

GASTROENTEROLOGY UPDATE

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FALL 2016



From the Division of Gastroenterology, Hepatology, and Nutrition



Message from the Chief

Dear Colleagues,

It is my pleasure to share with you recent news, events, and research from my colleagues in the Division of Gastroenterology, Hepatology, and Nutrition. In this issue we are highlighting three centers of excellence — Inflammatory Bowel Disease, Neurogastroenterology, and Gastrointestinal Cancer, and specifically colorectal cancer.

The development of a medical home program for IBD patients — UPMC Total Care-IBD — led by **Miguel Rugeiro, MD**, and co-director **Eva Szigethy, MD**, is the first such specialty program in the country. Expanding upon our high-volume, multidisciplinary care model, the medical home is reshaping the future of how IBD patients will be cared for, by addressing the full spectrum of biopsychosocial needs for complex, chronic patient care. In just its first full year of operation the program is demonstrating success.

David Levinthal, MD, PhD, along with colleagues in the Department of Neurobiology, have published new findings on the neural connections between the brain and the adrenal medulla. This groundbreaking research casts new light on pathways between the brain and the viscera, and how problems such as abdominal pain and nausea — in the absence of a physiological cause, may originate in the brain and conduct along heretofore previously unknown routes. More details of Dr. Levinthal's research follow in the pages below.

I am pleased to share findings of my colleagues and myself clarifying the risk of colorectal cancer in patients with a family history of colorectal cancer. In the gastrointestinal cancer center of excellence, we are deeply involved in biomarker research, looking for markers for early diagnosis and prognosis of cancer, as well as pursuing novel immuno-prevention studies, topics we hope to report on in the coming years.

Finally, for those of you who have attended in the past, we will once again host our *PancreasFest* conference in 2017 as well as our ongoing Gut Club speaker's series, details of both which can be found in this update.

I welcome comments and questions from our colleagues across the country, and I look forward to hearing from you in the future and visiting with you at our events.

Kind regards,

Robert E. Schoen, MD, MPH

Professor of Medicine and Epidemiology

Interim Chief, Division of Gastroenterology, Hepatology, and Nutrition

University of Pittsburgh School of Medicine

Total Care-IBD Program Shows Significant Results in First Year of Operation



The UPMC Total Care-IBD program is the first-of-its-kind, and currently the only subspecialty, patient-centered medical home for inflammatory bowel disease in the United States, and has shown significant and promising influence on patient care during its first year of operation. **Miguel Regueiro, MD**, (pictured at left) the IBD clinical medical director for the Division of Gastroenterology, Hepatology, and Nutrition, is the co-director of Total Care-IBD alongside **Eva Szigethy, MD, PhD**, founder and director of the Division's Visceral Inflammation and Pain Center (VIP). The Total Care-IBD program is a multi-aspect collaboration between the Division and the UPMC Health Plan to reimagine, and implement, a new model of care for individuals with chronic inflammatory bowel diseases including Crohn's disease, ulcerative colitis, and similar conditions.

Launched in 2015, Total Care-IBD is designed to take a team approach to whole-person care for this group of patients. This entails symptom and disease management of the underlying condition, taking into account the whole person's health and well-being, and rigorously addressing a patient's psychological and social or environmental factors that may contribute to acute changes in condition or even long-term symptom presentation. The program addresses and seeks to improve the patient experience, improve quality of care and patient quality of life, while reducing utilization and costs through targeted, patient-centric interventions at the same time.

In October, 2016, at the annual conference of the American College of Gastroenterology, Dr. Regueiro and colleagues presented recent findings and results from the first year of the Total-Care IBD program's operation in both plenary¹ and poster sessions.² The plenary session presentation titled "Decreased Emergency Room Utilization and Hospitalizations, and Improved Quality of Life in the First Year of an Inflammatory Bowel Disease (IBD) Patient Centered Medical Home (PCMH)" discussed key findings from year one of the program. Among the goals for the first year of the program was a marked reduction in emergency room utilization and hospitalizations, and improvements in

quality of life for 300 enrolled patients. The reduction goals at the outset for ED utilization and hospitalizations was 2% across the patient cohort of 308 (290 remained in the study cohort at the end of the first year). In the year prior to enrollment in the program, patients accounted for 322 ED visits and 160 hospitalizations. At the end of year one in the Total Care-IBD program, enrolled patients accounted for 155 ED visits, and 75 hospitalizations — a 51.9% and 53.1% reduction respectively — far exceeding the initial 2% goals at the outset.

With respect to the quality of life (QoL) measures,² patients with SIBDQ scores of < 50 (poor) and < 40 (very poor) at the time of their last visit prior to enrollment were analyzed with the hope that those individuals with the most impaired QoL would significantly improve through the coordinated, targeted, multi-faceted biopsychosocial interventions of the program. At the end of year one, those patients with SIBDQ scores < 40 (mean score for cohort = 41.3) saw that figure change to 43.9, after only three visits (the initial plus two follow up visits). Similarly, patient complexity, disease activity, and psychosocial impairment (depression) showed positive changes at visit three. (Table 1)

Continued on Page 6

Table 1. **Mean Clinical Scores at Baseline and Visit 3***

Measure	N	Baseline (B)		Visit 3 (V3)		Chg: B-V3		p-Value
		Mean	SD	Mean	SD	Mean	SD	
Complexity score: Overall	72	31.9	11.0	29.0	10.2	3.0	4.9	< 0.0001
Harvey Bradshaw Index (HBI)	70	7.7	7.6	6.1	8.9	1.6	5.3	0.01
PHQ9 depression score	62	9.8	7.5	8.1	6.0	1.7	4.6	0.005
SIBDQ score	70	41.3	12.5	43.9	13.2	-2.6	10.4	0.04

*The median number of days between the baseline and Visit assessment was 133 (interquartile range = 74 to 184; minimum = 17, maximum = 343).

Mapping the Neural Pathways that Connect Brain and Body



Groundbreaking new research by **David J. Levinthal, MD, PhD**, (pictured at left) director of the Neurogastroenterology and Motility Center, along with colleagues **Richard P. Dum, PhD**, research associate professor, and **Peter L. Strick, PhD**, distinguished professor and chair of the Department of Neurobiology, has for the first time identified the specific neural pathways connecting an area of the brain — the cerebral cortex — with an internal organ of the body — the adrenal medulla. Their research findings,¹ published in August 2016 by the Proceedings of the National Academy of Sciences of the United States of America under the title “Motor, Cognitive, and Affective Areas of the Cerebral Cortex Influence the Adrenal Medulla”, have profound implications for understanding the “anatomical basis for psychosomatic illness where mental states can alter organ function.”

Psychosomatic illness, its understanding and acceptance, or lack thereof, has largely been due to an unclear picture of what, if any, direct linkages existed along the body's neural networks from the brain through the central and peripheral nervous systems to specific organs.

Using mapping techniques developed by Dr. Strick, a highly purified rabies virus was injected into the adrenal medulla of non-human primates. As the rabies virus advances through the neural networks in the host in a purely retrograde direction and in a time-dependent manner, the transneuronal transport of the virus from the adrenal medulla allowed the researchers to ultimately visualize infected neurons in the cerebral cortex in several areas known to be involved in motor control, cognition, and mood. For the first time, this research has demonstrated the physical linkages between the brain and an organ, and exactly which areas of the brain and which nerve pathways are connected and able to influence organ function.

Dr. Levinthal points out several key findings and implications of the research, for the field of gastroenterology specifically, but also for the broader understanding of the mind/body connections. For patients with IBS or functional dyspepsia and the absence of any clear physiological pathology, such things as abdominal pain or nausea may really have origins in the brain. Multiple areas of the brain control or have an influence over an organ's function. In the case of the adrenal medulla, the cortical motor areas of the frontal lobe and somatosensory cortex are very involved in control of the organ, as well as areas of the prefrontal cortex associated with cognitive and affect control. “This is fascinating because not only is organ regulation linked to movement, but the motor cortical findings, from a neuroscience perspective, really challenge the view of what the motor areas of the brain even are. Prior to this research, it was thought these areas only controlled the muscles, but now I think we have to acknowledge that these areas may gain influence over the entire body,” says Dr. Levinthal. Movement matters; it has influence over organ function. While the specifics of this concept are not known at this point — for example what kinds of movement, how much, how frequently, and which neurons are

responsible and in what manner — the very fact that there is a connection is a striking finding of the research that should lead to new avenues of investigation far into the future.

Similarly, the finding that certain cortical regions involved with cognitive and affective control are linked with adrenal function puts into play and clarifies the physical, neural connections that conspire to allow thoughts, feelings, moods, and other mental states, both positive and negative, to exert some degree of influence on the organ in question.

Dr. Levinthal is a gastroenterologist and neuroscientist with specialties in functional bowel and motility conditions of the GI tract. He is interested in how various cognitive and emotional states can influence GI symptoms, the brain-gut axis, and the neural pathways through which thoughts, feelings, emotion, motion, and expectation can influence the GI tract – stomach contraction, acid production, colon motility, for example. Having the neural mappings of brain/organ connections may, in the future, allow for very targeted therapies focused solely on the specific pathways and functional determinants in question. “I think our work is providing a roadmap for future research and the development of therapies that could boost existing treatments, or perhaps even lead to completely novel interventions,” says Dr. Levinthal.

Dr. Levinthal and his research colleagues are continuing their studies with other organs to map their neural connections and determine which areas of the brain have control over the organs in question, and they expect to publish their findings over the next several years. Their foundational work in mapping brain/organ neural circuitry may one day go on to change not only the understanding and treatment for gastroenterological conditions, but those of the heart, lung, kidney, liver, and the entire body.

Reference

1. Dum RP, Levinthal DJ, Strick PL. Motor, Cognitive, and Affective Areas of the Cerebral Cortex Influence the Adrenal Medulla. PNAS. 2016; 113:35 9922-9927.

For patients with IBS or functional dyspepsia and the absence of any clear physiological pathology, such things as abdominal pain or nausea may really have origins in the brain.

IBD LIVE: Connecting Clinicians Across the Country



What began in 2009 as an internal collaborative effort between clinicians at two geographically separated UPMC hospitals (UPMC Presbyterian and Children's Hospital of Pittsburgh of UPMC) has since grown into a multi-institutional, interdisciplinary educational initiative with more than 30 institutions collaborating in an ongoing series of inflammatory bowel disease case reports and commentary. Designed to bring together clinicians from across the country in weekly discussions via video conference and quarterly live webcasts of case reports, IBD LIVE¹ was the idea of **Miguel Regueiro, MD** (pictured at left) IBD clinical medical director, and co-director of the UPMC Total Care-IBD patient-centered medical home, who continues to serve as the driving force of the education series, uniting disciplines in the discussion and providing ongoing education for clinicians evaluating and treating the complex needs of inflammatory bowel disease patients.

New cases are discussed on a weekly basis, every Thursday from 7 to 8 a.m. with a subset of participating institutions via video conference. These groups are typically multidisciplinary, involving various disciplines that were integral to the patient case under discussion.

On a quarterly basis, IBD LIVE is webcast to all participating institutions in partnership with the Crohn's & Colitis Foundation of America. Two cases are typically presented by members from one of the institutions, and a moderator is responsible for facilitating the discussion during the video conference.

"At the beginning, I did not foresee or anticipate how IBD LIVE has grown and become a recognized initiative all over the country. I've started to receive interest now from institutions in South America and Europe who

want to participate, and that is greatly encouraging to know that this initiative continues to grow and bring together individuals from our discipline. So many individuals have been extremely helpful in making IBD LIVE a success — **Andrew Watson, MD** has provided his expertise and support, **Julia Greer, MD** is instrumental in writing up the case reports for publication — everyone involved has continued to devote their time and energy, ultimately in the service of education and patient care," says Dr. Regueiro.

Past webcasts are archived and can be viewed by visiting services.choruscall.com/links/UPMC/ibd. Recent cases available for viewing include:

- **20-year-old Female with Severe Esophageal Crohn's Disease** — Presented by *Heba Isdandar, MD* — Emory University
- **15-year-old Female with Severe Colitis** — Presented by *Sapana J. Shaw, MD* — Children's Hospital of Pittsburgh of UPMC
- **Diagnostic Dilemma in a Patient with IBD** — Presented by *Shova Subedi, MD* — Dartmouth-Hitchcock Medical Center

CME-accredited case reviews are published in the Inflammatory Bowel Disease Journal and can be found on the journal's website or by searching PubMed using the IBD LIVE entry.

Reference

1. Regueiro MD, Greer JB, Binion DG, Schraut WH, Goyal A, Keljo DJ, Cross RK, Williams ED, Herfarth HH, Siegel CA, Oikonomou I, Brand MH, Hartman DJ, Tublin ME, Davis PL, Baidoo L, Szigethy E, Watson AR on Behalf of the IBD LIVE Physician Group. The Inflammatory Bowel Disease Live Inter-institutional and Interdisciplinary Videoconference Education (IBD LIVE) Series. *Inflamm Bowel Dis*. 2014; 20: 1687-1695.

UPMC LIFE CHANGING MEDICINE
FOUNDATION OF AMERICA

IBD Live

Slides Submit Question Support

Toxoplasmosis: Risk of reactivation?

- **Infliximab**
 - Post-marketing reports in patients receiving infliximab through February 23, 2005
 - 7 cases of toxoplasmosis among 634,000 patients (compared to 295 for 1,000,000)
- 43 yo male receiving methotrexate 20 mg weekly and prednisone 10 mg a day for RA. Methotrexate was switched to leflunomide which was then later switched to infliximab 5mg/kg.
 - Treated with chloroquine 3 months after being on infliximab
 - Found to have Toxo IgM and PCR positive in CSF
- 30 yo female receiving methotrexate weekly, prednisone 10 mg a day with addition of leflunomide a year later, infliximab was added at 10mg/kg every 6 weeks.
 - Treated with sulfone azo-dye symptoms including seizures 6 months later
 - Negative for Toxo IgM and positive for IgG
- All patients had normal CD4 and CD8 counts and improved with treatment of Toxo

For full screen video, double-click on the video.

Topics:
Case 1: Diagnostic Dilemma in a patient with IBD
Case 2: Neutropenia with new onset IUC

Recorded: September 29, 2016

Presenters:
Shova Subedi, MD, Dartmouth-Hitchcock Medical Center
A Nisha Malhotra, MD, University of Maryland

Moderator:
Miguel D. Regueiro, MD, University of Pittsburgh

Technical Support: 412-658-1350

02/16 UPMC

Understanding Familial History and Colorectal Cancer Risk



Family history is a risk factor for colorectal cancer (CRC). The risk increases with the number of first degree relatives (FDR) affected (parents, siblings, or children), and with a younger onset of cancer in the affected relative. Approximately 5% to 10% of the United States population has at least one FDR with prior incidence of colorectal cancer. However, few studies have assessed how CRC risk changes as people age.

A large study recently published in the journal *Gastroenterology* by **Robert E. Schoen, MD, MPH**, (pictured above) along with colleagues from the National Cancer Institute is adding new evidence to the knowledge base. The paper, "Incidence and Mortality of Colorectal Cancer in Individuals With a Family History of Colorectal Cancer,"¹ analyzed a large data set from the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial of flexible sigmoidoscopy. Specifically, Dr. Schoen's study explores the effects of family history on CRC incidence and mortality risk in individuals over age 55, that is, in individuals who have already reached age 55 and have not been diagnosed with cancer.

Dr. Schoen's study evaluated data on 144,768 individuals — 14,961 (10.3%) of which had reported a family history of CRC at enrollment in the PLCO study. Within the entire study group, 2,090 (1.4%) individuals contracted CRC, and, of those, 273 (13.1%) had a family history of CRC. Of the 273 individuals with CRC with a family history, 71 (13.2%) died of the disease compared with 538 (25.7%) CRC deaths overall.

Statistical analysis shows that individuals with a family history of CRC in one FDR, had a 30% increased risk of CRC compared to individuals with no family history. Individuals with two or more first degree relatives with CRC were at greater risk — with a two-fold risk for CRC compared to those with no family history. Further, the study shows that for individuals over age 55 with a family history of CRC, the age at which their relative was affected was not associated with increased risk.

For Dr. Schoen, the study data points to a need to review and address current screening guidelines for older patients with a family history. He notes that those individuals with two first degree relatives with CRC are still candidates for more frequent screening,



but guidelines for patients with one FDR affected, as they get older, could be relaxed. In an editorial reply to Dr. Schoen's study, Doubeni and Fletcher² provided a concurring opinion on the need to assess and realign screening guidelines for individuals > 55 years of age with only one FDR with CRC. Addressing updated guidelines, as well as balancing them with patient understanding and expressed wishes for care will require diligence on multiple fronts. However, new screening guidelines could avoid costs and procedural risks without adversely affecting outcomes.

References

1. Schoen RE, Razzak A, Yu KJ, Berndt DI, Firl K, Riley TL, Pinsky PF. Incidence and Mortality of Colorectal Cancer in Individuals With a Family History of Colorectal Cancer. *Gastroenterology*. 2015; 149(6): 1438-1444.
2. Doubeni CA, Fletcher RH. Family History of Colorectal Cancer: It Is Time to Rethink Screening Recommendations. (Editorial). *Gastroenterology*. 2015; 149(6) 1321-1322.

Inaugural Sherman Prize Awarded to Eva Szigethy, MD, PhD



Eva Szigethy, MD, PhD, associate professor of psychiatry, medicine, and pediatrics, and a co-director of the UPMC Total Care-IBD program was awarded the inaugural Sherman Prize for Excellence in Crohn's and Colitis by the Bruce and Cynthia Sherman Charitable Foundation. The \$100,000 award, announced in September 2016, is given to health care professionals, researchers, advocates, and teachers who have demonstrated exceptional and pioneering work with inflammatory bowel diseases.

Along with co-directing the Total-Care IBD program, Dr. Szigethy also is the clinical director of the Visceral Inflammation & Pain Center, and director of the Children's Hospital of Pittsburgh of UPMC Medical Coping Clinic. Dr. Szigethy's research interests center on the application and study of cognitive behavioral therapy to improve outcomes for adult and pediatric gastroenterology patients, as well as interventions for chronic pain control. Her work in the UPMC-Total Care IBD program with co-director and IBD clinical medical director, **Miguel Regueiro, MD**, is reshaping every aspect of the approaches to, and long-term care of, patients with inflammatory bowel diseases.

Dr. Szigethy indicates that, "It was wonderful to receive this prestigious award, and an even greater honor is that the award recognized, and allows for further research in the area of the behavioral challenges of having inflammatory bowel disease (IBD)."

Dr. Szigethy plans on using the award funding to examine the genetic and phenotypic predictors of the neurobiological manifestations of IBD. "These patients

will be drawn from our Total Care-IBD program, an innovative project funded by the UPMC Health Plan to provide collaborative medical and behavioral care for patients in the GI clinic using a medical home health care delivery model. The Total Care Program uses a biopsychosocial approach to understand the overall complexity of disease burden and develop appropriate treatment pathways," says Dr. Szigethy.

"By understanding the etiology of symptoms such as pain, depression, anxiety and fatigue in a setting where treatment plans are well characterized, we can begin to develop empirically driven targeted treatments for patients with this lifelong disease."

To learn more about Dr. Szigethy and her work, visit the Division website at pitt.dom.edu/gi. For more information about the Sherman Prize and Foundation visit shermanprize.org. For more information about the UPMC Total Care-IBD program, please refer to the article in this edition of *Gastroenterology Update*.

Total Care-IBD Program *(Continued from Page 2)*

Year one results for the Total Care-IBD program far exceeded Dr. Regueiro and his colleague's expectations. The changes in patient quality of life, and reductions in ED visits and hospitalizations are directly related to the complex, total patient care philosophy of the program and its attention to each individual's medical, social, and psychological needs resulting from their chronic IBD condition. In the future, Dr. Regueiro and colleagues will analyze the cost reduction ramifications of the program and its interventions to understand the full financial impact the program is having on the patients and the health system as a whole.

References

1. Regueiro M, Hashash JG, McAnallen S, Ramalingam S, Perkins S, Manolis C, Kogan J, Watson A, Binion D, McGowan M, Anderson A, Click B, Bell-Temin H, Weaver E, Fultz J, Graziani M, Smith-Seiler D, Szigethy E. Decreased Emergency Room Utilization and Hospitalizations, and Improved Quality of Life in the First Year of an Inflammatory Bowel Disease (IBD) Patient Centered Medical Home (PCMH). Poster presented at plenary session of the 2016 American College of Gastroenterology Conference, Las Vegas, Nevada.
2. Hashash JG, Szigethy E, McAnallen S, Kip K, Ramalingam S, Perkins S, Manolis C, Kogan J, Watson A, Binion D, McGowan M, Anderson A, Click B, Bell-Temin H, Weaver E, Fultz J, Graziani M, Smith-Seiler D, and Regueiro M. Patient Centered Medical Home (PCMH) Care Rapidly Improves Inflammatory Bowel Disease (IBD) Quality of Life, Depression, Disease Activity and Disease Complexity. Poster presented 2016 American College of Gastroenterology Conference, Las Vegas, Nevada.

Save The Date: July 26-28, 2017

PancreasFest 2017

Pittsburgh, Pennsylvania

The Division of Gastroenterology, Hepatology, and Nutrition will once again host the annual *PancreasFest* in July 2017. This annual research and clinical conference is designed for gastroenterologists, surgeons, researchers, and interested medical professionals. Lectures and discussion groups will mix with investigative research meetings to further the multidisciplinary understanding and treatment of pancreatic diseases.



Pittsburgh Gut Club

The Pittsburgh Gut Club is a gastroenterology education and networking series designed to bring novel and relevant subspecialty advancements to the greater Pittsburgh region. All gastroenterologists, physicians, and allied health professionals are encouraged to attend. All events are from 6 to 8:15 pm at the University Club, 123 University Place, Pittsburgh, Pa.

Upcoming Speakers

March 2, 2017

What To Do with a Patient with Suspected NASH

Arun Sanyal, MD

Charles Caravati Distinguished Professor of Medicine — Division of Gastroenterology, Hepatology and Nutrition — Virginia Commonwealth University School of Medicine

March 23, 2017

Comparative Effectiveness of Biologic Therapy in IBD: Which One, When?

Hans Herfarth, MD, PhD

Professor of Medicine — Center for Gastrointestinal Biology and Disease — University of North Carolina

April 20, 2017

Advances in Irritable Bowel Syndrome: Constipation and Diarrhea

Michael Camilleri, MD

Professor of Medicine, Pharmacology & Physiology — Department of Gastroenterology & Hepatology — Mayo Clinic, Rochester, Minn.

Learning Objectives

- Review state-of-the-art information on the pathogenesis of gastrointestinal and liver diseases
- Review the latest procedural and diagnostic advancements for gastroenterology practice
- Identify current treatments available for GI diseases and discuss future advancements

Sponsored By

- Division of Gastroenterology, Hepatology, and Nutrition, University of Pittsburgh School of Medicine
- UPMC Center for Continuing Education in the Health Sciences

Course Director

Robert E. Schoen, MD, MPH

Professor of Medicine and Epidemiology
Interim Chief, Division of Gastroenterology, Hepatology, and Nutrition
University of Pittsburgh School of Medicine

Contact Information

For more information about the Gut Club speaker series, or to reserve a seat for an upcoming event, please contact:

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About the Division

The Division of Gastroenterology, Hepatology, and Nutrition is one of the leading centers for gastrointestinal clinical care and research in the country.

The UPMC Digestive Disorders Center is a comprehensive care program for patients covering the full range of digestive health conditions including:

- Inflammatory Bowel Diseases
- Swallowing Disorders
- Cancer Prevention and Treatment
- Pancreatic and Biliary Diseases
- Functional Bowel Disorders
- Nutrition Support

The Division also includes eight Centers of Excellence providing specialized care for complex cases, as well as conducting research on numerous fronts to better understand, and develop treatments for, disorders and diseases of the gastrointestinal and related systems.

Centers of Excellence

- Pancreas and Biliary Center
- IBD Center and UPMC Total Care-IBD
- Center for Liver Diseases
- GI Cancer Prevention and Treatment Center
- Center for Intestinal Health and Nutrition Support
- Neurogastroenterology and Motility Center
- Center for Women's Digestive Health
- Visceral Inflammation and Pain Center

UPMC Division of Gastroenterology, Hepatology, and Nutrition

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For consults and referrals, please call UPMC's 24-hour physician OnDemand service at **1-866-884-8579**.

A world-renowned health care provider and insurer, Pittsburgh-based UPMC is inventing new models of patient-centered, cost-effective, accountable care. It provides nearly \$900 million a year in benefits to its communities, including more care to the region's most vulnerable citizens than any other health care institution. The largest nongovernmental employer in Pennsylvania, UPMC integrates 60,000 employees, more than 20 hospitals, more than 500 doctors' offices and outpatient sites, and a more than 3 million-member Insurance Services Division, the largest medical and behavioral health services insurer in western Pennsylvania. Affiliated with the University of Pittsburgh Schools of the Health Sciences, UPMC ranks No. 12 in the prestigious *U.S. News & World Report* annual Honor Roll of America's Best Hospitals. UPMC Enterprises functions as the innovation and commercialization arm of UPMC, while UPMC International provides hands-on health care and management services with partners in 12 countries on four continents. For more information, go to UPMC.com..