new endoscopic techniques and bypassing the need for surgery. Necrotic pancreatic tissue is removed by creating an opening via the stomach into the pancreas allowing the necrotic tissue to be debrided. Up to 80 percent of patients are cured using this approach. As part of our minimally invasive approach to gastrointestinal conditions, I am working with Ethicon Endosurgery Inc. to develop new devices and to design clinical trials for the use of Natural Orifice Translumenal Endoscopic Surgery (NOTES) for treatment of obesity and complications of bariatric surgery.



Andres Gelrud, MD, MMSc, is a visiting associate professor of medicine with the Division of Gastroenterology, Hepatology and Nutrition. He serves as the director of Therapeutic Endoscopy for the Division and provides primary clinical care at UPMC Shadyside. Dr. Gelrud is fluent in both English and Spanish.

References upon request.

What Is This? provided by Vinay Sundaram, MD, Gastroenterology Fellow

The CT scan of the abdomen and pelvis two years ago showed a lobulated, fat-attenuated mass in the ascending colon consistent with lipoma. The CT scan of the abdomen and pelvis during the current admission showed a colo-colonic intussusception with the ascending colon lipoma (5.8 x 4.6 cm) as the lead point. The patient underwent a laparoscopic-assisted right hemicolectomy with ileocolic anastomosis. Surgical pathology revealed a large submucosal lipoma with overlying mucosal ischemic changes.

Diagnosis: Colo-colonic intussusception secondary to a giant lipoma

Answer to *What Is This?* photos on page eight:

Information concerning **Pitt Digest** or requests for additional newsletter copies may be directed to Joy Jenko Merusi at joj2@pitt.edu or **1-866-4-GASTRO (1-866-442-7876)**. Visit our website at www.dom.pitt.edu/gi

What Is This?

Presentation: A 32-year-old woman presented with abdominal pain, bilious vomiting and watery diarrhea. CT scan of the abdomen and pelvis was performed (*Figure 1*). The patient had an abdominal CT scan two years earlier for workup of non-specific abdominal pain (*Figure 2*). What is your diagnosis?

Compare your answer to Dr. Sundaram's on page 6.



Figure 1



Figure 2

PancreasFest 2009: Personalizing the Pancreas

Advancements in Pancreatic Cancer and Pancreatitis for Physicians and Researchers

The University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition will again host one of the nation's most innovative pancreas education and research meetings, **PancreasFest 2009**. Education programs are interspersed with investigative research meetings (sponsored in part by NIDDK and NAPCG) to further the multi-disciplinary understanding and treatment of pancreas diseases.

This program will be held July 23–25, 2009 at The University Club in Pittsburgh, PA. Overnight accommodations will be available. For registration and overall program information, contact Joy Merusi at joj2@pitt.edu or (412) 578-9518 or visit www.dom.pitt.edu/gi/education.html.

