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**Pitt Quarterlyly Digest**

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

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As the fourth installment of a multi-part series, the **Pitt Quarterlyly Digest** features the UPMC Center for Intestinal Health and Nutrition Support this winter. We hope you will enjoy reading about the comprehensive clinical and research innovations of this group.

## CENTER FOR INTESTINAL HEALTH & NUTRITION SUPPORT

by Stephen J.D. O'Keefe, MD

**T**he UPMC Center for Intestinal Health and Nutrition Support was instituted two years ago and is currently staffed with three gastroenterologists, the Center director Stephen O'Keefe, MD, Hossam Kandil, MD, PhD and Toby Graham, MD, CNSP. The team's nurse practitioner is Brenda Owens, CRNP and the clinical dietician is Patty Centa, MS, RD, CNSD, LDN. Rose Kummer is the Center's administrative secretary. The Center is also assisted by GI fellows who rotate through the Nutrition Support Service to gain clinical experience in nutritional gastroenterology.

**The Nutrition Support Service**

Activity within the Nutrition Support Service has increased significantly over the past year, since this group is now responsible for all the endoscopic techniques required for patients with nutritional disorders. Traditionally, these procedures consisted almost entirely of PEG placements, but expertise has now been developed to place feeding tubes past upper GI obstructions and as far down as the mid-jejunum. The number of PEGs performed has doubled from 35 in 2002 to 68 in 2004, and the number of jejunal feeding tubes increased from 0 to 33. The Nutrition Support Service performs these procedures with complex techniques such as transnasal endoscopy and manipulation under fluoroscopic control within the GI lab. Many of



**Center for Intestinal Health & Nutrition Support Team**  
 (clockwise, from left): Patty Centa, MS, RD, CNSD, LDN, Stephen J.D. O'Keefe, MD, Hossam Kandil, MD, PhD, Brenda Owens, CRNP and Toby O. Graham, MD, CNSP

the procedures are performed on critically ill patients in the various medical and surgical hospital ICU's. The need for interventional tube feeding has increased dramatically with the recognition that the high use of TPN in critically ill patients is been associated with adverse side effects, particularly those of catheter-related septicemias and venous thrombosis. There is also concern that TPN increases infectious complications due to homeostasis and bacterial overgrowth. Many studies have shown that the cytosine response associated with critical illness is enhanced in patients solely given intravenous feeding. Concern

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## Division Highlights

Advancements in nutrition support research and ground breaking patient care have established the UPMC Center for Intestinal Health & Nutrition Support as one of the most important nutrition support programs in operation today. The scope of the Center involves the care of patients with severe intestinal diseases, short gut syndromes with or without parenteral nutrition and collaborations with the small bowel transplant program – all aided importantly by **Brenda Owens, CRNP, Patty Centa, MS, RD, CNSD, LDN** and Center assistant **Rose Kummer**.

Many of you share my admiration for **Dr. Toby Graham**, who started the Nutrition Support Service, so I know you will join me in wishing her well, as she has decided to work on a part-time basis with the Nutrition Support Service. She continues to teach and coordinate fellow educational activities and is also leading other administrative initiatives.

The mark of a great University program is the quality of the research and teaching. We therefore highlight the research efforts of **Dr. Stephen O'Keefe** and **Dr. Hossam Kandil** on page five. It is evident that newly sophisticated patient care is a direct result of their labs' efforts and achievements. Dr. O'Keefe also serves as the Chair of the Nutrition & Obesity Section for the American Gastroenterology Association.

I am also pleased to announce the following recent developments:

- Our current chief GI fellow, **Dr. Neeraj Kaushik**, will join our Division's faculty in July and will continue endoscopic ultrasound study and practice with **Dr. Kevin McGrath** and **Dr. Asif Khalid**.
- **Dr. Miguel Regueiro** and **Dr. Richard Duerr** were promoted to Associate Professors of Medicine.
- We welcome **Dr. Veronique Morinville** as the first recipient of *The Henry E. Haller, Jr. and Marjorie Burns Haller Advanced Fellowship in Pancreatic Medicine*. Dr. Morinville is a pediatric gastroenterologist from Montreal, Québec, Canada and will focus on the genetic causes of pancreatitis in children and families. This advanced fellowship is made possible by generous grants from the Haller family.



In good health,

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

**David C. Whitcomb, MD, PhD**  
*Professor of Medicine, Cell Biology & Physiology and Human Genetics  
Chief, Division of Gastroenterology, Hepatology and Nutrition*

## Expanding the Role of the Nutritional Endoscopist

by **Toby O. Graham, MD, CNSP**

Providing Nutrition Support by the enteral route plays a pivotal role in patient outcome in the critical care setting. With failure to obtain enteral access, the gut becomes a proinflammatory organ, increasing oxidative stress and risk of complications. Early enteral access promotes gut-associated lymphoid tissue as well as mucosal-associated lymph tissue at distant sites allowing preservation of immune function and decreased long-term complications.

Aggressive enteral tube feeding decreases the rate of complications when compared to standard therapy (oral diet as tolerated) or TPN. However, obtaining early enteral access in a critically ill patient may be difficult. While bedside placement of feeding tubes (FTs) may be adequate in a large number of patients, they are blinded and risky. More importantly, as disease severity increases, the success rate for bedside placement decreases, and blinded bedside techniques are less reliable for achieving deep jejunal or even trans-pyloric placements. Transporting patients for fluoroscopic placement of FTs leads to delays and increases complications.

The role of the nutritional endoscopist in these settings is critical. Using skills to place the FT at the appropriate level of the GI tract, most techniques can be performed at the bedside. With expertise in gut physiology, the nutritional endoscopist is better able to monitor enteral feeding, distinguish tolerance from intolerance and trouble shoot for complications.

During the past six months, the Nutrition Support Service (NSS) has seen a 25 percent increase in consult activity, largely related to requests for endoscopic nasoenteric tube placement in critically ill patients and those who require jejunal feeding because of acute and chronic pancreatitis with complications.

The growth and direction of nutritional endoscopy advances our commitment to early enteral access and initiation of early enteral nutrition. Enteral nutrition is capable of improving clinical outcomes in the critically ill by reducing nosocomial infection, multiple organ failure, hospital length of stay and use of TPN.

*Dr. Graham is an associate professor of medicine with the Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh.*



# Acute Hepatitis with an Unusual Etiology

by Jaideep Behari, MD, PhD

Fellow, Division of Gastroenterology, Hepatology and Nutrition

## Case Presentation

A 53-year-old male with a history of alcohol and intravenous drug abuse presented with jaundice, mental status changes, and transaminases of over 1000 IU/L. Three months earlier he was found to have alanine aminotransferase (ALT) of 100 IU/L (normal <40 IU/L), aspartate aminotransferase (AST) of 114 IU/L (normal <40 IU/L), and positive HCV antibody. Two weeks prior to admission ALT was 530 IU/L, AST 514 IU/L and alkaline phosphatase (AP) 575 IU/L (normal 40-125 IU/L).



**Figure 1:** CT scan showing ill-defined, heterogeneous, hyperintense areas in the liver

On admission and physical examination, he had jaundice, ascites, and asterixis.

Significant laboratory results were: ALT 1660 IU/L, AST 1176 IU/L, total bilirubin 13.5 mg/dL (normal .3-1.5 mg/dL), direct bilirubin 8.8 mg/dL, AP 552 IU/L, gamma glutamyltransferase 180 IU/L (normal <40 IU/L), INR 2.6, PTT 37.8 ammonia 56 µmol/L, albumin 2.3 g/dL, alpha fetoprotein 69 ng/ml, creatinine 1.5 mg/dL. Paracentesis was negative for spontaneous bacterial peritonitis.

### What is the differential diagnosis?

In this patient with acute hepatitis in the setting of chronic liver disease, differential diagnosis would include acute viral hepatitis (A, B, and herpes simplex), ischemic liver injury, acute portal vein thrombosis, drug-induced hepatotoxicity, autoimmune hepatitis, and rarely hepatocellular carcinoma (HCC).

History was negative for acetaminophen or herbal medication use. HCV PCR revealed genotype 3a and viral titer of 4373 IU/ml. Serologies for hepatitis A, B, HSV, autoimmune hepatitis and other etiologies of chronic liver disease were negative. Abdominal ultrasound showed no biliary ductal dilatation, and CT scan of the abdomen revealed a cirrhotic liver with multiple geographic areas of hypoattenuation thought to be diffuse fatty infiltration, chronic portal vein thrombosis, and moderate ascites (Figure 1).

During his hospital stay, the patient's transaminases remained markedly elevated (Figure 2). A trans-jugular liver biopsy showed moderately differentiated HCC. The final diagnosis was hepatitis C and alcohol related cirrhosis complicated by infiltrating HCC with an unusual presentation as acute hepatitis.

The patient was not a candidate for transplantation or palliative therapy, and he died eight weeks after his initial admission.

**Discussion:** Infiltrating, or diffuse-type HCC refers to a tumor with no clearly defined mass and infiltrating growth on imaging studies. The incidence of infiltrating HCC is 13-20 percent of all HCC cases. Mean age at tumor diagnosis is slightly lower for infiltrating than for nodular HCC (59.5 versus 66.2 years, respectively), and there are no differences in terms of gender, duration of chronic liver disease, stage of cirrhosis, histologic findings, or AFP levels.

Risk factors for development of infiltrating HCC are hepatitis B infection and HBV/HCV co-infection. Infiltrating HCC is associated with a high incidence of portal vein thrombosis. Gadolinium enhanced MRI scans are useful in imaging suspected cases of infiltrating HCC.

Infiltrating HCC is more aggressive than nodular HCC. In one series, all 22 patients with diffuse-type HCC had tumor involvement of at least four hepatic segments at diagnosis, while 12 had all eight segments involved. With survival rates of 33 percent at one year and 14 percent at three years, independent of treatment, compared with 75 percent and 46 percent for nodular HCC, infiltrating HCC carries a poorer prognosis.

Day	ALT	AST
1	2084	852
2	2750	1249
3	1839	1024
4	2829	1562
5	4946	2778
6	623	893
7	480	832
8	1660	1176

**Figure 2:** ALT and AST levels during hospital stay

**Summary:** Infiltrating HCC is a distinct sub-type of HCC which is difficult to diagnose and treat and carries a worse prognosis compared with nodular HCC. Rarely, as in our patient, it may present with marked elevation of transaminases mimicking acute hepatitis.

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## A Surgical Emergency?

**Kenneth E. Fasanella, MD**

*Fellow, Division of Gastroenterology,  
Hepatology and Nutrition*

### Case Presentation

**M**s. J. G. is a 52-year-old woman with a history of hepatitis C and prior abdominal surgery presented to the emergency room with a three-day history of nausea, anorexia, and severe epigastric abdominal pain. The pain was exacerbated by cough, belching, valsalva and movement, and was somewhat relieved by remaining still. GI review of systems was otherwise negative.

Examination revealed a well-nourished female in moderate distress, afebrile with stable vital signs. Her pulmonary and cardiac exams were unremarkable. Abdominal examination revealed active bowel sounds, exquisite tenderness even to light palpation in the mid epigastrium but no rebound or guarding. There were no organomegaly, mass or ascites on exam.

Laboratory workup revealed normal chemistries and normal CBC with no elevation in WBC or left shift. Liver enzymes showed stable elevation in transaminase levels (<2x upper limit) but no evidence of cholestasis. Amylase and lipase were also normal. Abdominal x-rays showed no obstruction or free air, and RUQ US and HIDA scan were negative for cholecystitis. The CT (*Figure 1*) was obtained.

**Question:** *Should this woman be taken for exploratory laparotomy?*

**What we did:** The CT scan was read as a rounded area of soft tissue infiltration in the omentum anterior to the left lobe of the liver, likely representing omental torsion or infarct. The radiologist interpreted this as a benign cause of abdominal pain, and surgery agreed that no surgical intervention was indicated. Comfortable on oral narcotics, the patient was discharged on hospital day three and was pain-free within two weeks.

**Discussion:** Omental torsion, segmental omental infarction and epiploic appendagitis represent a spectrum of omental pathology that can present as acute or subacute abdominal pain mimicking surgical emergencies such as acute cholecystitis, appendicitis, diverticulitis or perforated peptic ulcer. Most of the literature regarding this topic is surgical and suggest that omental infarction is a fairly rare condition

often found upon laparotomy. As radiologists become more comfortable with classic CT and ultrasound findings, more recent radiologic publications suggest that it is more common than previously thought. Median age is 41 years of age with males slightly more affected. Predisposing factors include obesity, direct trauma, enteritis, adhesions, hernias and venous thrombosis; it has even been associated with jackhammer use and marathon running. Torsion of the greater omentum presents with right upper quadrant pain, whereas epiploic appendagitis presents right or left lower quadrant pain, as the appendages are longest and most abundant in the cecum and sigmoid colon. Pain is usually sudden in onset, non-radiating and gradually worsens. Typically, venous occlusion leads to arterial compromise and hemorrhagic infarction which can lead to aseptic peritonitis. The natural history of this condition has not been defined, since, traditionally, most occurrences were not discovered until surgery. However, more recent case series suggest a benign course with a median time of 15 days to complete resolution of pain.



**Figure 1:** CT image depicting rounded area of soft tissue infiltration in the omentum adjacent to the left lobe of the liver representing area of omental infarction.

**Summary:** Omental infarction is a rare cause of abdominal pain, but may be more common than thought previously and can mimic other causes of abdominal pain classically thought to be indications for surgery. However, radiologists are becoming increasingly familiar with characteristic findings on CT and ultrasound, allowing for earlier diagnosis, and more recent experience suggests a benign natural course.

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## Nutritional Research

by Stephen J.D. O'Keefe, MD

**T**he Center for Intestinal Health & Nutrition Support is committed to improving nutritional care through basic research translated into clinical practice. I currently receive NIH support to investigate interactions between pancreatic exocrine function and dietary intake with particular reference to interventional tube feeding and intravenous feeding in the management of acute pancreatitis. Our investigations are aimed at developing the most effective ways to maintain Nutrition Support in patients with acute pancreatitis without stimulating the pancreas and worsening the disease process. My lab is also involved in another NIH-sponsored study to investigate changes in mucosal function in patients with massive intestinal loss during the 12-month post-resection adaptive period. This work is being done in collaboration with Emory University and the Cleveland Clinic. We also wish to examine why some patients with intestinal failure develop severe irreversible liver disease, leading to transplantation.

A second area of research is the relationship among diet, colonic bacterial flora and colon cancer risk, specifically differences in these parameters between native Africans and African-Americans. This research is supported by the American Institute of Cancer Research and is being conducted in centers in South Africa and Pittsburgh. Preliminary results suggest that the low animal fat (saturated fat) and animal protein consumed by native Africans may influence colonic bacteria to reduce the risk of colonic inflammation and cancer risk. Native Africans harbor high colonic populations of methanogenic bacteria in comparison to African-Americans, and there is evidence that the combination of metabolically generated hydrogen by bacteria into methane reduces hydrogen toxicity and mucosal damage. Further studies concerning DNA polymorphisms and specific bacterial species is being conducted.



*Dr. O'Keefe is a professor of medicine and is director for the Center for Intestinal Health & Nutrition Support at the University of Pittsburgh.*

## Reducing Intestinal Transplant Complications

by Hossam Kandil, MD, PhD

**N**utrition support and dietary modification are essential to improve dietary tolerance and intestinal rehabilitation in patients with intestinal failure. Conversely, patients dependent on parenteral nutrition (TPN) are at high risk of severe complications such as recurrent line sepsis, vanishing venous access and hepatic complications. Intestinal transplantation has become acceptable management for patients with intestinal failure who are unable to be maintained on TPN. Our nutrition support team collaborates with the intestinal transplant service to optimize the management of patients with short bowel syndrome and intestinal failure.

TPN-induced hepatic complications, common among candidates awaiting isolated small bowel transplants, may necessitate multivisceral transplant and affect waiting time on the transplant list. Our team is investigating the risk factors for progression of TPN-associated liver disease after isolated small bowel transplant. Recently, we have shown that significant hepatic steatosis prior to isolated small bowel transplant is associated with persistent hepatic abnormalities post transplant. Better understanding of

these factors will help to improve patient management and organ utilization.

Intestinal biopsies are the gold standard for the diagnosis of rejection after small bowel transplantation. Preliminary studies indicate that the ileum remains the most sensitive site for diagnosing rejection. When ileal biopsies are negative in the presence of high clinical suspicion for rejection, jejunal biopsies are of additional diagnostic value.

We are also studying how dietary modifications in fatty acid composition may affect active metabolites such as prostaglandins and cytokines. This may affect the pathogenesis of diseases such as colitis. Utilizing a mouse model of spontaneous colitis, we observed a significant decrease in colitis-associated dysplasia and inhibition of cyclooxygenase-2 (COX-2), when animals are fed olive oils. This may be related to the anti-oxidant effects of olive oils or the direct inhibition of COX-2 expression. Further studies are underway to increase our understanding of the nutritional effects on colitis and colitis-associated cancer.



*Dr. Kandil is an assistant professor of medicine in the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition.*

## INTESTINAL HEALTH & NUTRITION SUPPORT

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about the overuse of TPN within the hospital system has lead the hospital safety committee to empower our section to supervise all TPN-fed patients to increase efficiency and reduce complication rates.

Another activity of our Nutrition Support Service is the home care program. Many of the Center's patients develop permanent feeding disorders requiring long term tube or intravenous feeding at home. To provide this care, we work closely with home care agencies. With regard to home TPN, patients first begin intravenous feeding while in the hospital and then, once stabilized, are trained to look after their own catheters and infusions at home. Following discharge, the Nutrition Support Service continues to provide metabolic monitoring to maintain nutritional homeostasis and avoid the serious complications of sepsis, thrombosis and liver disease.

As part of the education program for GI fellows, the GI nutrition fellow presents cases for discussion and future management at the weekly Nutrition Grand Rounds program. It is our goal to ensure that all GI fellows trained at the University of Pittsburgh will be fully competent to manage the most difficult GI nutritional problems.

### **Small Intestinal Rehabilitation and Transplant Service**

Small bowel transplantation is a unique area of gastroenterology not shared by many other institutions around the world. The University of Pittsburgh's 14 years of experience with 323 intestinal transplantations leads the field. While one-year graft and host survival until five years ago was only 50 percent, most recent figures show a dramatic improvement to over 90 percent. Medicare's approval of small bowel transplantation for TPN failure has resulted in increased referrals to our Center. Increases in candidates for assessment and subsequent transplantation have increased the need for additional personnel and resources.



Traditionally the GI Division was only involved in endoscopic biopsy to assess graft function and rule out rejection. Now Drs. O'Keefe and Kandil are also intricate members of the small bowel transplant team, and the Center has a leading role in the assessment of candidates for transplantation and the management of patients with permanent intestinal failure before transplant occurs. With the development of an ileoscopy unit in UPMC Montefiore Hospital, the urgent ileoscopies have been moved out of the GI lab to free up GI endoscopists for more traditional work. Dr. Kandil has recently moved from the VA to a full-time position in the Division of Gastroenterology, Hepatology and Nutrition and now devotes most of his time to the clinical and academic parts of the intestinal transplant program. We are also developing a more comprehensive website to emphasize that the Center provides help with small bowel transplantation and difficult cases of intestinal failure. Alternature techniques such as drug and hormone therapy, jejunostomy placement or reconstructive surgery may help restore intestinal function and therefore nutritional autonomy.

The transplant clinic operates daily with two full-time nurses, a social worker, and a psychiatrist to provide the support required by patients with intestinal failure before and after transplantation. The program will be strengthened further by the addition of Laura Matarese, a leading national dietician, who has recently moved from her position as Director of Intestinal Rehabilitation at the Cleveland Clinic.

To consult with a Center for Intestinal Health & Nutrition Support physician or to schedule patients, call the UPMC Digestive Disorders Center, toll-free, at 1-866-4GASTRO (1-866-442-7876).

*Dr. O'Keefe is a professor of medicine and is director for the Center for Intestinal Health & Nutrition Support at the University of Pittsburgh.*

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



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