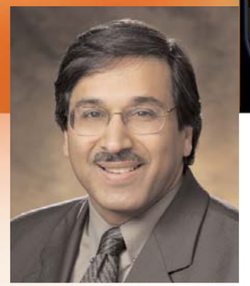

CHIEF'S CORNER

Anil K. Rustgi, MD
T. Grier Miller Professor of Medicine and Genetics, Chief, Division of Gastroenterology

The gastroenterology team at the University of Pennsylvania School of Medicine and Penn Medicine is nationally recognized for clinical research and superlative care for its patients. I am pleased to announce the following recent honors and awards accorded our faculty, as well as additions to our team.

JOHN DRAGANESCU, MD, has joined the Penn Division of Gastroenterology. A graduate of the University of Pennsylvania School of Medicine, Dr. Draganescu completed a fellowship in gastroenterology at the Hospital of the University of Pennsylvania. He sees patients at Penn Medicine at Radnor, where he treats a wide array of diseases and disorders of the esophagus, stomach, intestine, colon and pancreas.

JAMES LEWIS, MD, MSCE has been elected to the American Society for Clinical Investigation (ASCI). Comprised of physician scientists devoted to translational medicine and the advancement of clinical practice, ASCI is one of the nation's oldest and most respected medical honor societies.

K. RAJENDER REDDY, MD, has been inducted as an honorary fellow in the Royal College of Physicians (RCP) in London. Founded by Henry VIII in 1518, the RCP serves medical professionals throughout the United Kingdom.

OCTAVIA PICKETT-BLAKEY, MD, will join the Penn Division of Gastroenterology in the fall of 2010. Dr. Pickett-Blakely is a graduate of the University of Maryland School of Medicine and completed a fellowship in gastroenterology at Johns Hopkins Hospital. Her clinical interests include obesity, nutrition and small bowel disorders. She will see patients at the Perelman Center for Advanced Medicine.

Penn Medicine
3600 Market Street, Suite 210
Philadelphia, PA 19104

GASTROENTEROLOGY NEWSLETTER 2010

Penn Digestive & Liver Center
Penn Medicine

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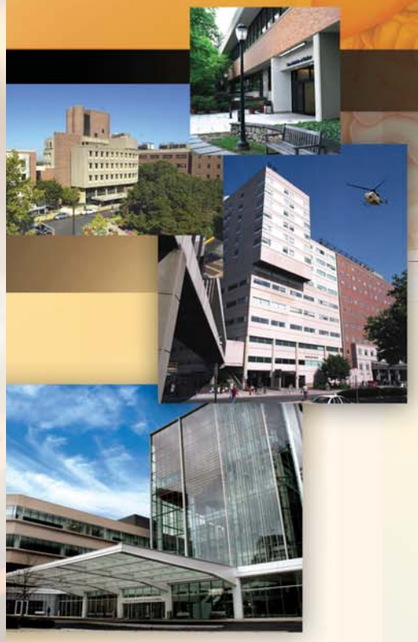
CLINICAL REPORTS



GASTROENTEROLOGY NEWSLETTER

AN INTERVIEW

with Gary W. Falk, MD, MS

Gary W. Falk, MD, MS

Gary W. Falk, MD, MS, joined the staff of the Division of Gastroenterology at Penn Medicine in January 2010 after almost 25 years at the Cleveland Clinic, where he was Director of the Center for Esophageal and Swallowing Disorders. A graduate of the University of Rochester School of Medicine, Dr. Falk is nationally and internationally recognized for treating esophageal diseases, including achalasia, eosinophilic esophagitis, gastroesophageal reflux disease, swallowing disorders and Barrett's esophagus. He has served as president of the American Society for Gastrointestinal Endoscopy and is a member of several national societies. He has published extensively in leading journals and his research has received NIH funding. Dr. Falk was interviewed in his office at the Hospital of the University of Pennsylvania, near the Ruth and Raymond Perelman Center for Advanced Medicine, where he currently sees patients.

† *Before we discuss your experience in research, can you provide a brief overview of your background in clinical practice?*

Certainly. I had a tertiary care referral practice in Cleveland for both esophageal and foregut diseases that drew patients locally, regionally and nationally. My goals were to provide state-of-the-art expertise in esophageal diseases in a collaborative and interdisciplinary fashion. Along the way, I had the opportunity to develop new clinical skills in areas such as high resolution manometry, advanced endoscopic imaging and endoscopic interventions for Barrett's esophagus that have represented paradigm shifts in the care of patients with esophageal diseases.

† *What was the genesis of your interest in clinical research?*

I learned from my mentor, Joel Richter, MD, (former Chief of Gastroenterology at Cleveland Clinic and now Chair of Medicine at Temple University), how questions coming from clinical care are a fertile source of hypothesis driven clinical research. Over the course of 15 years, I became involved in thematic clinical research in Barrett's esophagus, gastroesophageal reflux disease, esophageal motility disorders, advanced esophageal imaging and therapeutics, eosinophilic esophagitis—and importantly, the early detection and prevention of esophageal cancer. These investigations ultimately resulted in participation in a number of NIH- and nonNIH-funded studies, as well as publications on the significance of high-grade dysplasia (HGD) in Barrett's esophagus and other subjects. I have long been interested in HGD, and have examined the disorder from a variety of perspectives, including biopsy forceps yield, findings of unsuspected cancer at esophagectomy, and the use of cytologic sampling as an alternative to biopsy-based surveillance. An investigation of the development of the concept of cytology

CONTINUED ON PAGE 2

LOCATIONS

The Perelman Center for Advanced Medicine
3400 Civic Center Boulevard
Philadelphia, PA 19104
Phone: 215.349.8222

Penn Presbyterian Medical Center
38th and Market Streets
218 Wright-Saunders Building
Philadelphia, PA 19104
Phone: 215.662.8900

Penn Medicine at Radnor
250 King of Prussia Road | Module B
Radnor, PA 19087
Phone: 610.902.1500

"The research environment at Penn offers many opportunities to pursue translational research in Barrett's esophagus and esophageal cancer." —Gary W. Falk, MD, MS

CONTINUED FROM PAGE 1

specimens as a platform for molecular-based biomarker studies led to collaborations with the Mayo Clinic, where investigators have advanced this conceptual model further. Other studies in Barrett's esophagus focused on epidemiologic observations related to the role of *Helicobacter pylori* in the disease along with issues of age and gender in the development of cancer.

How has the way you pursue clinical research changed over the course of your career?

As my work in Barrett's esophagus progressed, it became clear to me that single-center studies were no longer sufficient to truly advance the field. This led me to seek out collaborations with other centers to examine areas such as familial risk, molecular imaging paradigms, chemoprevention, radio-frequency ablation and endomicroscopy. Along the way, I was fortunate enough to receive a career development grant from the Cleveland Clinic in 2002 that allowed me to obtain additional training in clinical research skills leading to a Master of Science degree in Clinical Research. I currently chair the ongoing NCI multicenter chemoprevention study examining the role of high-dose proton pump inhibitor therapy in conjunction with aspirin in Barrett's esophagus. Recently, translational research studies in collaboration with basic scientists in immunology and smooth muscle physiology have commenced in order to study the role of inflammatory mediators in eosinophilic esophagitis.

"Here, I will continue to focus on early detection, prevention and treatment of Barrett's-associated neoplasia, and the establishment of a tissue biorepository as a resource for future studies…."

—Gary W. Falk, MD, MS

Was there a link between your search for collaborative environments at this time and your subsequent service at the national level?

My service at the national level exposed me to the diverse viewpoints of individuals from many different institutions, and allowed me to develop a "30,000-foot view," so important in developing strategies to adapt to the many changes in the field of medicine that have been a constant in my entire career. The single most satisfying part of this service was my year as president of the American Society of Gastrointestinal Endoscopy, a true once-in-a-lifetime experience that allowed me to provide national level leadership and strategic vision to the field. That year provided me the opportunity to interact with colleagues throughout the world, which further broadened my perspectives.

What, then, are your near- and long-term objectives at Penn Medicine?

As I transition to the Penn Division of Gastroenterology, I'm excited about the possibility of leading a multidisciplinary center of excellence in esophageal diseases and enhancing its recognition regionally, nationally and internationally. The research environment at Penn offers many opportunities to pursue translational research in Barrett's esophagus and esophageal cancer. I look to develop synergies here with the individuals already in place to continue to evaluate strategies for early detection and prevention of esophageal cancer, and to that end, I hope to provide the clinical bridge. I will be involved, as well, with researchers at the Children's Hospital of Philadelphia to address a variety of issues in the fascinating relatively new disease, eosinophilic esophagitis. Penn is uniquely positioned by virtue of its type II Joint Center in Digestive, Liver and Pancreatic Medicine to confront many of the key unresolved issues in eosinophilic esophagitis, especially the question of what happens to children with this disease when they become adults. The group at CHOP has already pedigreed a large pediatric population with this disease that will help address this question.

Among my long-term objectives are multi-disciplinary studies of Barrett's esophagus. Here, I will continue to focus on early detection, prevention and treatment of Barrett's-associated neoplasia, and the establishment of a tissue biorepository as a resource for future studies of potential biomarkers of increased risk for the development of cancer in Barrett's patients. I've brought several trials with me to Penn that should benefit from the research-enriched and interdisciplinary environment here. These include: an NCI-supported study on chemoprevention of esophageal cancer; a multicenter, NIDDK-supported study seeking to define the epidemiology and genetics of Barrett's esophagus and adenocarcinoma; and a multicenter trial examining a novel new imaging technique, confocal endomicroscopy for virtual optical biopsies in Barrett's esophagus.

Will you be seeing patients at Penn, as well?

Of course. Clinical practice is among the most gratifying parts of what I do.

RESOURCES

- Penn GI division patient website: **PennMedicine.org/GI**
- Penn GI division academic website: **www.med.upenn.edu/gastro**
- Penn Abramson Cancer Center website: **PennMedicine.org/abramson**
- Penn cancer information: **www.oncolink.org**
- NCI program project on esophageal cancer at Penn: **www.med.upenn.edu/gastro/nci**

THE GI PHYSIOLOGY *and* MOTILITY LABORATORY

The GI Physiology and Motility Laboratory at Penn was developed to provide ancillary diagnostic procedures unrelated to endoscopy and biopsy or other physical investigations for specific diseases of the upper gastrointestinal tract, including achalasia, *Helicobacter pylori* gastritis, gastroesophageal reflux disease, hypersecretory states and disaccharide intolerance. The laboratory is among the few in the region to specialize in these advanced diagnostic procedures that, alone or in combination, can be used to create individualized and effective patient treatment plans. Patients can be seen in consultation before being scheduled for studies by the GI consultant physicians, but open-access scheduling is also available.

The tests currently available at the GI Physiology and Motility Laboratory at Penn, and their respective uses, include:

1] AMBULATORY pH TESTING — currently the best method to diagnose gastreoesophageal reflux disease (GERD) these tests are used to demonstrate abnormal esophageal acid exposure as well as the correlation between episodes of acid exposure and symptoms. Traditional pHmetry involves passage of a transnasal catheter connected to an external monitoring device that records the pH in the esophagus and stomach over a 24-hour period. Today, pHmetry can be accomplished with improved catheter-based tests that also measure impedence, or with catheterless (wireless) tests that are more comfortable.

a) **BRAVO™ RADIOTELEMETRY ESOPHAGEAL pH TESTING** — used to measure pH in the esophagus, the Bravo system transmits information from a capsule temporarily attached to the wall of the esophagus; the capsule transmits readings to a receiver worn on the patient's belt or waistband. This technique allows prolonged (48 hr) studies and even permits testing OFF and then ON therapy in a sequential manner. Bravo is better tolerated than catheter testing and may therefore provide better outcomes. Bravo testing cannot identify non-acidic or weakly acidic reflux episodes.

b) **ESOPHAGEAL pH/IMPEDANCE TESTING** — performed to detect reflux of acidic or non-acidic material in the upper GI tract, impedance testing measures alterations in electrical current. When combined with traditional ambulatory pH testing, the resultant impedance/ pHmetry allows the identification of acid and weakly acidic (or even alkaline) reflux events. This study is ideally suited for patients with persistent symptoms despite the presence of antisecretory therapy and is commonly done ON therapy.

2] GASTRIC ANALYSIS — performed by very few other medical centers in the region, gastric analysis is used to evaluate gastric secretory function and to identify Zollinger-Ellison syndrome. Studies are commonly performed in patients with hypergastrinemia to distinguish achlorhydria (appropriate hypergastrinemia commonly due to medication therapy or pernicioua anemia) from Zollinger-Ellison syndrome (inappropriate hypergastrinemia).

3] HYDROGEN BREATH TEST — used to measure hydrogen levels in the breath to identify bacterial overgrowth (lactulose testing), as well as for disaccharidase intolerance (lactose, sucrose or fructose). A recent advance in this area is the inclusion of methane testing together with hydrogen testing which improves the accuracy of these studies.

4] MANOMETRY — the gold standard for the evaluation of esophageal motor activity and motility, manometry measures the strength of esophageal contractions and is used to investigate dysphagia and particularly to diagnose achalasia. A new procedure, high-resolution esophageal manometry (HRM), measures pressure events simultaneously along the entire length of the esophagus and is both faster and more accurate than standard manometry. According to David Metz, MD, of the Penn Gastroenterology Division, HRM has greatly improved the ability of gastroenterologists to diagnose and treat patients with achalasia. With the new Chicago Classification, Dr. Metz adds, the test now has prognostic value in achalasia patients because it can identify patients who are likely to do well with surgery. HRM has been further advanced recently by being combined with impedance testing to permit more accurate assessment of bolus transit (movement of swallowed contents) in patients with dysphagia (difficulty swallowing) who may have abnormalities other than achalasia (*e.g.*, ineffective motility which is commonly associated with GERD).

5] UREA BREATH TESTING — an accurate non-invasive test for the presence of *H. pylori* infection, this test involves the detection of gastric urease—the enzyme used by *H. pylori* to metabolize urea—in the patient's breath. Since humans do not normally metabolize urea, the test easily discriminates between infected and uninfected individuals according to the presence or absence of urease breakdown products in expired breath.

The members of the GI Physiology and Motility Laboratory include:
David Metz, MD; **Gary Falk, MD, MS** (co-directors);
Yu-Xiao Yang, MD, MSCE and **Octavia Pickett-Blakely, MD** (Fall, 2010).

"High-resolution esophageal manometry has greatly improved the ability of gastroenterologists to diagnose and treat patients with achalasia, and has prognostic value in some patients." – David Metz, MD, Penn Gastroenterology Division