Training Tomorrow’s Gastroenterologists and Hepatologists:

Today’s University of Pittsburgh Fellowship Program

by Miguel D. Regueiro, MD and Arnold Wald, MD

The gastroenterology fellowship at the University of Pittsburgh Medical Center currently has 14 fellows with one additional tertiary-year hepatology fellow. The program provides rigorous training in clinical gastroenterology, hepatology, and nutrition as well as specialized training in pancreaticobiliary diseases, inflammatory bowel diseases and neurogastroenterology. Fellows may also receive training in advanced endoscopic procedures, ERCP and endoscopic ultrasound.

Large and Diverse Faculty

The strength of this training program is based on a large and diverse faculty, who are recognized as experts in their fields. Currently, there are 27 clinical faculty and six research faculty. Over the past five years, research grants have jumped from $2 million to $5 million, with clinical income increasing by more than $2.6 million to a total of $5.6 million. Fellows interact daily with faculty and receive research training in their second and third years.

Three career track programs have been established to allow fellows to achieve individual career goals within the structured three-year training program. Importantly, career tracks can quickly advance fellows interested in third-tier, specialized training programs.

▶ The **physician scientist** track prepares a fellow for a career as a physician scientist in a university/academic center. Under faculty mentor supervision, the fellow will receive 18 months of bench research and will be prepared to become an independent investigator.

▶ The **clinical research and investigation** track establishes a fellow’s career as a clinical researcher in an academic medical center. In the second and third training years, each fellow defines a niche specialty within gastroenterology, hepatology, or nutrition and identifies an area of research that will continue into his/her career.

▶ The **clinician education and informatics** track prepares a fellow for a career as a clinician educator. During the second and third training years, the fellow learns how to become an effective clinician educator with an emphasis on learning informatics as an educational tool.

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As you have probably noticed, we have changed the format of our Division’s physician newsletter, Pitt Digest. We have added more pages to provide more information, and our editors will feature different aspects of the University of Pittsburgh’s gastroenterology, hepatology and nutrition advancements in each issue.

This fall, we are featuring our Gastroenterology Fellowship Program. This program has flourished under the direction of Dr. Arnold Wald, and the program’s co-director, Dr. Miguel Regueiro. During Dr. Wald’s tenure as program director, fellowship numbers have increased and outstanding new initiatives such as the T-32 NIH grant and fellow clinical tracks have been designed and implemented. Informatics opportunities have also become available through the mentorship of Dr. James B. McGee. And, importantly, all regulatory fellowship information has been automated, including all fellow and attending evaluations. As the new year turns, Dr. Regueiro will assume full directorship of this Gastroenterology Fellowship Program, and we thank him for accepting this challenge.

Of particular note in this issue are the contributions from Dr. Niraj Jani, chief GI fellow, and Dr. Daniel Chung, a Pitt Digest editor, who discuss the participatory involvement of the fellows in their own curriculum development and program plans.

Please join our Division for its fifth annual physician education program Update in GI and Hepatology: What’s New and What To Do on December 2 & 3 at Pittsburgh’s Sheraton Station Square Hotel. A copy of the course brochure and registration materials may be found online at [http://ccehs.upmc.edu/formalCourses.jsp](http://ccehs.upmc.edu/formalCourses.jsp).

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

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**Pitt Fellowship Program continued from page one**

Creation of the career tracks has been a popular addition to the gastroenterology, hepatology, and nutrition fellowship training program and has attracted outstanding fellowship candidates to the University of Pittsburgh.

All fellows are expected to publish or submit for publication at least one peer-reviewed article by the end of fellowship. For example, fellows who just graduated in July 2005 had 19 peer-reviewed publications, seven abstracts, four presentations at national conferences and seven awards resulting from their research.

**Varied Clinical and Research Experiences**

Pitt GI fellows benefit from varied clinical and research experiences during their three training years. The first fellowship year typically involves clinical training. Fellows rotate on inpatient consult services and begin a longitudinal outpatient clinic. An enriched hepatology outpatient experience has also been added to Year I. Fellows meet with the program director early in the first year enabling them to “hit the ground running” with their research projects in Year II. Second year fellows average six months of protected time to begin their research project. Additionally, fellows receive an enriched outpatient experience at UPMC Shadyside Hospital to provide exposure to clinicians in various aspects of community practice. Year III fellows continue their research projects with an average of six months of protected time. Fellows pursuing a career in academic gastroenterology may apply for a career award or other research grants. Those electing to receive additional tertiary (fourth year) training in pancreaticobiliary, EUS or hepatology may participate in clinical investigation in these disciplines. Please see page eight of this issue for the class of 2005’s post-graduate work.

Recently the division has implemented an online fellowship program evaluation system, which provides enhanced ease of use, “real time” evaluation of fellows and faculty and an improved evaluation process compliant with the ACGME guidelines. Duty hours are also captured on this system, and procedure logs and electronic portfolios will soon be incorporated.

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**Dr. Regueiro is associate professor of medicine, is the Division’s associate chief for education, and co-directs both the IBD Center and GI Fellowship Program.**

**Dr. Wald is professor of medicine with the Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh and directs the GI Fellowship Program.**
Ever since the passage of the 1997 Balanced Budget Act, autumn has not only brought the colorful splendor of falling leaves and crisp fall evenings but, for physicians, the annual rite of anxiety over impending political battles for fiscal viability. Given the enormous impact of this fall’s congressional decisions, I will review the genesis and mechanism of the Medicare Physician Fee Schedule (MPFS) as well as what to expect from the American Medical Association’s Relative Value Update Commission (RUC).

As the largest insurer of health care in the America, the MPFS significantly influences the reimbursement rates of all private insurers and, consequently, global reimbursement for physician services. This year, unease about Medicare is particularly high, since the RUC will re-evaluate the Relative Value Units (RVUs) assigned to five key services provided by gastroenterologists: simple endoscopy (CPT-43235); endoscopy with PEG placement (CPT-43246); endoscopy with lesion removal by hot biopsy forceps or cautery (CPT-43750); simple flexible sigmoidoscopy (CPT-45330); and simple colonoscopy (CPT-45378).

The 1997 Balanced Budget Act completed the transition of Medicare reimbursement from its original open ended, fee-for-service model in 1965 to a globally budgeted system, in which physician reimbursement is limited by a Sustainable Growth Rate (SGR). Since 1997, Medicare payments to physicians are not solely dependent on provider activity but on the performance of the U.S. economy as measured by the Gross Domestic Product (GDP) and the physician’s ability to provide care within a defined dollar limit. The SGR factors four items to determine annual revisions of the MPFS:

1. Physician fees for services to Medicare beneficiaries;
2. Number of fee-for-service beneficiaries;
3. Estimated ten-year average annual growth rate in real GDP per capita; and
4. Estimated changes in expenditures due to law or regulation changes.

The use of the SGR as a basis for annual physician reimbursement calculations resulted in a 4.8 percent MPFS decrease in 2002 to keep Medicare reimbursement in line with climbing senior services costs. It is currently estimated that Medicare payments to physicians cover only 65 percent of the actual cost of services performed. If left unchanged, implementation of the Balanced Budget Act will result in a 4.3 percent decrease in Medicare reimbursement for 2006 and a whopping 26 percent decrease in Medicare payments over the next six years. This will occur over a period in which inflation is estimated to be 15 percent. Therefore, the real MPFS will have declined by 41 percent by 2002.

The activities of the RUC will impact not only the procedures discussed above but also the enhancements rendered through these services such as simple endoscopy with added biopsy (CPT-43239), and colonoscopy with polypectomy (CPT-45385). The total RVUs assigned to a given service reflect the time spent providing the procedure. If the RUC is convinced that the current service time component is too generous, then a decrease in the RVU value assigned to these procedures will occur in 2007.

The potential of a decreased MPFS, now proposed at minus 4.3 percent, will lower the dollar value of each RVU. A drop in RVU values for GI procedures further devalues these reimbursements. An example of this impact on cash flow is given in Table 1 on page six.

continued on page six
Case Presentation

A 35-year-old man with a history of type 1 diabetes mellitus and prior cadaveric renal transplant presented with a one-week history of upper back pain, bloating, and early satiety, followed by nausea with epigastric abdominal pain. The pain was not worsened post-prandially or with position, and was unaccompanied by changes in bowel habits, fevers, chills, night sweats, or vomiting.

Examination revealed a well-nourished, muscular Caucasian man in no acute distress. HEENT, neck, chest, and cardiovascular exams were all normal. His abdominal exam revealed a non-tender, firm mass in the epigastrum, but was otherwise normal. There was no evidence of portal hypertension, jaundice, or cirrhosis on exam.

Laboratory workup consisted of normal CBC and chemistries except for a mild elevation from his baseline creatinine, and liver enzymes which markedly rose over a four-day period. AST increased from 54 IU/L to 1069 IU/L (nl <40 IU/L), ALT from 45 IU/L to 845 IU/L (nl <40 IU/L), alkaline phosphatase from 71 IU/L to 295 IU/L (nl 40-125 IU/L), and total bilirubin from 0.2 mg/dL to 2.0 mg/dL (nl .3-1.5 mg/dL). Amylase, lipase, and INR were normal.

A CT scan initially done at an outside hospital demonstrated mild ascites and thickening of the antrum and duodenum.

Question: What would you do next?

What we did: An upper endoscopy was performed to evaluate the abnormalities seen on his prior CT. The endoscopy revealed partial gastric outlet obstruction and a stricture in the duodenal bulb which was able to be traversed with a 27 endoscope (Figure 1). The post-bulbar duodenum was endoscopically normal. Biopsies of the stricture were taken. Given the worsening liver enzymes, a repeat CT was performed and demonstrated a large soft-tissue mass involving the porta hepatitis, omentum, and lesser sac (Figure 2). Biopsies revealed EBV-associated, strongly CD-20 positive, monomorphic, post-transplant lymphoproliferative disease (PTLD). The patient was referred to oncology, who treated him with high-dose steroids followed by a modified CHOP protocol and rituximab (anti-CD-20 monoclonal antibody).

Discussion: PTLD is a lymphoproliferative disorder that encompasses a spectrum of diseases from a mild infectious mononucleosis-like illness to an aggressive non-Hodgkins B-cell lymphoma. The distinguishing characteristic of these illnesses is the victim’s post-transplant status, for which the immune suppression is the predisposing factor. Immunosuppressant medications impair the normal cytotoxic T-cell response to EBV-infected cells, resulting in Th-2 like responses, allowing uncontrolled proliferation of the EBV-transformed B-cell clone. The risk is highest among patients on aggressive immune suppression, and those with transplanted organs which are rich in lymphoid tissue, such as small bowel. 1-10% of renal transplant patients are affected. EBV-seronegative organ recipients are 25-50 times more likely to develop the illness, and are more likely to develop it earlier after transplant. 47% of cases occur within six months after transplant, and 90% within five years. Treatment ranges from reduction in immune suppression in mild cases to chemotherapy in more severe cases. In one series of ten patients with late PTLD after kidney transplant, six achieved complete remission receiving CHOP therapy with a median survival of 27 months. The addition of rituximab to chemotherapy is fast becoming the standard of care.

Future directions in therapy center on adoptive immunity, in which EBV-specific cytotoxic T-lymphocytes (CTLs) are derived in vitro using the patients’ own lymphoblastoid B-cells as the immune stimulus. While promising, this has the drawback of a prolonged preparation time. To overcome
this hurdle, there have been proposals to bank CTLs of various HLA-types or to derive patient-specific clones in high-risk patients prior to the development of disease.

**Summary:** PTLD is a common disease affecting both solid and liquid organ transplants, and is due to proliferation of EBV-infected B-cells which grow unchecked in the absence of adequate cytotoxic T-cell surveillance. Therapy is based on decreasing immunosuppression in mild, mononucleosis-like cases, whereas chemotherapy plus anti-CD20 monoclonal antibody (rituximab) is indicated in more severe cases.

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**Crohn’s Disease: Postoperative Maintenance of Remission**

**by Rachelle Johns, MD**  
**Fellow, Division of Gastroenterology, Hepatology and Nutrition**

**Case Presentation**

A 28-year-old man presented for a second opinion for his Crohn’s disease which had presented eight months earlier with pneumaturia and fecaluria. A CT scan revealed an enterovesicular fistula and a colonoscopy showed an inflamed, ulcerated terminal ileum. Biopsies confirmed the diagnosis of Crohn’s disease. He was treated with oral prednisone and started on mesalamine. Subsequently, he was hospitalized on multiple occasions with recurrent small bowel obstructions involving ten cm of the terminal ileum. He again was treated with oral prednisone but continued to be symptomatic. On presentation the patient complained of abdominal pain, bloating, anorexia with 15-pound weight loss and four to ten bowel movements per day. He denied current pneumaturia or fecaluria. He admitted smoking one pack per day. As the patient had complicated Crohn’s disease unresponsive to treatment, he underwent laparoscopic resection of 33 cm of ileum and 5 cm of cecum with an ileocolonic anastomosis. Post-operatively, the question arose as to whether medical treatment was indicated to reduce the frequency of postsurgical relapse.

**Postoperative Relapse**

After ileocolonic resection, Crohn’s disease typically recurs at the site of resection and often extends proximally. In up to 93 percent of cases, recurrent endoscopic lesions occur in the neoterminal ileum at 1 year, and up to 68 percent of patients experience symptomatic relapse within three years. The risks of reoperation range from 18-38% at five years, 36-57% at ten years and 48-71% at 20 years. Smoking cessation is essential since it increases the probability of disease reactivation and further surgical intervention.

Given the high likelihood of recurrent disease and repeat surgery, much attention and research has focused on prophylactic postoperative therapy. There are currently no guidelines concerning postoperative maintenance therapy in Crohn’s disease and considerable uncertainty remains as to the efficacy of such treatment. Potential treatment options include probiotics, corticosteroids, budesonide, nitroimidazole antibiotics (metronidazole and ornidazole), immunomodulators (Azathioprine/6-MP) and infliximab.

Probiotics and conventional steroids have no role in postoperative prophylaxis. A randomized controlled trial (RCT) with probiotic therapy using lactobacillus given for one year in 45 patients did not alter either the clinical or endoscopic recurrence rate, or the severity of endoscopic lesions compared to placebo. Similarly, two RCT’s investigating budesonide 3 mg/day and 6 mg/day failed to show significant difference in preventing endoscopic or clinical relapse at one year.

As fecal bacteria are believed to play a role in the pathogenesis of recurrent disease, nitroimidazole antibiotics have been studied to determine if inflammation can be modulated to prevent new lesions. One RCT comparing metronidazole 20 mg/kg with placebo for 3 months in 60 patients showed no significant differences over three years. More promising results were found using ornidazole, a drug not available in the USA. Eighty patients were given ornidazole 1g/d or placebo for one year. There was a statistically significant decrease in both endoscopic (53.6 vs. 79%, p=0.037) and clinical recurrence (7.9 vs. 37.5%, p=0.0046) at 12 months in patients taking ornidazole. However, these differences disappeared at two and three years and there was a significant drop out rate due to side effects in the ornidazole group.

The largest number of trials have involved mesalamine. There have been four placebo controlled trials and one meta-analysis. The trial designs were heterogeneous using variable dosing regimens, interval between surgery and start of therapy, and duration of follow-up. Although the

*continued on page six*
**Crohn’s Disease** continued from page five

meta-analysis showed a trend favoring mesalamine, all study confidence intervals crossed zero except for the one which had the least rigorous study design.

There have been few studies of immunosuppressive therapy. One RCT randomized 131 patients to 6-MP 50 mg/day, mesalamine 3 g/d, or placebo for two years. 6-MP was superior to placebo and mesalamine in preventing clinical recurrence at two years (50%, 58% and 77% for 6-MP mesalamine and placebo respectively, p=0.045).

Another open-label study involved 142 patients who were randomized to either mesalamine 3 g/d or azathioprine 2 mg/kg for two years. As clinical and surgical relapse rates at two years were similar in both groups, the authors concluded that azathioprine is not superior to mesalamine in preventing clinical relapse after surgery.

**Summary:** No guidelines exist for postoperative maintenance therapy in Crohn’s disease. No benefits have been shown for probiotics, budesonide or mesalamine. There are limited data concerning immunosuppressive therapy (azathioprine or 6-MP), but a recent study shows a trend toward benefit over placebo. There may be a short-term benefit with ornidazole but not metronidazole.

There are currently no trials of infliximab as prophylaxis in postoperative Crohn’s disease. Dr. Miguel Regueiro is principal investigator of an ongoing IRB-approved study at UPMC evaluating infliximab for the prevention of recurrent Crohn’s disease after surgery. Our patient agreed to enroll in the study.

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**GI Reimbursements** continued from page three

In an effort to avert the proposed cuts in the MPFS, bills regarding the *Preserving Patient Access to Physicians Act* have been introduced into the House of Representatives (H.R.2356) and Senate (S.1081). These bills would replace the MPFS’s SGR calculation with a fee schedule reflecting changes in cost provision (The Medicare Economic Index). This cost provision calculation is approved by the Medicare Payment Advisory Commission (MedPAC), which is composed primarily of physicians.

Physician support for these items of legislation is vital for all physicians as a group and for gastroenterologists in particular. The importance of political activism on the part of physicians has never been greater.

### Table 1: Impact of Revenue Changes Derived from Simple Colonoscopy

<table>
<thead>
<tr>
<th>Year</th>
<th>RVU</th>
<th>RVU (facility based)</th>
<th>Proposed RVU</th>
<th>Proposed RVU (facility based)</th>
</tr>
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<tbody>
<tr>
<td>2005</td>
<td>37.90</td>
<td>5.46</td>
<td>36.27</td>
<td>5.00</td>
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</table>

<table>
<thead>
<tr>
<th>2005 $ from 1,000 colonoscopies:</th>
<th>Proposed 2007 $ from 1,000 colonoscopies:</th>
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<tbody>
<tr>
<td>1,000 x 37.90 x 5.46 = 206,930</td>
<td>1,000 x 36.27 x 5.00 = 181,350</td>
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Dr. Kisloff is Clinical Assistant Professor of Medicine and serves as the Director of Clinical Services and Director of the Digestive Disorders Center for the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition. Dr. Kisloff also serves on the American Gastroenterological Association’s Clinical Practice and Economics Committee.
Clinical Investigator: A Pitt Fellowship Track with Many Options
by Klaus Bielefeldt, MD, PhD

About 50 years after Watson and Crick unraveled the structure of DNA, the entire human genome has been decoded. Abnormalities in single or multiple genes can lead to diseases, which—at least in some cases—may be effectively treated by drugs targeting the very molecules these genes encode. As physicians, we have the opportunity to apply the growing body of new scientific insight in clinical practice. The required integration of basic and clinical science requires in depth exposure to both facets of medicine, and we are proud to share our University’s wealth of information and experience with gastroenterology fellows.

At the University of Pittsburgh, we are able to create an outstanding learning environment that combines clinical expertise and scientific investigation in pancreatic diseases, inflammatory bowel disease and functional disorders of the gastrointestinal tract. As we are trying to identify and train the next generation of investigators, we combine additional effort and resources to develop educational opportunities for interested fellows. In collaboration with the other University divisions and departments, we now offer an intensive program that provides in depth training in epidemiology, study design, statistics, and research ethics. The National Institutes of Health recently recognized the academic accomplishments of our division, awarding us a highly competitive grant to train future physicians who want to become clinical investigators. Several of our recent and current fellows took advantage of this opportunity, studying genetic factors that may predispose to more severe forms of acute pancreatitis, sensory mechanisms that potentially contribute to prolonged postoperative ileus, the role of programmed cell death in the development of hepatocellular neoplasms and the regulation of adaptive immunity in patients with inflammatory bowel disease.

The experience in the laboratory and the challenge of solving clinically relevant questions have sparked ongoing interest in these trainees, who will continue to pursue careers as clinical investigators.

Dr. Bielefeldt is associate professor of medicine and is the director of the Neurogastroenterology & Motility Center for the University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition.

Gastroenterology, Hepatology and Nutrition T-32 Training Grant: Basic Research in a Clinical Department
by Brian M. Davis, PhD

Clinical academic units like the Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh are in a unique position to contribute to the welfare of the general population in two ways: 1) through direct intervention in the disease process of their patients; and 2) by contributing to research concerning the basis of those diseases. Six PhD scientists complement the clinical mission of this Division, and the result is an exciting synergy between clinicians and basic science researchers which has accelerated research in gastrointestinal diseases.

One example of this collaboration is the recently funded NIH T-32 training grant. This grant was awarded to the University of Pittsburgh for its recognized research program quality and its ability to train young investigators. This grant enables fellows to think about the impact of basic science studies on clinical problems and how basic science can be used to identify and treat disease mechanisms. NIH realizes that the most exciting basic research will not reach its full potential if not brought into the clinic.

Gastroenterology fellow Kenneth Fasanella, MD is currently working with Julie Christianson, PhD, an expert anatomist, in my laboratory to identify the distribution of a calcium channel that has been linked to chronic pancreatitis pain. Dr. David Whitcomb has identified a single nucleotide polymorphism (SNP) in the DNA sequence of this channel that appears to predict the intensity of this pain. Drs. Fasanella and Christianson are working together to identify the neuronal components that express this channel and the role of these components in chronic pain.

The faculty participating in the T-32 program are widely known experts in many research fields including cellular and molecular basis of motility dysfunction, molecular/genetic basis of inflammatory bowel diseases, genetics of pancreatic disease and visceral pain. By combining such diversity of experience with the UPMC huge patient database, fellows have the opportunity to not only treat disease, but to develop the next generation of therapies to realize the promise of molecular medicine.

Dr. Davis is associate professor of medicine with the Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh.
We are proud to recognize the new appointments of the following 2005 University of Pittsburgh Gastroenterology Fellowship Program graduates and welcome them as colleagues:

<table>
<thead>
<tr>
<th>Fellow Name</th>
<th>Current Institution/Practice</th>
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<tbody>
<tr>
<td>Mehul Lalani, MD</td>
<td>Private Practice in Lancaster, PA (Regional Gastroenterology Associates of Lancaster)</td>
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<tr>
<td>Neeraj Kaushik, MD</td>
<td>Assistant Professor – University of Pittsburgh Medical Center</td>
</tr>
<tr>
<td>Georgios Papachristou, MD</td>
<td>Advanced GI Fellowship (4th year) in Endoscopic Ultrasound (EUS) – Mayo Clinic, Rochester, MN</td>
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<tr>
<td>Jennifer Curtis Radin, MD</td>
<td>Private Practice in Cheshire, CT</td>
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<tr>
<td>Rupam Sharan, MD</td>
<td>Private Practice in Monroeville, PA</td>
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New Fellows in University of Pittsburgh Division of Gastroenterology, Hepatology and Nutrition training program for the 2005-2006 year include:

<table>
<thead>
<tr>
<th>Name</th>
<th>Fellowship</th>
<th>Medical School/Residency</th>
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<tbody>
<tr>
<td>Scott Cooper, MD</td>
<td>Gastroenterology</td>
<td>University of Pennsylvania</td>
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<tr>
<td>Mark Lazarev, MD</td>
<td>Gastroenterology</td>
<td>University of Pittsburgh</td>
</tr>
<tr>
<td>John Lyons, MD</td>
<td>Gastroenterology</td>
<td>University of Southern California</td>
</tr>
<tr>
<td>James Park, MD</td>
<td>Gastroenterology</td>
<td>State University of New York – Buffalo</td>
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<tr>
<td></td>
<td></td>
<td>New York University Medical Center</td>
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<tr>
<td>Raja Chadalavada, MD</td>
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Raja Chadalavada, MD is also completing a one-year Hepatology Fellowship this year.

What Is This?

A 30-year-old white male was admitted with shortness of breath. Four weeks prior, he was diagnosed with advanced AIDS and was started on highly active anti-retroviral therapy (HAART). Admission hemoglobin was 9.3 g/dL, as compared to a baseline of 12.1 g/dL several months earlier. He had guaiac positive stool and was having three to four loose, watery bowel movements per day. The following lesions were seen on upper endoscopy and skin.

Compare your answer to Dr. Mullady’s answer on page six.