



Pitt

Digest

Fall 2009



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Pitt Digest

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

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Barrett's Esophagus Specialty Treatment (BEST) Clinic

by Kevin McGrath, MD

Barrett's Esophagus (BE) is a premalignant condition of the esophagus, where normal squamous epithelium is replaced by specialized columnar epithelium (intestinal metaplasia). This metaplastic change occurs due to chronic insult from gastroesophageal reflux in certain patients, and it is the major risk factor for the development of esophageal adenocarcinoma (EAC). EAC is increasing at an alarming rate. Given the lethality of this disease, early detection and treatment are critical in improving outcomes and ultimate survival.

The Barrett's Esophagus Specialty Treatment (BEST) Clinic was launched officially in Fall 2008. Created from our Division's Endoscopic Ultrasound Program and housed under the Gastrointestinal Cancer Prevention and Treatment Center of Excellence, the BEST Clinic offers consultation for the evaluation and management of the patient with BE, including endoscopic therapy (ET) for the appropriate patients with dysplasia. Due to recent technologic advancements in endoscopic ablative techniques and mucosal resection along with a growing body of literature supporting excellent safety and patient outcomes, ET is now an accepted management option for BE with high-grade dysplasia (HGD) and intramucosal adenocarcinoma. Specifically, for dysplastic BE and superficial cancer, we employ endoscopic mucosal resection (EMR), radiofrequency ablation (RFA), and cryotherapy alone or in combination after initial mapping endoscopy.

Treatment decisions are based on the individual morphology of the Barrett segment and are guided by EUS, narrow band imaging and/or chromoendoscopy. Since introduction of this new technology, we have performed more than 150 ablative procedures over the past two years.

The BEST Clinic, staffed by myself and Kenneth Fasanella, MD, has been integrated with the UPMC GI Pathology Center of Excellence.



Dr. Kevin McGrath (right) discusses BEST Clinic advanced technology with BEST colleague, Dr. Kenneth Fasanella.

We have developed a template that reports EMR histology results to aid in interpretation, risk stratification and clinical decision making. We also meet weekly to review biopsy and EMR specimens. Collaborations with the Division of Thoracic and Foregut Surgery are in development as well. In the near future, we will partner with Blair Jobe, MD, a surgeon who has clinical and research expertise in Barrett's esophagus and heads the Esophageal Diagnostic Center at UPMC Shadyside.

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As part of our ongoing series of communications to keep the gastroenterology community aware of the clinical and research activities of the Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh Medical Center (UPMC), I am pleased to share this Fall 2009 issue of *Digest*.

This issue of *Digest* highlights the pioneering upper GI expertise of Dr. Kevin McGrath and Dr. Kenneth Fasanella with the innovative Barrett's Esophagus Specialty Treatment (BEST) Clinic, offering a multidisciplinary approach to Barrett's Esophagus diagnosis and disease management. Pancreaticobiliary researcher, Dr. Vijay Singh, discusses his developing lab studies and potential new treatment paradigms for acute pancreatitis as well. Our fellows' complement the attendings' contributions with unusual GI and hepatology case presentations.

Plan to join us in Pittsburgh this November to see what the G20 excitement was all about! Our Division's eighth annual physician education course, *What's New in GI and Hepatology*, will be held at the University of Pittsburgh's newly renovated University Club on Nov. 12 & 13, 2009. Liver disease treatment advancements, novel approaches to IBD management and cutting edge procedure updates will be discussed.

We hope *Digest* proves to be a useful resource in your practice. We would be happy to discuss our work here at the division, offer consultations, or accept patient referrals. To contact us, please call UPMC's 24-hour physician referral service at **1-800-544-2500**.



Sincerely,

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*

New Approaches:

Acute Pancreatitis

by Vijay P. Singh, MD

Despite considerable advancements in molecular targeting and individualized medicine, pancreatic diseases remain unpredictably devastating and disabling, with unacceptably high morbidity and mortality rates. The emphasis in my clinical practice and research is to improve outcomes for pancreatitis patients.

Several decades of clinical trials have shown that drugs targeting a single mechanism treat acute pancreatitis ineffectively. However, in acute pancreatitis, several deleterious mechanisms progress simultaneously and rapidly. While a multi-drug approach may be helpful, no such drugs are approved currently, and the availability of such options will be much delayed. Our lab is working on a single drug therapy to target multiple players involved in deleterious outcomes.

Approximately half of pancreatitis mortality results from local complications occurring later in the disease course. Therefore, we are developing a device which uses a minimally invasive, easily reversible approach to induce local hypothermia in the pancreas. Local hypothermia slows several deleterious mechanisms simultaneously while not affecting vital systems. Preliminary results are promising.

With its multidimensional infrastructure and expertise, our Center for Excellence in Pancreatic Diseases offers an ideal environment to address patient needs, while researching new therapies to provide hope for this devastating group of diseases that, otherwise, has no effective treatment.



Dr. Singh is an assistant professor of medicine with the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition. He cares for patients at the UPMC Presbyterian and UPMC McKeesport hospitals.

Unusual GI Bleed



by **Kofi Clarke, MD**
Gastroenterology Fellow

Case Presentation

A 64-year-old female presented with two episodes of hematemesis in the prior month. She also had fatigue, recent onset of early satiety, and dyspnea with minimal exertion. She had no history of NSAID or ASA use and reported no recent steroid use. Her appetite was good, and weight was unchanged. A nun who works as a college administrator, she is a nonsmoker and has no history of alcohol use or other high risk behavior.

Past medical history was notable for Hashimoto's disease, lumbar laminectomy with residual foot drop, cholecystectomy and a lower extremity DVT. She was taking the following medications: sythroid, prevacid, coumadin, ativan and potassium supplements.

Examination was unremarkable except for decreased breath sounds in the right lung base. Initial lab work showed normal chemistry, hypochromic microcytic anemia of 9.5gms/dl with normal platelets and white cell count. EKG showed low voltage complexes and first degree heart block. Chest X-ray and CT scan of chest confirmed a right sided pleural effusion, and a transthoracic echocardiogram showed a thickened interventricular septum. Upper GI endoscopy revealed an ulcer with

raised irregular edges in the gastric body. Biopsies confirmed gastric amyloidosis.

Amyloid consists of small, low molecular weight fibrils (8-10um) which are subunits of human and animal protein precursors supported by a glycosaminoglycan and protein matrix. Twenty-five human and eight animal proteins have been identified. Clinical presentation of amyloidosis is protean depending on organ involvement. The most common organ involvement in the GI tract is the liver. Gastric amyloidosis which is less common can present as GI bleeding, gastroparesis, or malabsorption. Bleeding is usually a result of factor X deficiency, direct hepatic or blood vessel wall

infiltration, and acquired von Willebrand Disease.

Types of amyloidosis include primary/AL disease, secondary/AA disease (seen less commonly in the developed world), hemodialysis related, senile and hereditary disease.

Apple green birefringence on Congo red staining of biopsy material is 57 to 85 percent sensitive and 92 to 100 percent specific for diagnosis. Amino acid sequencing, mass spectroscopy and serum amyloid P scanning are under evaluation as newer methods for diagnosis.

Treatment options though limited include supportive care and organ transplant within the first year of diagnosis. Future treatment options may include experimental agents to disrupt fibril formation or hasten degradation of existing deposits.

This patient's AA disease is likely secondary to multiple myeloma which was diagnosed during evaluation. She had a successful stem cell transplant for her underlying multiple myeloma.

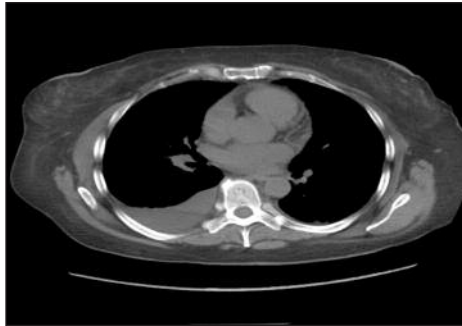


Figure 1: CT scan of chest showing R pleural effusion.



Figure 2: Ulcer in gastric body at upper GI endoscopy.

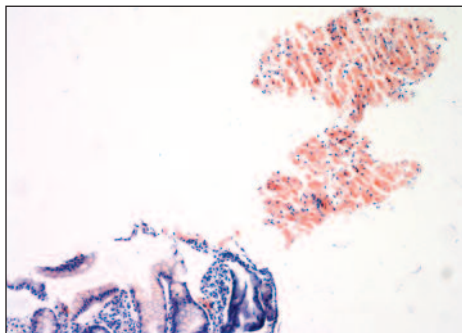


Figure 3: Gastric biopsy with positive stain.

A Mysterious Case of Pancreatitis



by **Julie Holinga, MD**
Gastroenterology Fellow

Case Presentation

In Winter 2009, a 57-year-old female presented to the emergency room with presyncope and one day of fever and diarrhea. Her past medical history was significant for hypertension and HIV. She was followed at the Infectious Disease clinic regularly and was compliant with HAART. Her medications included efavirenz, emtricitabine, tenofovir and hydrochlorothiazide. Social history was negative for tobacco and recreational drugs and was positive for one to two alcoholic drinks per week. She reported that other family members had recently been ill with flu-like symptoms.

Physical examination revealed a temperature of 38.4, heart rate in the 120s, and a 2 liter oxygen requirement to maintain saturations greater than 92%. She was awake and oriented, but had slurred speech. Cardiopulmonary and abdominal exam were unremarkable. Neurologic exam was negative for focal weakness, nuchal rigidity and asterixis. Initial laboratory data showed an elevated BUN, creatinine consistent with pre-renal azotemia. She had a leukocytosis of 15,000 cells/mm with 93% neutrophils. A lumbar puncture was performed with normal opening pressure and cell count.

Upon admission, she received several liters of intravenous fluids with resolution of tachycardia and transient improvement in her symptoms. Blood cultures, sputum cultures, urine cultures, and stool cultures were obtained, and she was started on empiric antibiotics including rocephin, vancomycin, azithromycin and acyclovir empirically. Forty-eight hours after admission, her clinical status began to deteriorate. She reported new onset abdominal pain, had progressive renal failure necessitating hemodialysis and required intubation. Consecutive chest X-rays initially showed a lacey infiltrate without focal consolidation and subsequent development of bilateral airspace disease consistent with ARDS. Concurrent with these developments, her lipase rose from 63 to over 5,000, amylase rose from 46 to 655.

The GI consult service was contacted for further recommendations.

The patient's hydrochlorothiazide had been stopped several days earlier upon admission, but her antiretroviral medications were continued (as they were not ones known to precipitate pancreatitis). Her renal failure precluded an abdominal CT with contrast, but an abdominal ultrasound was done. This showed a normal liver, contracted gallbladder, no gallstones, no biliary ductal dilatation, and a "suboptimal view of the pancreatic parenchyma." Calcium, triglycerides, ANA, IgG4 were all within normal limits.

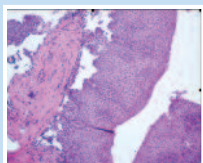
She remained in the intensive care unit and was supported with fluids, antibiotics, mechanical ventilation and hemodialysis. Soon, her cultures began to return. Blood (including fungal isolate cultures), sputum, urine and stool cultures were all negative. Her urine Legionella antigen was positive. Of note, it had been incidentally checked a few months prior and was negative. Meanwhile, one of her family members was also admitted to the intensive care unit at Montefiore hospital with milder, but similar presenting complaints and with infectious workup also positive for Legionella. For this reason, her antibiotic treatment was narrowed to coverage for Legionella with moxifloxacin and rifampin. Over the next several days she began a very gradual recovery and was discharged home after a three week hospitalization.

While Legionella infection is an uncommon cause of acute pancreatitis, it still has a well-established link. The majority of cases are difficult to prove, because other causes of acute pancreatitis cannot be excluded adequately and because definitive diagnosis requires surgical biopsy or pathology taken from pancreatic tissue at autopsy. In this case, the patient's illness emerges as an acute presentation of Legionnaire's disease with both pulmonary and extra pulmonary features including mental status changes, renal failure, diarrhea, and pancreatitis.

While Legionella infection is an uncommon cause of acute pancreatitis, it still has a well-established link. The majority of cases are difficult to prove, because other causes of acute pancreatitis cannot be excluded adequately and because definitive diagnosis requires surgical biopsy or pathology taken from pancreatic tissue at autopsy. In this case, the patient's illness emerges as an acute presentation of Legionnaire's disease with both pulmonary and extra pulmonary features including mental status changes, renal failure, diarrhea, and pancreatitis.



CXR on Hospital Day #2:
Lacey infiltrate and bilateral airspace disease consistent with ARDS



Diagnosis: Eosinophilic Esophagitis – The EGD images show endoscopic findings of linear furrowing and small white papules (eosinophilic microabscesses). Multiple biopsies, taken at 25cm and 35cm, showed more than twenty eosinophils per high-power field.

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

What Is This? provided by Julie Holinga, MD, Gastroenterology Fellow. References upon request.

LHAS Supports UPMC GI Cancer Programs

In 1898, the Ladies Hospital Aid Society (LHAS) began its long history of community service when 17 women met to address the pressing needs of the sick and the poor living in their neighborhoods. These women also were concerned with the troubles facing the immigrant population, which suffered from indigence, homelessness and lack of adequate medical care. LHAS was instrumental in the opening of the original Montefiore Hospital in 1908 and the construction of the current hospital in 1929. Today, UPMC Montefiore is the site of our Division's Center for Liver Diseases, Thomas E. Starzl Transplantation Institute and inpatient wards for medicine, transplantation and GI surgery.

LHAS supports innovative and worthy UPMC programs through an annual gala. Recent recipients of aid include the McGowan Institute of Regenerative Medicine and UPMC



LHAS Come Fly With Us gala attendees from the UPMC GI Cancer group: L to R first row: Dr. A. James Moser, Dr. David Whitcomb, Chris Whitcomb, Carrie Slivka. Second row: Dr. Susanna Hartmann, Dr. Miguel Regueiro, Dr. Carol Regueiro, Dr. Adam Slivka, Linda McGrath, Dr. Kevin McGrath.

concession research. This year, the LHAS *Come Fly With Us* annual gala benefited our Division of Gastroenterology, Hepatology and Nutrition's clinical service, the Digestive Disorders Center (DDC), through a specific philanthropic focus on GI cancers.

The LHAS August 2009 gala's honorary chair was Jai Pausch, the wife of the late Carnegie Mellon University professor and author Dr. Randy Pausch, who died of pancreatic cancer within a year of his "Last Lecture." Jai Pausch gave a moving account of the need for renewed research to prevent and treat this terrible disease. David Whitcomb, MD, PhD represented the UPMC GI cancer team and spoke about the tremendous progress being made in pancreatic cancer research and overall GI cancer treatments at the University

of Pittsburgh through the tireless effort of dedicated physicians, surgeons and scientists.

The event was an overwhelming success, raising over \$800,000 to support research and patient care. Proceeds from this LHAS gala will support the replacement of core research equipment that is now over 20 years old as well as patient-directed programs in the Digestive Disorders Center. The Division of Gastroenterology, Hepatology and Nutrition faculty express gratitude for the good work of the LHAS and its support of translational research and patient care for pancreatic and colon cancer and other digestive diseases.



Dr. David Whitcomb discusses University of Pittsburgh Medical Center GI cancer advancements at the gala.

BEST Clinic *continued from page 1*

Clinical research is a major focus of the Division of Gastroenterology, Hepatology and Nutrition and of our specialty clinic. We have an active IRB-approved patient registry, which allows us to track endoscopic therapy outcomes. Additionally, meetings with our expert GI pathologists have fostered collaborative research efforts to examine the phenomenon of "buried glandular mucosa" after ablative therapy. We are also working with Randall Brand, MD, and Yang Liu, PhD, utilizing light scattering spectroscopy to detect field defects, which may help to predict which Barrett patients will develop dysplasia and/or cancer.

This is an exciting time for physicians specializing in BE patient management. With continued research efforts and effective endoscopic therapy, our ultimate goal is to identify and ablate the at-risk patient with BE to eliminate EAC risks. Hopefully, this will become a reality in the near future.

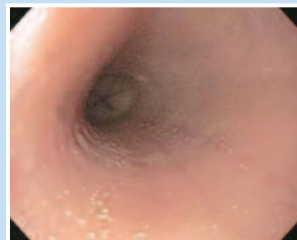


Dr. McGrath is an associate professor of medicine with the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition. He also directs the Division's Endoscopic Ultrasound (EUS) Program as well as the UPMC GI Lab.

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 28-year-old woman presented with a three-year history of “burning in my throat.” She denied dysphagia, odynophagia, heartburn, and abdominal pain. She had been seen by multiple physicians including an allergist, ENT specialist and outside gastroenterologist. Previous fiberoptic laryngoscopic exam and EGD were unremarkable. Current EGD showed the following:



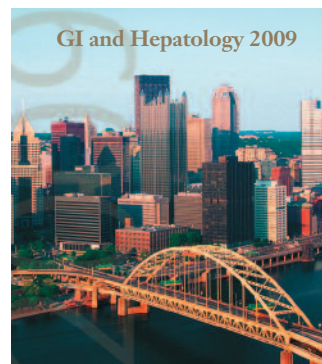
What is your diagnosis?

Compare your answer to Dr. Holing's on page 4.

Annual Physician Education Course:

What's New in GI & Hepatology? November 12 & 13, 2009

The University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition will host its annual fall education



update for physicians and medical professionals interested in gastroenterology and hepatology on November 12 & 13, 2009. This program will be held at the University Club in Pittsburgh.

The Thursday evening, November 12 program will feature

liver diseases. The full-day Friday, November 13 program will feature inflammatory bowel disease and upper-GI endoscopy. Special endoscopy workshops are planned.

For more information, please contact UPMC's Center for Continuing Education in the Health Sciences at CCEHS@upmc.edu or (412) 647-8232.