Pitt Digest

Winter 2008

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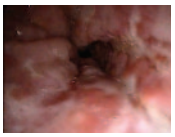

Centers of Excellence:

- 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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The Digestive Disorders Center

by Barry Kisloff, MD

On July 1, 2007, the University of Pittsburgh Medical Center (UPMC) opened a completely refurbished and expanded Digestive Disorders Center (DDC) to support patient care. The new DDC features sixteen exam rooms, a procedure room and two team rooms for conferencing. The Center has been redesigned completely and has been fully integrated into the health system's electronic health record (EHR).

The DDC has retained its location adjacent to the UPMC Presbyterian gastroenterology laboratory to maintain easy access to the resources of that facility. EHR capability allows for immediate availability of all notes, laboratory and radiology materials from the entire UPMC system.

The new DDC demonstrates UPMC's commitment to provide for the increasing demand of gastroenterologic services. During the twelve months preceding the new DDC opening, 12,000 patient visits were made at the old facility!

The DDC is home to the general gastroenterology clinic as well as "Centers of Excellence" in Inflammatory Bowel Disease, Pancreaticobiliary Disease, Visceral Pain and other GI specialties. Additionally, the DDC serves as the main outpatient site for General and Thoracic Surgery. This "one stop shop" permits single-visit patient access to gastroenterologists and surgeons

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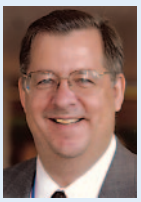
The DDC's Leadership Team: Linda Nelson, MA, Tracey Ryan, RN, Barry Kisloff, MD, Steven Hughes, MD (assistant professor of surgery and DDC Co-Director with Dr. Kisloff), and Mary J. Wilson, RN, MS. Absent from this photo: April King, MA.

Previous issues of *Pitt Digest* have highlighted the cutting edge programs offered by our Division's clinical Centers of Excellence. These programs are made possible through the strong support of academic physicians and scientists, UPMC leadership and the various schools and colleges of the University of Pittsburgh. In this issue, **Dr. Barry Kisloff** introduces you to the successful and beautiful renovation of the Digestive Disorders Center (DDC), the Division's primary GI clinic located on the third floor of UPMC Presbyterian Hospital. The DDC was designed to enhance and facilitate the function of our multi-disciplinary Centers of Excellence in IBD, pancreas & biliary diseases, neurogastroenterology and functional disorders, nutrition support and digestive cancer evaluation and prevention.

Patient care is further optimized by a multimillion dollar investment in electronic medical records, a system-wide program that is being spearheaded, in part, by **Dr. Michael Dunn**, a new faculty member with the Division of Gastroenterology, Hepatology and Nutrition. The future of medical education includes electronic media, and the new initiatives from **Dr. James (J.B.) McGee** are also featured. In addition, we highlight two new cases from our weekly, and more traditional "*GI Grand Rounds,*" educational series presented by two of our outstanding gastroenterology fellows, **Dr. John Lyons** and **Dr. Sandra El-Hachem**.

When I first moved to the University of Pittsburgh fresh from my North Carolina training more than 15 years ago, I was told that two themes characterized the culture of western Pennsylvania: *innovation* and *hard work*. To these, I add *cooperation* – not only the internal partnerships among University faculty, but also the clinical and research collaborations evident in our physicians' daily service. I believe that this issue of *Pitt Digest* reflects these three values and the major successes evident in our Division's unrelenting search to "discover new knowledge in digestive diseases" to provide "the best of tomorrow's medicine, *today*."



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

The Digestive Disorders Center

continued from page 1

Clinic rooms are spacious and well-appointed.

and fosters an environment encouraging professional collaboration across diverse areas of expertise.

The new DDC has been designed to enhance patient experiences by providing ease of registration, discounted parking and a comfortable and well-appointed waiting area. It offers efficient services such as future scheduling and phlebotomy.

Dr. Kisloff adds to a patient chart. The new DDC enjoys rigorous HIPAA compliance features, such as this secure-access chart shelf, which folds up after use to provide patient privacy.

The new DDC also contains medical record design features which reflect a heightened awareness of and commitment to medical record security.

The facilities of the new DDC at UPMC Presbyterian will provide opportunities for gastroenterologists and surgeons to offer up-to-date, efficient and patient friendly services for the diagnosis and treatment of gastrointestinal diseases.

Dr. Kisloff is an Clinical Assistant Professor of Medicine with the Division of Gastroenterology, Hepatology and Nutrition and serves as the Director of Clinical Services and Director of the Digestive Disorders Center.

Connecting the Dots: Electronic Record Interoperability at UPMC

by Michael A. Dunn, MD

Electronic records can improve the accuracy and efficiency of care, and UPMC is adopting electronic medical records. However, such value is limited without the free exchange of key information. At UPMC, eRecord applications include three separate inpatient systems in 19 hospitals, and a different version is being used by physicians in the outpatient setting. More than 100 other data stores are in daily use, such as the system containing our Division's endoscopy reports and digital images.

The practical reality in such a complex system is that we simply cannot replace our prior multiple existing systems with a one-size-fits-all application. Yet we need to provide users with easy access to the data required for good decisions. Last fall, UPMC partnered with an interoperability firm, dbMotion, which supports electronic health information exchange in Israel. Our joint interoperability initiative will "go live" in February 2008 with displays of data from multiple sources for UPMC's emergency department physicians and a pilot group of outpatient providers including those in UPMC's Center for Liver Diseases.

Simple exchanges of data among systems, while helpful, fall short of the power of true exchange of meaning, called semantic interoperability. For example, full exchanges of meaning ensure that an allergy entered into system A automatically enters system B and triggers the same alerts and actions. To achieve this high level of performance, we will map critical data, messages and documents using national standards. Standardization will let us exchange electronic information with referring providers, while protecting patient privacy and security.

The University of Pittsburgh Medical Center is among the nation's leaders in translational science, putting new understanding of the human genome into action to improve the lives of persons with pancreatic, liver and inflammatory bowel diseases. At present, it is challenging to "connect the dots" between the new genomic databases that define a person's risk for heritable diseases and the electronic records of what patients actually experience (i.e., phenotypic expressions) of these same diseases. Interoperability among information systems will be a key support to help our clinical investigators to make rapid progress in this exciting new field.

Dr. Dunn is the Medical Director of Interoperability for UPMC. He is a Clinical Professor of Medicine in the Division of Gastroenterology, Hepatology and Nutrition, and practices in the Division's Digestive Diseases Center. He comes to UPMC after Army service as a Brigadier General that included leadership of successful initiatives for interoperability between military and veterans' health records, as well as command of the Walter Reed Health Care System and the Army's hospitals in the Western United States.

GI Rounds Online
University of Pittsburgh School of Medicine
http://girounds.pitt.edu

New Additions to Online Series

The Division of Gastroenterology, Hepatology and Nutrition is pleased to announce new additions to its interactive, online physician education series, *GI Rounds Online* @ **http://girounds.pitt.edu.**

GI Rounds Online was founded by James B. McGee, MD, associate professor of medicine, through the publication of six inflammatory bowel disease cases. This educational series is based on researched educational theories and has received excellent reviews from online participants.

Pancreas and functional bowel modules are now available as well, and expanded cases exploring diagnosis and treatment strategies for a variety of GI and liver diseases will be available in the future. The six-case pancreas series also offers a hardcopy educational monograph to complement each online pancreas module.

If you have questions or would like to have the hardcopy pancreas monograph series mailed to you, contact **girounds@dom.pitt.edu**. But remember: the best way to experience *GI Rounds Online* is to visit **http://girounds.pitt.edu** first hand. Just get online and learn!

A Disease that is Far from Home

by John M. Lyons, MD
Chief Gastroenterology Fellow

Case Presentation

A 53-year-old woman with a history of dyspepsia presented to an outside hospital with a one-day history of acute onset, severe epigastric pain associated with nausea, bilious emesis and diarrhea. The pain awakened her and was constant. She denied fever, chills, NSAID use or recent antibiotics use. She never had a similar pain episode in the past. Physical examination demonstrated an Asian woman in significant distress. She was doubled over in pain, afebrile, and mildly tachycardic. Her abdominal exam was notable for epigastric tenderness without peritoneal signs and normoactive bowel sounds. The remainder of the exam was unremarkable. Of note, she was born in rural Korea but immigrated to the US 30 years ago.

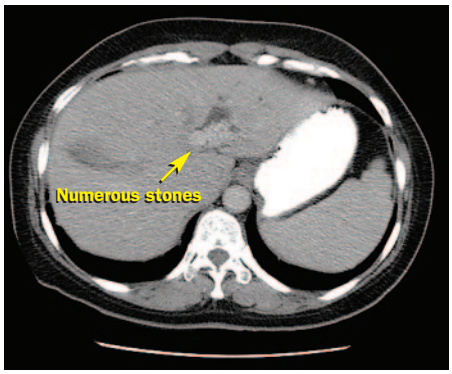


Figure 1. CT demonstrating left intrahepatic stones in dilated biliary system.

Initial laboratory data revealed WBC of 11,000, normal hemoglobin, normal electrolytes, total bilirubin of 1, AST 34, ALT 65 (nl 30-65), alkaline phosphatase 143 (nl 39-117), and normal pancreatic enzymes. A right upper quadrant ultrasound, abdominal CT, and MRI/MRCP were performed at the outside facility. The combined impression of these studies was left intrahepatic biliary duct dilation due to an obstructing hyperdense area near the biliary hilum *(see Figure 1)*. Extrahepatic biliary duct dilation was also present.

She was transferred to UPMC five days after initial presentation for further care. Her notable labs upon arrival were: ALT 151, AST 41, alkaline phosphatase 351, gamma-glutamyl transferase 627 (nl<40), total bilirubin 0.4, and CA 19-9 1215 (nl<37).

A diagnosis of recurrent pyogenic cholangitis (also known as oriental cholangiohepatitis) was made, and the patient was treated with broad spectrum antibiotics. Given the presence of extrahepatic biliary duct stones and increasing LFTs, an ERCP with choledochoscopy was performed for duct clearance, sphincterotomy and evaluation for malignancy. Examination revealed near complete obstruction of the common hepatic duct due to a large stone and massively dilated left intrahepatic system. Balloon sweeps retrieved small stones and purulent material. Due to worsening cholangitis, she underwent surgery for a left liver lobectomy bile duct exploration with stone removal and placement of a T-tube. She did well post-operatively and was discharged one week later with plans for outpatient follow-up and T-tube cholangiogram. No evidence of cholangiocarcinoma was found in the resected specimen.

Recurrent pyogenic cholangitis (RPC) is a disease typified by intrahepatic biliary pigment stone formation with bouts of cholangitis, biliary obstruction, dilation and stricturing. Immigration is leading to an increased incidence in western countries, but RPC still occurs in patients from Southeast Asia almost exclusively. Men and women are affected equally, and the peak incidence is between 20 to 40 years of age. The exact pathogenesis remains poorly understood. A commonly proposed etiology is that parasitic infections, such as Clonorchis sinensis, lead to biliary epithelial damage and obstruction which predisposes patients to bacterial infections, biliary stasis and stone formation. Dietary differences may also play a role but cannot explain the entire disease process.

The diagnosis of RPC is established in patients who present with a consistent constellation of symptoms, have lived in Southeast Asia and have imaging-confirmed intrahepatic biliary stones. One study reports cholangitis (44%) and abdominal pain without obvious cholangitis (32%) as the most common presenting symptoms. Acute management often involves antibiotics and biliary decompression/stone clearance. The long-term goal of therapy is to cease future attacks to eliminate disease progression (e.g., biliary cirrhosis). Complicating management concerns include recurrent stone formation and increased annual incidence of cholangiocarcinoma (~5%/year) in RPC patients. Proper management requires a multidisciplinary approach comprised of gastroenterologists, surgeons and radiologists, since multiple endoscopic (ERCP), radiologic (PTCs) and surgical (hepatic resection/possibly transplant) interventions are usually required.

Beyond the ABC's of Viral Hepatitis

by Sandra El-Hachem
Gastroenterology Fellow

Case Presentation

A 47-year-old male was referred for a second opinion concerning cirrhosis. In 1979, he was diagnosed with acute hepatitis B infection secondary to intravenous drug use (IVDU). He did not receive treatment but did well except for chronic fatigue. In February 2007, his transaminases were mildly elevated on routine blood work. A CT of the abdomen, showed a cirrhotic liver with no masses or ascites. Blood work confirmed the history of chronic hepatitis B (HBsAg: positive, HBs Ab: negative, HBcAb [Total/IgG]: positive, HBV DNA : 1410 IU [285 copies], HBeAg: negative, HBeAb: positive). A liver biopsy showed chronic viral hepatitis with moderate activity (modified HAI: 10/18) as well as mild fibrosis (stage 2/6). The immunohistochemistry revealed scattered cells expressing HBsAg with no HBcAg.

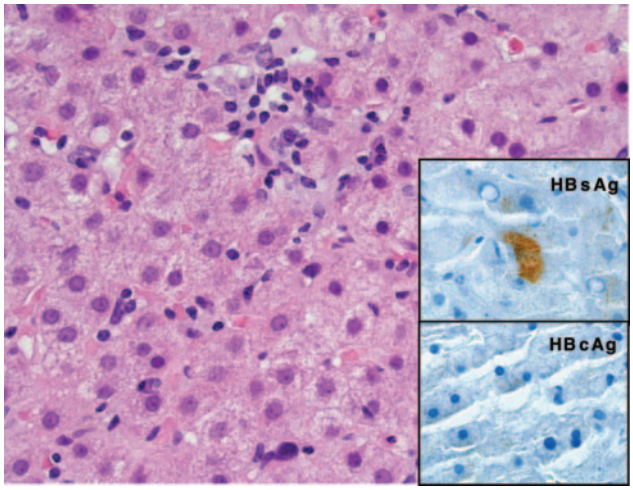


Figure 1: Immunostain for HBsAg is positive in only rare hepatocytes and is negative for HBc Ag.

In view of his history of IVDU, serologies for hepatitis D were sent, and the results showed HDAb IgM positive, HDAg negative, and HDV PCR positive. The diagnosis of hepatitis delta superinfection was made.

Hepatitis D (Delta) virus was described initially in 1977. Approximately four to five percent of the 400 million patients with chronic hepatitis B are coinfected with Hepatitis D. Prevalence is decreasing worldwide due to HBV vaccination and AIDS awareness programs. Risk factors for the transmission of the delta virion are intravenous drug use, blood transfusions, sexual promiscuity and living in endemic areas. Eight current genotypes are described, which affect prognosis as well as clinical course of the infection.

The delta virion is a 'defective virus' which implies that it requires hepatitis B to replicate and cause infection. It has a simple structure built within the outer lipoprotein envelope being provided by HBsAg and a core comprised of an RNA genome and the hepatitis D antigen. It replicates in hepatocytes and suppresses hepatitis B infection.

Three primary clinical entities are described:

Coinfection implies acute infection with both hepatitis B and D. In order to make the diagnosis, Anti-HBc IgM must be present. Up to five percent mortality is associated with co-infection secondary to fulminant hepatic failure. Most cases will resolve as the hepatitis B resolves.

Superinfection implies the infection of a chronic HBV patient with delta virion. Cirrhosis develops at a faster rate in these patients. Anti-HDV IgM is brisk and long lasting, while Anti-HBc IgM is negative.

Helper Independent Latent Infection is described in the transplant setting initially. The allograft is re-infected with HDV, and the virus remains dormant until rescued by HBV reactivation or infection.

Hepatitis D infection imparts a three-fold increased risk of HCC and doubles mortality making correct diagnosis essential. The aim of therapy in Hepatitis D is suppression of replication. Unfortunately, no effective regimen has been discovered to date. Current standard therapy, which has limited efficacy, uses IFNa at high doses to suppress HDV replication. Studies done with pegylated interferon had a 21 percent clearance of virus after 72 weeks. Patients without cirrhosis and without prior exposure to interferon seemed to have a higher response. Ribavirin, lamuvidine, adefovir and acyclovir are ineffective against the virus.

Physicians should consider checking for hepatitis D in patients with chronic HBV with risk factors or unexplained worsening of their hepatitis. Some evidence exists to support hepatitis D treatment with interferon in patients with abnormal liver function tests but without cirrhosis. The best therapy remains prevention of HBV infection through immunization and education.

Radiofrequency Ablation for Barrett's Esophagus

by Kevin McGrath, MD

Barrett's esophagus (BE) is a premalignant condition and is the main risk factor for esophageal adenocarcinoma. The incidence of adenocarcinoma has been rapidly increasing in the United States. There is no treatment for BE per se, but acid suppression has been the mainstay for symptomatic control of GERD, which is the cause of BE. Patients are generally offered endoscopic surveillance for detection of dysplasia and early cancer. The risk of developing adenocarcinoma is 30 to 125 times higher in people with BE, with an estimated incidence of 0.5 percent per year. Surveillance intervals are based on the cancer risk, which increases with worsening grades of dysplasia. Low grade dysplasia (LGD) and high grade dysplasia (HGD) carry cancer risks of 7 percent and 22 percent, respectively, in patients followed for up to seven years.

While LGD is surveyed more frequently (six to 12 month intervals), HGD has been treated by esophagectomy traditionally. In the last decade, endoscopic ablative treatments for HGD have emerged, and photodynamic therapy (PDT) has been the most rigorously evaluated. The goal of endoscopic ablative therapy is eradication of HGD with little to no morbidity. A large randomized multicenter PDT study reported an eradication rate of 77 percent for HGD. However, this treatment modality is also plagued by morbidity, chest pain requiring narcotic analgesia, photosensitivity and an esophageal stricture rate of 30 percent.

A new FDA-approved therapy for dysplastic BE has recently emerged, commercially known as the HALO ablation system (BARRX Medical, Sunnyvale, CA). This system, powered by an automated generator, rapidly delivers radiofrequency energy to the bipolar electrode of a treatment catheter. The energy application (treatment time) is approximately one second, resulting in a uniform depth of injury (< 1 mm) no deeper than the muscularis mucosae. The HALO^{360} system uses a balloon-based ablation catheter, enabling a uniform circumferential treatment length of 3cm per application. Short term studies report a > 90 percent ablation rate for dysplastic Barrett's esophagus. The HALO^{90} system utilizes a small electrode mounted on the tip of the endoscope, which can treat very short Barrett segments or residual islands.

The Digestive Disorders Center at UPMC has used this treatment since April 2007. The therapy is outpatient and is well tolerated, with minimal to no chest discomfort afterward. Patients are given acetaminophen for treatment-related discomfort, as opposed to the narcotics used for PDT-related chest pain. Call **(412) 648-9325** to refer a patient for treatment consideration.

Dr. McGrath is an associate professor of medicine with the Division of Gastroenterology, Hepatology and Nutrition and serves as the Director of the GI Lab and Director of Endoscopic Ultrasound (EUS).

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

The EGD shows erythematous friable mucosa with multiple erosions and discreet circumscribed ulcers with slightly raised edges. Biopsies were consistent with herpes esophagitis. This condition was first reported by Johnson, et. al. in Archives of Pathology in 1940. While often seen in immunocompromised patients, it is rare in immunocompetent hosts. The typical clinical presentation involves odynophagia and dysphagia. Other symptoms include fever, epigastric pain, nausea, vomiting and heartburn. Co-existent genital/oropharyngeal herpetic lesions may be found in some patients, but this is atypical. Endoscopic appearance may vary depending on time of the procedure in relation to the course of the disease; early lesions are more likely to be vesicles, while later lesions tend to be discreet, circumscribed ulcers with raised edges. Biopsies can establish diagnosis, and the pathology can show typical findings of inflammation, ground-glass appearance in the nuclei, Cowdry type-A nuclear inclusion bodies and multinuclear cells. Immunohistochemical stains for HSV confirm diagnosis. Serologies are usually not helpful unless seroconversion is proven. Typically, erythematous friable mucosa is a self-limiting illness in immunocompetent hosts, and benefits of antiviral therapy are unknown. Therapy may shorten the duration of the illness.

This patient had significant esophagus ulcerations, and biopsies showed inflammation, multinucleated cells and Cowdry type-A inclusion bodies. Immunohistochemical stains were positive for HSV. He completed a course of acyclovir with resolution of his symptoms.

What Is This? provided by Eli Aoun, MD, Gastroenterology Fellow.

References upon request.

The Division of Gastroenterology, Hepatology and Nutrition is pleased to welcome the following faculty members:

Randall E. Brand, MD
Rhonda Brand, PhD
Julie Christianson, PhD
Michael A. Dunn, MD
Kenneth E. Fasanella, MD
Julia Greer, MD, MPH
Sacha Malin, PhD
Mitchell B. Max, MD
Ian M. McGowan, MD, PhD
Amit Raina, MD
Ernest L. Sutton, MD, MPH

To learn about the clinical and research priorities for these new faculty, visit the Division's website at **http://www.dom.pitt.edu/gi.**

Kapil B. Chopra, MD, associate professor of medicine with the Division's Center for Liver Diseases, has received the Commonwealth of Pennsylvania's *2007 Viral Hepatitis Award of Excellence* for being an excellent patient and physician advocate. This award is presented annually to physicians demonstrating outstanding clinical care. Dr. Chopra received this award in October 2007 at the 2008 PA Viral Hepatitis Conference.

Dr. Chopra is the medical director of the Comprehensive Liver Program with UPMC's Liver Pancreas Institute, is the medical co-director for Transplant Hepatology and directs the Division's Transplant Hepatology Fellowship Program. For more information about Dr. Chopra and the Center for Liver Diseases, call 412-647-1170 or visit the Division's website at **http://www.dom.pitt.edu/gi.**

James B. McGee, MD, associate professor of medicine, has been named the founding editor of the American Gastroenterological Association's (AGA) Online Education Program. As one of the premier gastroenterology associations in the world, the AGA offers outstanding opportunities for global education through novel online initiatives. Dr. McGee will lead reviews concerning accredited education programs, physician recertification and related online projects. Online resources will be offered for both clinical physicians and research scientists.

In addition to his gastroenterology appointment, Dr. McGee serves as the assistant dean for Medical Education Technology and directs the Laboratory for Educational Technology for the University of Pittsburgh School of Medicine. Dr. McGee may be contacted at **mcgee@medschool.pitt.edu**.

Stephen O'Keefe MD, MSc has been awarded a major R-01 NIH grant entitled *Feeding and Pancreatic Rest in Acute Pancreatitis* (DK07580). This five-year award involves a multi-center clinical trial comparing the effects of nasogastric versus distal jejunal feeding with pancreatic rest on outcome in patients with severe acute pancreatitis. Collaborating centers are University of Louisville/KY (Dr. S. McClave), VA Commonwealth University (Dr. D. Kirby), Medical University of SC (Dr. M. DeLegge), Mayo Clinic/Rochester (Dr. S. Vege), Harvard University (Drs. P. Banks and S. Freeman), University of FL/Gainesville (Dr. C. Forsmark), and UCLA (Dr. S. Pandol). The study will be coordinated from the University of Pittsburgh (Dr. S. O'Keefe, PI).

FELLOWSHIP UPDATE

The Division of Gastroenterology Hepatology and Nutrition is pleased to announce the successful graduation and placements of the following gastroenterology fellows:

Allen Banegura, MD – Private Practice, Digestive Disease Associates, Baltimore, MD

Yasser Bhat, MD – Interventional Endoscopy Fellowship, University of Pennsylvania, Philadelphia, PA

Kenneth Fasanella, MD – Instructor of Medicine and Associate Program Director for the GI Fellowship Program, Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh, Pittsburgh, PA

Rachelle Johns, MD – Westmoreland Gastroenterology Associates/Excela Health, Greensburg, PA

Daniel Mullady, MD – Advanced Endoscopy Fellowship, Massachusetts General and Brigham and Women's Hospitals, Boston, MA

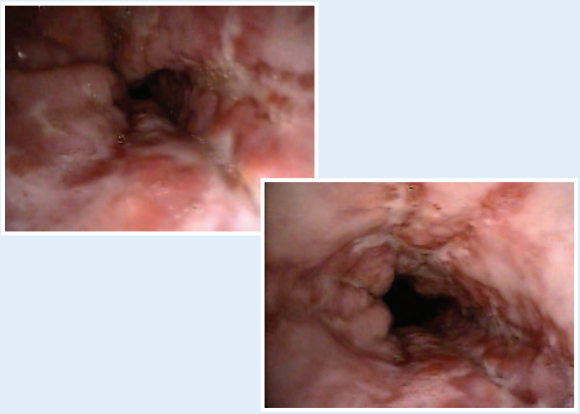
Benjamin Siemanowski, MD – Private Practice, Madrona Medical Group, Bellingham, WA.

continued on page 8

What Is This?

Presentation: A 35-year-old previously healthy male presented with severe odynophagia and epigastric pain of five days duration. A viral prodrome preceded the onset of these symptoms. He denied any frank dysphagia but has not been able to tolerate oral intake due to the pain. There are no significant alleviating factors. He had two episodes of non-bloody emesis the day prior to presentation. His physical exam was significant only for mild epigastric tenderness. An EGD was done.

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



FELLOWSHIP UPDATE continued from page 7

The Division is also pleased to welcome the following outstanding Year I gastroenterology fellows to our program:

Elie Aoun, MD – M: American University of Beirut; R: University of Pittsburgh Medical Center

Sandra El-Hachem, MD – M: American University of Beirut; R: Cleveland Clinic Lerner College of Medicine

David Lo, MD – M: Northwestern University Feinberg School of Medicine; R: Barnes-Jewish Hospital

Shahid Malik, MD – M: Drexel University College of Medicine; R: University of Pittsburgh Medical Center (and 2006-07 University of Pittsburgh Transplant Hepatology Fellow)

Joseph Rodemann, MD – M: Loyola University Chicago Stritch School of Medicine; R: Barnes-Jewish Hospital

Vinay Sundaram, MD – M: New York University School of Medicine; R: University of Virginia Health System.

The Division's 2007-08 Transplant Hepatology Fellow is **Anastasios Mavrakis, MD** (M: University of Athens Greece Medical School; R: Caritas St. Elizabeth's Medical Center/Tufts).

(M) = Medical School *(R) = Residency*

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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