



**Pitt**

# Digest

Winter/Spring 2010



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**What Is This?**

## CENTERS OF EXCELLENCE:

- PANCREAS & BILIARY DISEASES
- INFLAMMATORY BOWEL DISEASE
- LIVER DISEASES
- NEUROGASTROENTEROLOGY & 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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 Kofi Clarke, MD  
 Bahar Madani, MD  
 Joy Jenko Merusi, MA

## Center for Liver Diseases:

# Clinical Expansion in Response to Patient Demand

by **Kapil Chopra, MD**

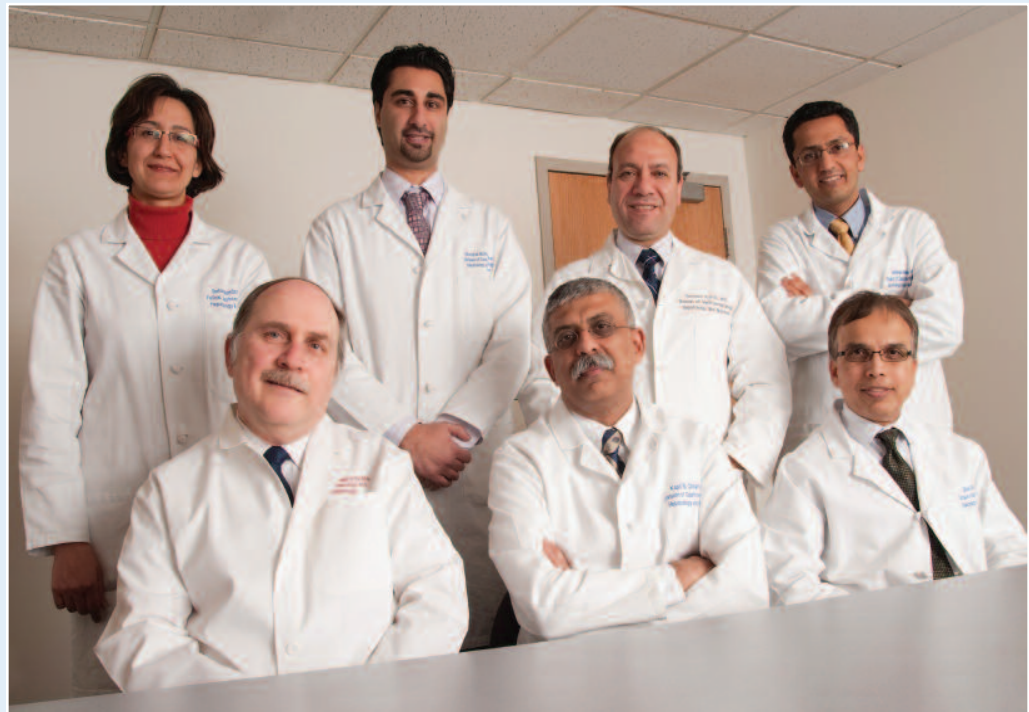
The hub of UPMC's hepatology program is the Center for Liver Diseases (CLD), a "Center of Excellence" for the University's Division of Gastroenterology, Hepatology and Nutrition. Located in the Kaufmann Medical Building in the Oakland section of Pittsburgh, this site has eleven exam rooms, a phlebotomy service and has been fully integrated into the UPMC electronic health record.

The CLD team cares for patients with all known liver disorders including acute and chronic liver disease before, during and

after liver transplantation. Working in close collaboration with the Thomas E. Starzl Transplantation Institute, this team of six physicians, three mid-level providers (CRNP/PA), seven clinical nurse coordinators (four of whom are dedicated to viral hepatitis alone), two clinical research coordinators, an LPN, a clinic manager and coordinator provide patients with state-of-the-art diagnostic and therapeutic options.

More than 10,000 patients visit the CLD each year, and 2,000 new patients receive care annually. Importantly, every patient is invited to participate in a research registry,

*continued on page 6*



Left to right (1st row): Mordechai Rabinovitz, MD; Kapil B. Chopra, MD; Obaid S. Shaikh, MD. (2nd row): Bahar Madani, MD; Shahid Malik, MD; Hossam Kandil, MD, PhD; Jaideep Behari, MD, PhD.

**A**s Chief of the Division of Gastroenterology, Hepatology and Nutrition, it is gratifying to be associated with outstanding physicians and scientists who continue to demonstrate the best of medicine and surgery.

In this issue, we focus on our Center for Liver Diseases, which has quietly built one of most outstanding clinical medical hepatology units in the world. Two articles discuss different aspects of the program. The first is an overview of the medical hepatology program by **Kapil Chopra MD**, and the second details Living Donor Liver Transplantation by the new Chief of Transplantation Surgery, **Abhinav Humar, MD**. Discussion of the hepatology group's NASH research advancements is provided by **Shahid Malik, MD**, a Year III gastroenterology fellow who will join Division faculty this summer. Case reports are presented by two additional gastroenterology fellows, **John Nasr, MD** and **David Brokl, MD**.

Our Division will sponsor two major GI conferences in 2010:

- > The international **PancreasFest 2010** symposium on July 29, 30 & 31; and
- > **Postgraduate Course: Multidisciplinary Strategies for Common Digestive Diseases** on October 21 & 22. Both programs will be held in Pittsburgh. Contact [joj2@pitt.edu](mailto:joj2@pitt.edu) for more information.

As always, we seek your feedback on how we may best serve you and your patients. This increasingly complex and difficult time in medicine can offer great opportunities for sub-specialists to do remarkable things, and we look forward to hearing from you. Meanwhile, enjoy this issue of *Digest*.



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*

## News & Updates

### Transplant Hepatology Fellowship Program

The Transplant Hepatology Fellowship Program at the University of Pittsburgh Medical Center is now accredited by the ACGME. This one-year program is designed to provide clinical training to enable the candidate to meet the requirements for certification in Transplant Hepatology. This program functions within the Division of Gastroenterology, Hepatology & Nutrition in close collaboration with the Thomas E. Starzl Transplantation Institute. Applicants must have completed training in both internal medicine *and* gastroenterology. For additional information, visit [www.dom.pitt.edu/gi/fellowship/hepatology](http://www.dom.pitt.edu/gi/fellowship/hepatology).

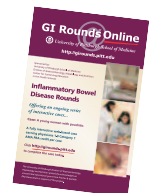
### Dr. Kandil & Islamic Center Work to Eradicate Hepatitis C

Hosted by the Islamic Center of Pittsburgh, Hossam Kandil, MD, PhD, Mercy Behavioral Health and other providers coordinated a successful hepatitis C screening program in January, 2010. This program raised public awareness about the risks of hepatitis C infection and provided treatment options. More than 100 people participated, and 40 attendees were screened anonymously. Dr. Kandil was the keynote speaker for this seminar. He discussed how immigrants and minorities may be at a greater risk of hepatitis C infection but may be less likely to receive early and appropriate care. Dr. Kandil is an assistant professor of medicine and cares for nutrition support and liver disease patients.

### GI Rounds Online

**GI Rounds Online** is a unique and highly interactive online physician education course which provides globally accessible, state-of-the-art educational case studies through Internet technology. These programs are designed for the continuing medical education needs of gastroenterologists.

For more information, please visit <http://girounds.pitt.edu>.



# Living-Donor Liver Transplantation (LDLT)

**T**he single greatest problem in liver transplantation today is the shortage of deceased donors. Consequently, as the waiting lists have grown, so have the number of people who die awaiting transplant. This shortage has also lengthened the waiting time for candidates, often resulting in deterioration of their overall medical status before transplantation can be performed.

Attempting to increase the total number of livers available for transplant, several centers now perform liver transplants using living donors. Although most commonly used for kidney transplantation, living donation is also possible for liver transplantation. Typically, one of the two liver lobes (or certain segments) may be removed from a living donor and transplanted successfully. Initially this option was reserved for pediatric recipients, but now it is possible to perform this surgery for both pediatric and adult patients.

Most patients with severe liver disease who are candidates for a deceased donor transplant may be considered for a living-donor liver transplant (LDLT). The greatest advantage of an LDLT is the avoidance of waiting time for a deceased donor transplant. More than 17,000 people are awaiting liver transplantation in the United States currently, but only 5,000 transplants are performed per year. Roughly 25 percent of these candidates will die of liver disease before having the chance to undergo transplantation. For those who do receive a deceased donor transplant, the average waiting time is one to two years. With an LDLT, this waiting time is bypassed, allowing the transplant to be performed before the recipient's health deteriorates and before the transplant becomes impossible. Importantly, LDLT increases the number of overall livers available for transplantation. The utilization of LDLT enables surgery programs to provide the deceased donor livers to those candidates lacking a suitable living donor.

## The LDLT Process

The LDLT process begins with a rigorous medical, surgical and psychosocial evaluation of the potential donor. Relatives are preferred, since they are often the most committed to the candidate's health. However, non-relatives such as good friends or spouses may be considered. The donor must have a compatible blood type and be in good physical and mental health, with no significant history of major medical problems, liver disease or excessive alcohol use. The liver is carefully imaged to ensure that the anatomy and size of

the donor's liver supports the transplant procedure. If the recipient is an adult, the right lobe of the donor's liver is generally used for the transplant. If the recipient is a child weighing less than 25 kg, the left lateral segment of the donor's liver is used typically. Another important part of the donor evaluation process is to ensure that the donor is psychologically fit. The decision to donate should be made entirely by the potential donor, with no coercion from anyone, after careful consideration of procedure risks and potential complications.

The operative procedure involves isolation of the blood vessels supplying the portion of the liver to be removed and transection of the hepatic parenchyma, followed by removal of the portion to be transplanted. The donor operation generally takes six to eight hours. The usual recovery time is five to seven days of hospitalization. The donor operation is a major procedure, and potential complications

exist, with incidence ranging from 20 to 30 percent. Adult donors have a higher risk of complications, since a larger piece of the donor's liver is removed. Possible complications include bleeding, bile leaks, incision problems and infections. There is also a small risk (<0.5%) of donor death. While the risk of death is small, it is very real and must be considered seriously.

The Thomas E. Starzl Transplantation Institute has long been performing LDLTs and is one of the largest programs in the country offering this option to patients. Well over 250 LDLT surgeries have been performed at UPMC over the past ten years. In 2009, approximately 30 percent of our pediatric liver transplants and ten percent of adult transplants occurred with a living donor. Patients and graft survival results are encouraging.

Current local and national data suggest that results in LDLT recipients are superior to those in deceased donor recipients, largely due to these recipients being healthier at the time of their transplant. However, LDLT surgical complications tend to be more common. It is encouraging to note that LDLT results are improving, as centers gain more experience with this procedure.



*Dr. Humar is a Professor of Surgery in the University of Pittsburgh School of Medicine. He serves as Chief for the Division of Transplantation within the Department of Surgery and is the Clinical Director for the Thomas E. Starzl Transplantation Institute.*



## A Not-So-Common Liver Cyst



by **David Broki, MD**  
Gastroenterology Fellow

### Case Presentation

A 64-year-old female presented with a one-day history of upper abdominal pain, nausea and one episode of bilious vomiting. Her past medical history was notable for HTN, obesity, and rheumatoid arthritis. Her medications included methotrexate 7.5 mg PO weekly for about one year, folic acid, amlodipine, benazepril and labetalol. She smoked one pack per day for about 50 years and denied alcohol use. She also denied illicit drug use, recent travel, sick contacts or contact with animals. Family history was unrevealing. During a review of systems, she confirmed subjective fevers and chills but denied weight loss, diarrhea, night sweats, history of jaundice, fatigue or weakness.

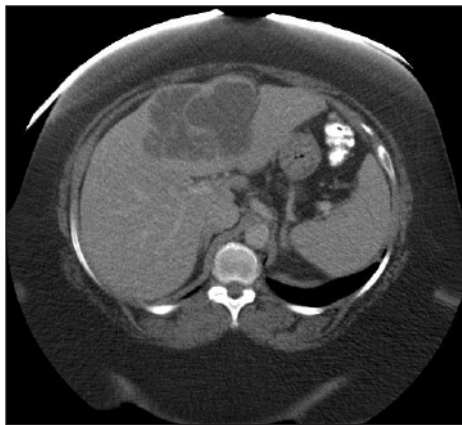
She was afebrile with normal vital signs. Her examination revealed epigastric and RUQ tenderness to palpation without palpable masses, hepatosplenomegaly or findings of chronic liver disease. EKG was unremarkable. CXR was normal. Lab testing showed bilirubin 0.8, AST 117, ALT 81, AP 177 albumin 3.6, normal electrolytes and renal function. CBC revealed WBC of 19,800 with a left shift and normal platelet count. INR was normal. Abdominal triphasic CT scan revealed a large, low-attenuation, complex cystic lesion with multiple septations in the left liver lobe within normal appearing hepatic parenchyma. She was started on intravenous ampicillin-sulbactam and metronidazole. Further laboratory studies revealed an elevated CA 19-9 at > 20,490, with a negative work up for chronic liver disease. AFP levels were normal, and Echinococcus serologies were

negative. The patient underwent U/S-guided needle aspiration of the cystic lesion which revealed 360 WBCs/mm<sup>3</sup> (100% neutrophils) and CA 19-9 level > 20,490. Cultures were negative as was cytologic analysis of the aspirated fluid. She subsequently underwent a left hepatic lobectomy.

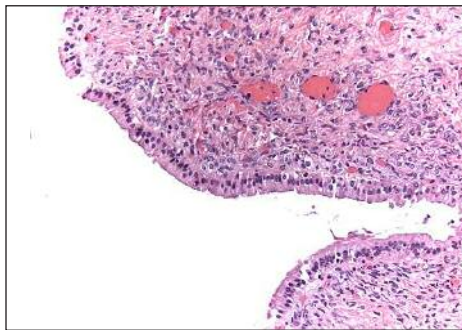
Histopathologic analysis of the resected tissue revealed biliary type mucus-secreting cuboidal epithelium supported by a dense cellular (mesenchymal) fibrous stroma resembling ovarian tissue without evidence of malignancy consistent with intrahepatic biliary cystadenoma. The patient did well post-operatively and was discharged two weeks after initial presentation.

Biliary cystadenomas represent less than five percent of cystic liver lesions. They are benign, are hypothesized to arise from a congenital defect of the bile ducts or gallbladder, and usually involve no luminal communication with the biliary tree. About 80 percent manifest among middle-aged women. Typical clinical manifestations are due to mass effect of the cysts. Complications are rare and include cyst infection, hemorrhage or rupture. LFTs are generally normal unless infection is present or compression of the biliary system occurs. Serum and cystic levels of CA 19-9 are usually elevated, sometimes markedly. Diagnosis is suggested by imaging findings of a multilocular anechoic (on U/S) or low attenuation (on CT scan) fluid-filled cystic lesion with thick walls and multiple septations. The vast majority of these lesions are located in the liver. Histology is essential for diagnosis and often reveals cysts lined by biliary type mucus-secreting cuboidal or columnar epithelium supported by a dense cellular (mesenchymal) fibrous stroma resembling

ovarian tissue. Preferred treatment of hepatic biliary cystadenomas is surgical resection due to the potential for malignant transformation (up to 15%). Surgical options include enucleation (excision of the mass with a thin layer of normal tissue) or anatomic resection. Incomplete resection results in high risk of recurrence (> 50%).



**Figure 1:** CT scan of abdomen with contrast in portal venous phase showing cystic lesion.



**Figure 2:** Cystic lining showing biliary type mucus-secreting cuboidal epithelium supported by a dense cellular (mesenchymal) fibrous stroma resembling ovarian tissue.

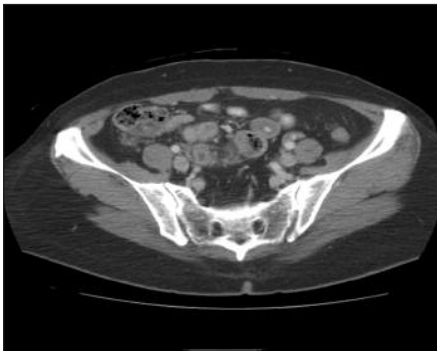
# Endometriosis Masquerading as Crohn's Disease



by **John Nasr, MD**  
Gastroenterology Fellow

## Case Presentation

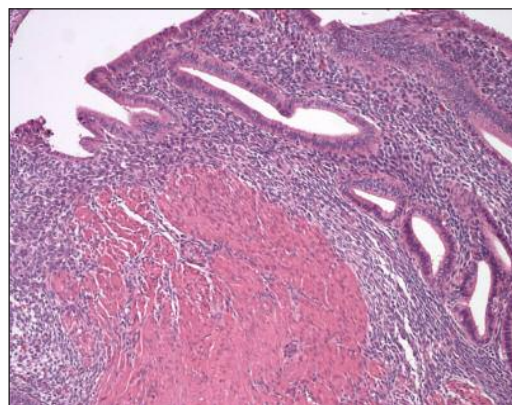
**A** 47-year-old female presented with a six-month history of intermittent abdominal pain associated with nausea and vomiting. The pain occurred monthly and lasted four to five hours. This pain was located on the left side of the abdomen initially and was not associated with food intake. Later, the pain became generalized and resulted in three prior hospitalizations. The patient denied



**Figure 1:** Focal area of wall thickening in the distal ileum several centimeters prior to the ileocecal valve.

obstipation or constipation but did report three to four loose bowel movements associated with her pain episodes. Her past medical history included hypertension controlled with medications, and her only prior surgeries were hysterectomy and cholecystectomy. An upper endoscopy and colonoscopy (with terminal ileal intubation) were normal. Abdominal ultrasound did not show cholelithiasis or biliary dilatation, and liver function tests were normal during episodes of pain.

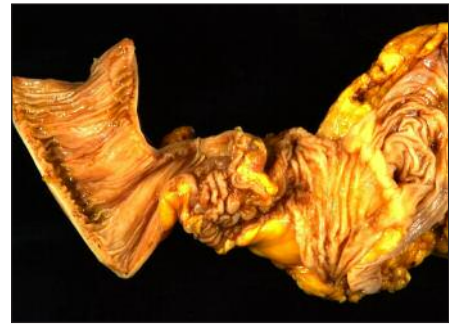
Abdominal Computed Tomography (*Figure 1*) showed thickening of the terminal ileum. Her abdominal symptoms were thought to be due to fibrostenotic Crohn's disease involving the terminal ileum. She underwent laparoscopic resection of the terminal ileum and cecum.



**Figure 3:** Histology showing endometrial glands in cellular stroma within muscularis propria.

Gross specimen (*Figure 2*) revealed area of thickened small bowel, with stricture formation and small focal hemorrhages. Histology (*Figure 3*) revealed endometrial glands within bowel wall consistent with small bowel endometriosis.

Endometriosis is a condition defined by the presence of functional endometrial glands and endometrial stroma, localized outside the uterus. It affects up to 15 percent of women of menstruating age. Endometriosis is diagnosed based on high clinical suspicion and consistent histology.



**Figure 2:** Gross pathology of resected small and large bowel, with areas of small bowel thickening, stricture formation and small focal hemorrhages.

Endometriosis affects 12 percent of patients with this condition, with the rectosigmoid area being the most commonly involved intestinal area. Intestinal endometriosis diagnosis is based on clinical suspicion in the appropriate clinical setting accompanied by typical histological features of endometriosis. Involvement of the terminal ileum is seen in seven percent of patients with intestinal endometriosis. Gastrointestinal endometriosis patients present with relapsing bouts of abdominal pain, distention, tenesmus, constipation or diarrhea, and, rarely, with perforation. Endometriosis of the terminal ileum usually presents in young nulliparous women with abdominal pain, in conjunction with signs of obstruction.

Definitive treatment of endometriosis of the small bowel is surgical resection of the involved bowel portion. Therapy with danazol- or gonadotropin-releasing hormone analogs is only a temporizing measure.

Endometriosis should be considered in the differential diagnosis of a young patient presenting with terminal ileal disease mimicking Crohn's disease.

## UPMC CLD: Clinical Expansion in Response to Patient Demand *continued from page one*

and, to date, 5,000 patients are enrolled in the CLD research registry. The UPMC CLD has expanded to satellite centers beyond Oakland as well. Liver patients are now seen at UPMC Passavant (North Hills), UPMC McKeesport and UPMC

*More than 10,000 patients visit the CLD each year, and 2,000 new patients receive care annually.*

Horizon (Greenville). Given the tremendous success of the CLD's outreach services, additional sites are scheduled to be added soon.

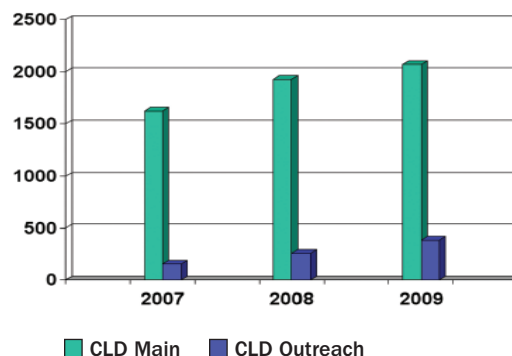
Starting January 2010, Fatty Liver Disease (FLD) and Bile Duct Disorders (BDD) clinics will focus on patients with alcoholic

and non-alcoholic fatty liver disease and patients with cholestatic liver disease (primary biliary cirrhosis and primary sclerosing cholangitis). These clinics will utilize protocol-driven clinical care and research study participation.

CLD physician scientists participate in investigator-initiated and industry-sponsored clinical research protocols to provide patients with the best current treatment options, such as newer antiviral therapies for hepatitis C and B, hepatic encephalopathy management, and the use of thrombopoietin for chronic liver disease. Additionally, our researchers are exploring the role of intracellular signaling pathways in the pathogenesis of liver diseases, new treatments for non-alcoholic and alcoholic fatty liver diseases, and studying the metabolic syndrome after orthotopic liver transplantation.

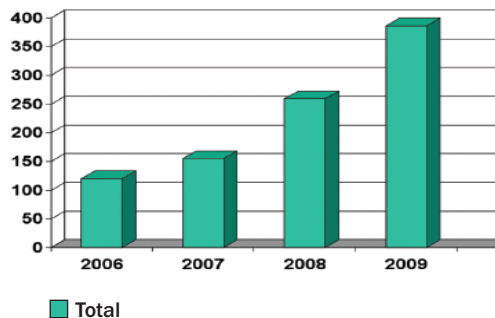
The UPMC CLD is poised to provide patients and their families with a comprehensive approach to all disorders of the liver. Its collaborative clinical and research partnerships within UPMC provide a unique opportunity to better understand the basic mechanisms causing liver diseases and provide excellent care/options for our patients. To refer a patient, physicians may call MedCall at 412-647-7000 or

### CLD – New Patient Visits



### CLD Outreach Program

(Passavant; McKeesport; Horizon)



1-800-554-2500 and ask for the liver consult attending. Patients may call 412-647-1170 for a direct appointment.



*Dr. Chopra is an Associate Professor of Medicine with the University of Pittsburgh School of Medicine, Division of Gastroenterology, Hepatology & Nutrition. He is the Clinical Director of Hepatology and Medical Director of Liver Transplantation, Transplant Hepatology Fellowship Program Director, and Medical Director of the Comprehensive Liver Program for the UPMC Liver-Pancreas Institute.*

*What Is This? by Kofi Clarke, MD, Gastroenterology Fellow. References upon request.*

**Diagnosis:** The CT scan shows a gastroduodenal fistula, a well-described major complication of PEG tube placement. This fistula is more common in patients with several pre-existing co-morbid conditions and is usually discovered after weeks to months following tube replacement. If diagnosed early, treatment involves tube removal, allowing the tract to close naturally. Another option is surgical closure.

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



# NASH and Liver Transplantation



by **Shahid Malik, MD**  
Gastroenterology Fellow

**A**t the beginning of my hepatology fellowship, a patient asked me:

“So doc, how do patients like me do after transplant?”

Although I knew the general outcomes of liver transplantation (LT), I could not quote specific outcomes for patients with nonalcoholic fatty liver disease (NAFLD). I performed a thorough literature search and was surprised to find no information on this subject. Addressing this patient’s question and the noted lack of available literature became the impetus behind most of my research for the next several years.

LT is the standard of care for patients with decompensated cirrhosis. Outcomes following LT are excellent with one- and five-year survival rates of 85-90 percent and 70-80 percent respectively for the most common causes of cirrhosis in the United States, namely cholestatic liver disease (PBC/PSC), alcoholic liver disease (ALD) and hepatitis C virus (HCV). Outcomes following LT in patients with NASH cirrhosis have yet to be described.

NAFLD has become the most common cause of chronic liver disease in the developing world, affecting nearly one in every three individuals. Nonalcoholic steatohepatitis (NASH), the progressive form of NAFLD, can eventually lead to cirrhosis and end stage liver disease. NASH affects approximately 10 million Americans, substantially higher than the prevalence of HCV infection. As a result, NASH is projected to surpass HCV as the leading indication for LT within the next ten years.

Utilizing a prospectively collected database, we identified 98 biopsy-proven NASH patients who underwent LT at the University of Pittsburgh during the last ten years. These patients were compared to a model for end stage liver disease (MELD) matched controls comprised of the other most common indications for LT: PBC/PSC, ALD, HCV and cryptogenic cirrhosis.

Our series focused on mortality, hepatocellular carcinoma (HCC), and recurrent disease and led to these results and conclusions:

**1) Outcomes:** NASH patients had comparable short- and long-term mortality as patients undergoing LT for the other most common causes of cirrhosis. However, we categorized a subset of NASH patients as ‘high-risk’ (defined as age  $\geq$  60 years, BMI  $\geq$  30 kg/m<sup>2</sup>, pre-transplant diabetes and hypertension). One-year mortality following LT in these “high-risk” NASH patients was 50 percent compared to 16 percent in the overall NASH population (K-M Curve).

**2) Hepatocellular Carcinoma (HCC):** The incidence of HCC in patients with NASH cirrhosis at the time of LT was 17 percent and was comparable to controls. Outcomes following LT in patients with NASH cirrhosis and HCC (within Milan criteria) were excellent with 88% survival at a mean follow-up of 2.5 years following LT.

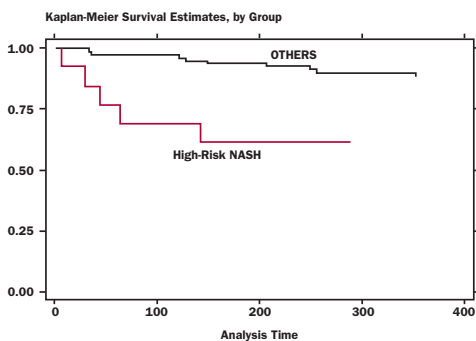
**3) Recurrent Disease:** Recurrence of fatty liver following LT is common, affecting up to 70 percent of patients.

Recurrent NASH occurred in 25 percent of patients at a mean follow up of three years. One-third of patients with recurrent NASH had normal liver enzymes at the time of biopsy. To detect recurrent disease, yearly protocol biopsies should be performed on all patients transplanted for NASH cirrhosis.

Currently, we are generating a database for all NASH patients seen at the UPMC Center for Liver Diseases and Thomas E.

Starzl Transplantation Institute. Database information will be used to categorize these patients and determine future therapies to prevent progressive disease in both the pre- and post-LT populations.

**Kaplan-Meier Survival Curve for 98 Patients Transplanted for NASH According to High Risk vs. Non-High Risk**  
P<0.005 by log rank (analysis time in days)



- 1) Malik SM, deVera ME, Fontes P, Shaikh O, Ahmad J. Outcomes After Liver Transplantation for NASH Cirrhosis. *Am J Transplant* 2009; 9:782-793
- 2) Malik SM, Gupta PA, de Vera ME, Ahmad J. Liver Transplantation in Patients with NASH-Related HCC. *Clin Gastroenterol Hepatol* 2009;7:800-806.
- 3) Malik SM, deVera ME, Fontes P, Shaikh O, Sasatomi E, Ahmad J. Recurrent Disease Following Liver Transplantation for NASH Cirrhosis. *Liver Transpl* 2009;15:1843-1851.

Information concerning **Pitt Digest** or requests for additional newsletter copies may be directed to Joy Jenko Merusi at [joj2@pitt.edu](mailto:joj2@pitt.edu). Visit our website at [www.dom.pitt.edu/gi](http://www.dom.pitt.edu/gi)

## What Is This?

**Presentation:** A 74-year-old man with an extensive past medical history including ventilator dependent respiratory failure with a tracheotomy presented with discomfort around a PEG tube that had been placed several weeks earlier. Clinical exam of the abdomen was unremarkable except for minor irritation at the PEG tube site.



Figure 1



Figure 2

**What is your diagnosis?**

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

## Annual Physician Education Opportunities

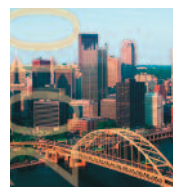
### PancreasFest 2010: July 29, 30 & 31, 2010



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 2010**. Education programs are interspersed

with investigative research meetings to further the multidisciplinary understanding and treatment of pancreas diseases.

### What's New in GI & Hepatology?



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 **October 21 & 22, 2010**.

Both programs will be held in Pittsburgh, Pennsylvania. For more information about either program please contact Joy Jenko Merusi at [joj2@pitt.edu](mailto:joj2@pitt.edu).