



Pitt

Digest

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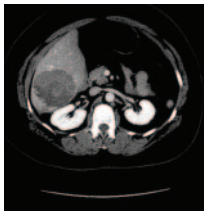
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What Is This?

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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Kenneth Fasanella, MD
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Innovative New Programs in Development

GI Services at Magee-Womens Hospital of UPMC

by Steven R. Abo, MD

The University of Pittsburgh Medical Center includes Magee-Womens Hospital, one of only a few women's hospitals in the U.S. and a major clinical and research center for women's health. Magee effectively addresses the needs of women and is dedicated to women in the Pittsburgh area. This has spawned the development of innovative new programs, especially those including understudied digestive disorders in women.

An emerging biomedical research conclusion is that gender differences may explain the prevalence of diseases as well as various disease manifestations among men and women. Certainly, one field in which this is clinically relevant is gastroenterology. Functional bowel disorders including irritable bowel syndrome (IBS), the most common such disorder, are more common in women than men.

Inpatient and Outpatient Consultation

At Magee, the Division of Gastroenterology, Hepatology and Nutrition currently provides inpatient and outpatient consultation for both women and men. While focused on women's GI health, men are seen for various GI conditions as well. Two attending gastroenterologists, Janet Harrison, MD and I, consult on all general

gastroenterology cases and focus care on functional bowel conditions and inflammatory bowel diseases. Magee's GI service collaborates

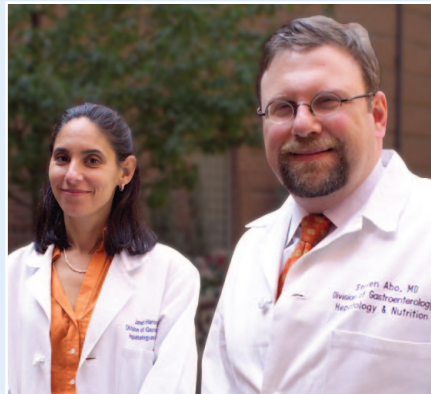
with the pelvic floor group and uro-gynecologists (e.g., coexisting fecal and urinary incontinence). Additionally, pre- and post-operative evaluations of obese patients are offered in collaboration with the Division of Minimally Invasive Bariatric and General Surgery Program based at Magee. Please see page five of this issue for additional

information about Magee's surgical solutions for patients with severe obesity.

Looking to the Future

Future research plans include exploring and applying behavioral therapies for functional bowel disorders, expanding the program's endoscopic laboratory and instituting studies on pregnancy-related gastroenterologic disorders such as hyperemesis gravidarum.

Dr. Abo is an assistant professor of medicine with the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition. He also directs the Center for Women's GI Health at Magee-Womens Hospital of UPMC.



The Magee Center for Women's Digestive Health gastroenterology team: Dr. Janet R. Harrison and Dr. Steven R. Abo.

Thank you for your continued interest in Pitt Digest!

This current issue highlights women's digestive health with its focus on GI services at Magee-Womens Hospital provided by Division of Gastroenterology, Hepatology and Nutrition faculty members, **Steven Abo, MD** and **Janet Harrison, MD**. Our recognized collaborations with our surgical colleagues in the Division of Minimally Invasive Bariatric and General Surgery are featured as well.

Two important clinical vignettes and an interesting endoscopic unknown are presented by three of our accomplished senior gastroenterology fellows. We thank our readership for their positive feedback concerning these features, and we are pleased to continue to offer these case reviews.

In addition, we report two major breakthroughs in the translational research effort in complex disorders conducted by our Division. **Dr. Regueiro** discusses the success of **Dr. Duerr's** lab team on this page. Additionally, my lab in cooperation with the University of Washington Medical Center lab of **Terri Brentnall, MD**, has located a critical pancreatic cancer gene linked to familial pancreatic cancer. These efforts and those of key collaborators at several other institutions should have major impact on the diagnosis and treatment of Crohn's disease and pancreatic cancer.



In good health,

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*

IBD Gene Breakthrough

Researchers at the University of Pittsburgh have made a novel inflammatory bowel disease genetic discovery, which features an association of mutations in the gene encoding the receptor for the pro-inflammatory cytokine interleukin-23 (IL-23) in patients with Crohn's disease. There was an increased rate of a different mutation in the IL-23 receptor in healthy controls without IBD. These findings suggest that a person with one type of mutation in the gene for the IL-23 receptor gene (IL-23R) are at *increased risk* for developing Crohn's disease, whereas another mutation *protects* against Crohn's disease formation. This gene was found through the collaborative efforts of lead investigator Richard H. Duerr, MD, M. Michael Barmada, PhD, myself and the NIDDK IBD Genetics Consortium.

IL-23, a pro-inflammatory cytokine mediated by T cells, is a key immune chemical responsible for inflammation. Animal models have demonstrated its importance in colitis-induced mice, and high levels of IL-23 have been found in the gastrointestinal tracts of Crohn's disease patients. The discovery of IL-23R would suggest that blocking the function of this cytokine may help to treat patients with IBD. This gene likely also plays an important role in other autoimmune and immune-mediated diseases.

This finding was made possible only through our University's solid research relationships. Dr. Duerr provided genetics expertise and collaborative study leadership. I was honored to lead the study's phenotyping and patient processing efforts, while Dr. Barmada provided the mathematical and technological platforms. This work could not have been accomplished without the tremendous efforts of all of our IBD physicians, clinical nurses, research nurses, database coordinators, nurse practitioners and phenotypers.

Through the efforts of Dr. Duerr, our collaborators and myself, a new IBD research paradigm has emerged. IBD patients presenting at our clinic not only receive specialized clinical care but are entered into a research registry. As such, patients with Crohn's disease and ulcerative colitis are phenotyped with blood samples taken for genotyping. These genetic discoveries hopefully will herald new treatments and, potentially, a cure for Crohn's disease and ulcerative colitis.



Richard H. Duerr, MD
lead study author



Dr. Regueiro is an Associate Professor of Medicine with the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition. He also serves as the Division's Associate Chief for Education and Gastroenterology Fellowship Program Director and is the Co-Director and Clinical Head of the Division's IBD Center.

The Unusual Suspect



by **Yasser M. Bhat, MD**
Gastroenterology Fellow

Case Presentation

An 81-year-old gentleman presented to the emergency room with right upper quadrant pain of two days duration. The pain exacerbated when lying on his right side and with movement and was associated with right shoulder tightness. He denied fevers, chills or jaundice. Previously, he was in excellent health with no past medical history, medication use, habitual risk factors for liver disease, or pets. He has traveled to Italy, Spain, the Caribbean, Mexico and Cuba during the past four years.

Physical examination indicated jaundice, and his liver edge was tender and palpable 5cm below the right costal margin. He had no splenomegaly, ascites or signs of chronic liver disease. CBC, pancreatic enzymes and coagulation profiles were normal. Liver function tests included total bilirubin 10.2 mg/dl, AST 1392 IU/L, ALT 437 IU/L, AP 90 IU/L, GGT 37 IU/L and albumin of 2.1 gm/dl.

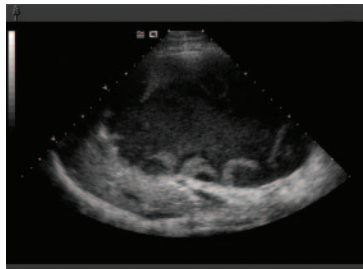


Figure 1 – Hepatic cyst. RUQ ultrasound reveals a large cyst

Right upper quadrant ultrasonography showed a large right hepatic lobe cyst with daughter cysts and hydatid sand (*Figure 1*). A representative computed tomography image in *Figure 2* confirmed a large unilocular cyst in the right hepatic lobe. Subsequent serology (ELISA IgG) was positive for *E. granulosus* confirming hepatic hydatid disease.

Discussion

Hydatid disease is endemic in sheep-rearing areas of the world, including Mediterranean Europe, Asia and the Middle East. Dogs or other canines are definitive hosts for the helminth and shed embryonated eggs in stool. Sheep, goats or swine are intermediate hosts, in which eggs develop into organ cysts before being re-ingested by the primary host. Humans are accidental hosts infected by

ingestion of embryonated eggs. Hydatid disease most commonly affects the liver (70%) and lungs (25%) and rarely involves the brain, bones or heart. More than two-thirds of hepatic hydatidosis involves the right lobe. Cysts are unilocular and can grow up to 20cm in diameter.

Patients may be asymptomatic, but a majority (60%) have right hypochondrial pain. Jaundice is seen in 15 percent of cases. As the cyst grows, patients may develop low-grade fevers and tender hepatomegaly. Other clinical features relate to invasion of the cyst into other organs like the lungs (e.g., dyspnea, hemoptysis or bronchobiliary fistulae) or the biliary tree (e.g., cholangitis or biliary obstruction). Invasion into the peritoneum can cause anaphylaxis, and superinfection of cysts can lead to pyogenic liver abscesses (20%). Other features include skin rashes, pruritus and allergic reactions.

Diagnosis is based on a combination of imaging and serology. CT and ultrasonography may demonstrate unilocular or multilocular cysts, sometimes with fine intracystic shadowing (hydatid sand) or degenerative changes and mass-like collapse of cyst structures. Serology is fairly accurate, with sensitivity up to 90 percent in hepatic echinococcosis. Immunodiffusion and immunoelectrophoresis demonstrate antibodies to antigen 5 and provide specific confirmation of reactivity.

Medical therapy alone, using benzimidazole drugs (i.e., albendazole, mebendazole), is effective in cyst eradication in ten to 30 percent of cases. Total or partial cystectomy surgery achieves the best results, during which the cyst cavity is injected with scolicidal agents for 30 minutes prior to suction and cyst removal. Percutaneous drainage, a newer technique termed **PAIR** (**P**uncture of the cyst cavity generally under ultrasound guidance, cyst **A**spiration, **I**njection of a scolicidal agent [20% saline, 95% alcohol or chlorhexidine] and cyst **R**e-aspiration) has been compared to surgery. Both achieve good eradication rates, but PAIR is associated with fewer complications.

This patient completed a one month course of albendazole and then underwent surgical cystectomy. He did well and had no further symptoms.

References on request.

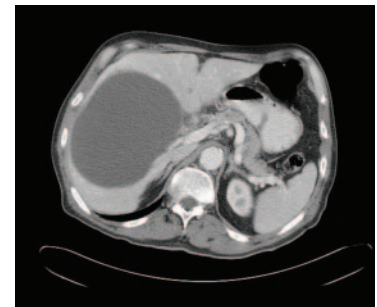


Figure 2 – Contrast-enhanced spiral CT scan

Small Bowel Complications During Pregnancy After Laparoscopic Gastric Bypass



by **Allen Banegura, MD**
Gastroenterology Fellow

Case Presentation

A 26-year-old woman at 28 weeks gestation presented with sudden onset nausea, vomiting and severe mid-epigastric abdominal pain. She had undergone a successful laparoscopic Roux-en-Y gastric bypass 18 months earlier. She lost 125 pounds and now weighed 147 pounds. Initial evaluation revealed mild epigastric tenderness without rebound or guarding. On rectal exam, stool was guaiac positive. Hemoglobin was 8.8 g/dL with low MCV. White blood cell count, amylase, lipase, liver enzymes, basic metabolic panel and fetal heart rate were within normal limits. A right upper quadrant ultrasound was negative for gallstones, and the initial CT scan of the abdomen and pelvis was negative for perforation or obstruction.

The patient continued to complain of severe abdominal pain out of proportion to the physical exam. An EGD was performed which revealed diffuse ischemia and decreased motility in the Roux limb (*Figure 1*). The patient underwent an urgent exploratory laparotomy, and, intra-operatively, the entire small bowel appeared dusky but viable, with further inspection revealing a small bowel

volvulus. The small bowel was detorsed and fixed to the transverse colon, subsequently regaining its normal pinkish color. Her post-op course was uncomplicated, and the patient and fetus were discharged home in stable condition.

As the prevalence of morbid obesity has increased, the number of bariatric surgeries has also increased dramatically in recent years. Among patients undergoing Roux-en-Y gastric bypass, 84 percent are women, and most are of childbearing age. The estimated 30-day post-op mortality for this procedure is less than one percent. However, the procedure is associated with multiple early and late complications. The most common early complications include anastomotic

leakage or bleeding, infection, deep vein thrombosis, pulmonary embolism and gallstone disease. Common late complications include marginal ulcers, stomal stenosis, nutritional/mineral deficiencies, bacterial overgrowth, small bowel obstruction and small bowel ischemia. The leading cause of small bowel obstruction after laparoscopic Roux-en-Y bypass is an internal hernia, which can occur either between the jejuno-jejunos-tomy anastomosis, the transverse meso-

colon and Roux-limb or in the transverse mesocolon. Internal hernias have been reported to occur in pregnant women after gastric bypass resulting in both maternal and fetal death.

The incidence of small bowel volvulus during normal pregnancy is rare. This incidence is even more unique in pregnant women with a Roux-en-Y gastric bypass. The small bowel volvulus is attributed to decreased

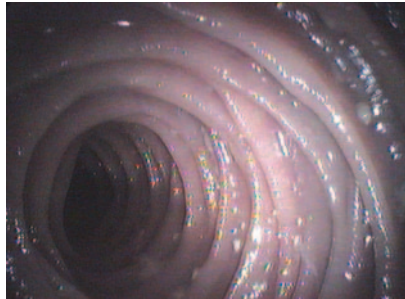


Figure 1 – EGD: Roux Limb ischemia

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Figure 2 – Postoperative image several months after right hepatic lobectomy.

The CT scan reveals a ruptured hepatic adenoma in segment 6 of the right lobe. Three smaller lesions were also identified in the right lobe and one in the left. The patient reported oral contraceptive use for approximately 30 years due to menorrhagia. An angiogram with selective embolization of the right hepatic artery was performed in preparation for a right hepatic lobectomy. After right lobectomy, the patient recovered fully and was discharged after two weeks. Hepatic adenomas are strongly associated with use of oral contraceptives. Major complications include malignant transformation in eight to 13 percent, and spontaneous hemorrhage or rupture, which is associated with up to 20% mortality. Hemorrhage rates are much higher in lesions greater than 4cm, and surgical resection should be recommended for lesions 5cm or greater. *References upon request.*

Answer to What Is This photo on page six:

The Division of Minimally Invasive Bariatric and General Surgery at Magee

by **Carol A. McCloskey, MD**

The Division of Minimally Invasive Bariatric and General Surgery, based at Magee-Womens Hospital of UPMC, specializes in advanced laparoscopic techniques to treat a variety of conditions such as obesity, colorectal disease, gallbladder disease and other general surgical needs, including hernia repairs and gastro-esophageal reflux disease (GERD). Benefits of a minimally invasive surgical approach include smaller incisions, reduced length of hospital stay and overall faster recovery.

The Division's Bariatric Surgery Program is a comprehensive program committed to improving the health of morbidly obese patients. Bariatric surgery achieves a sustained weight loss, reduces or eliminates obesity-related medical problems and improves the patient's overall quality of life. Respected nationally, the program offers a variety of bariatric surgical procedures including laparoscopic Roux-en-Y gastric bypass and laparoscopic adjustable gastric banding. Designed for obese patients specifically, facilities at Magee-Womens Hospital include bariatric operating suites, an outpatient clinic area and inpatient units. Other specialists such as dietitians and psychologists work closely with the surgical team to prepare patients for weight loss surgery and guide patients through the approval process of medical insurers. Following surgery, supportive care is provided with support groups available to assist patients and their family members through the entire counseling and surgery process.

The surgical team consists of six fellowship-trained surgeons who collectively perform more than 1,000 procedures per year. **Anita Courcoulas, MD, MPH, FACS** directs the Division of Minimally Invasive Bariatric and General Surgery and specializes in minimally invasive bariatric, foregut and general surgeries. Her studies on surgical outcomes are widely published, and she is currently the principal investigator for the NIH-funded Longitudinal

Assessment of Bariatric Surgery (LABS), which studies effects and outcomes following bariatric surgery.

George Eid, MD, FACS specializes in minimally invasive bariatric, colorectal and general surgery. His research interests include surgical outcomes following laparoscopic colon surgery, assessment of comorbid conditions following weight loss in bariatric patients, applications of robotic

surgery and device development in endoluminal surgery. Specializing in bariatric and minimally invasive general surgery, **Giselle Hamad, MD, FACS** has a special interest in surgical education including the development of laparoscopic skills and surgical simulation. Her research interests include prevention of venous thromboembolism in bariatric surgery and alterations in pharmacokinetics following gastric bypass surgery. The

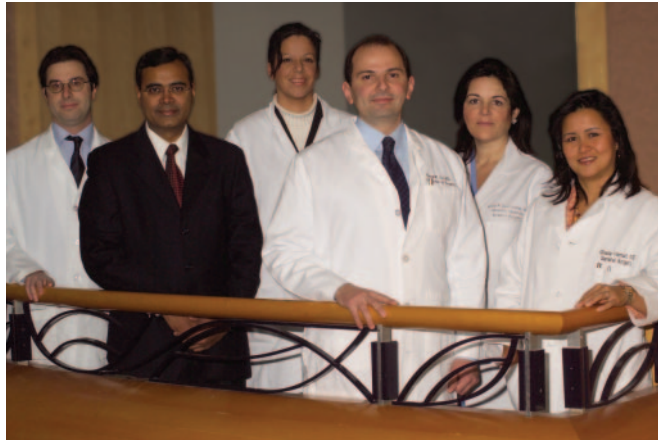
research of **Ramesh Ramanathan, MD, FRCS** focuses on minimally invasive bariatric, colorectal and surgical oncology; his research interests include the assessment of comorbid conditions following bariatric surgery.

Ioannis Raftopoulos, MD, PhD specializes in minimally invasive bariatric, colorectal and general surgery. His research interests include surgical outcomes and pharmacokinetics following bariatric surgery. Rounding out this list, I specialize in minimally invasive bariatric and general surgery, including colon and hernia surgery. My basic science interests relate to obesity and inflammation, and my clinical research interests include surgical outcomes as well as device development in endoluminal surgery.

Our division's wide range of surgical expertise, combined with minimally invasive technology, strives to provide excellent outcomes for its large variety of patients.

More information about this program and its surgeons is available by calling 412-641-3632. Or, visit the Division Web site at <http://mageebariatrics.upmc.com>.

Dr. McCloskey is an Assistant Professor of Surgery with the Division of Minimally Invasive Bariatric and General Surgery at Magee-Womens Hospital of UPMC.



The Division of Minimally Invasive Bariatric and General Surgery Team (L to R): Ioannis Raftopoulos, MD, PhD, Ramesh Ramanathan, MD, FRCS, Carol McCloskey, MD, George Eid, MD, FACS, Anita Courcoulas, MD, FACS, MPH, and Giselle Hamad, MD, FACS.

Graduating Fellows

The University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition welcomes the following summer 2006 graduating fellows as colleagues. **Niraj Jani, MD** and **Jaideep Behari, MD, PhD** have joined the Division as an Instructor and Assistant Professor of Medicine, respectively. **Daniel Chung, MD** has entered private practice with Kaiser Permanente in California, and **Ajay Pabby, MD, MPH** has entered private practice in Williamsburg, VA. Congratulations!

New Fellows

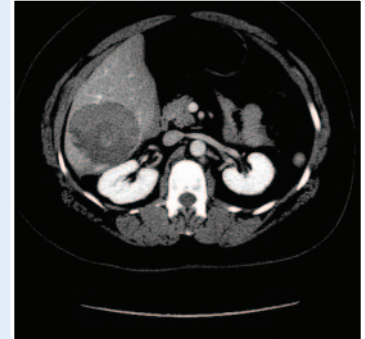
The Division also welcomes the following Year I fellow trainees. **Arthur "Tripp" Barrie, MD, PhD** attended medical school at the University of Cincinnati, and completed his residency at Duke University. **Karen Collinson, MD** went to medical school at the University of Medicine & Dentistry of New Jersey, and completed residency at the Boston University Medical Center. **Carmen Meier, MD** attended medical school at the University of Cincinnati, and **Brian Ng, MD** attended medical school at the State University of New York at Syracuse. Both Dr. Meier and Dr. Ng completed their residency program at the University of Pittsburgh Medical Center.

New Faculty

The Division is pleased to announce the following new faculty members:

- Jaideep Behari, MD, PhD
- Raja Chadalavada, MD
- Kapil Chopra, MD
- Michael Gold, PhD
- Refaat Hegazi, MD, PhD
- Niraj Jani, MD
- Michael O'Connell, PhD
- Georgios Papachristou, MD
- Michael Sanders, MD
- Dhiraj Yadav, MD, MPH

What Is This? **Presentation:** A 47-year-old woman presented with right upper quadrant abdominal pain for 24 hours. Laboratories revealed an initial hemoglobin of 11 g/dl, which dropped to 9.1 g/dl over 12 hours. A CT scan of the abdomen was obtained. *Images and explanation provided by Kenneth Fasanella, MD, chief gastroenterology fellow. Compare your answer to Dr. Fasanella's answer on page four.*



Small Bowel Complications

continued from page four

mesenteric fat from rapid weight loss and increased abdominal pressure from uterus enlargement. The highest risk of volvulus occurs in the third trimester and at puerperium. Fetal mortality has been reported to occur in up to 64 percent of cases, while maternal mortality rates range between six and 20 percent. To avoid complications, the American College of Obstetricians and Gynecologists recommended that women delay pregnancy for at least 12 to 18 months after gastric bypass in a 2005 report.

A number of childbearing age women are having this surgery, and the incidence of internal hernias and small bowel volvulus during pregnancy may increase in this patient population. Any pregnant women with history of gastric bypass and abdominal pain should be considered at risk for these complications.

References upon request.

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



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