

INNOVATIONS | 2008 EDITION



Gastroenterology & Hepatology



JOHNS HOPKINS
MEDICINE



Mission

The mission of Johns Hopkins Medicine is to improve the health of the community and the world by setting the standard of excellence in medical education, research and clinical care. Diverse and inclusive, Johns Hopkins Medicine educates medical students, scientists, health care professionals and the public; conducts biomedical research; and provides patient-centered medicine to prevent, diagnose and treat human illness.

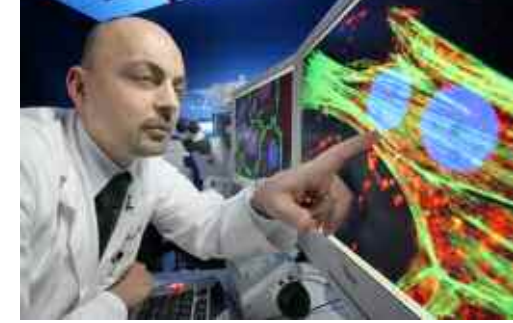
Vision

Johns Hopkins Medicine provides a diverse and inclusive environment that fosters intellectual discovery, creates and transmits innovative knowledge, improves human health, and provides medical leadership to the world.

Core Values

Excellence & Discovery
Leadership & Integrity
Diversity & Inclusion
Respect & Collegiality

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Gastroenterology & Hepatology

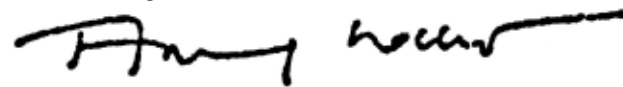
Dear Colleague:

Research and discoveries lead to improved health for our patients. We strive to be one of the most innovative divisions in the country. Working hand in hand with our gastroenterology and hepatology staff, including a solid partnership with our nurses, our physician scientists have developed and patented many innovations here at Hopkins over the past five years. A few recent examples include a device and method for treating gastrointestinal muscle disorders, a gastrojejunal feeding tube and an endoscopic cryospray device.

And we continue to dream. The possibilities seem endless, and we won't accept "impossible" as an answer. In this booklet, you'll find the results of some of these dreams—research and clinical innovations helping to improve patient treatment that go far beyond what was deemed unachievable only 10 years ago.

We hope you take away some inspiration from this booklet. As always, we are here as a resource for you and your patients. We look forward to working with you to better the health of GI and liver patients all over the world.

Warm regards,



Anthony Kalloo, M.D.

Chief, Division of Gastroenterology and Hepatology

If you have any questions or would like to speak with Anthony Kalloo or any of the Gastroenterology & Hepatology faculty, please call 410-955-9697.

For more information on Johns Hopkins Gastroenterology & Hepatology, visit www.hopkins-gi.org. To refer a patient, call 410-955-4166.



Department Overview

The Johns Hopkins Hospital Division of Gastroenterology & Hepatology

The Johns Hopkins Hospital Division of Gastroenterology & Hepatology is consistently recognized nationally and internationally for our achievements in advancing the understanding and treatment of gastrointestinal and liver disease. Every year since 1999, we have been named among the top three GI programs in the United States in *U.S. News & World Report's* Best Hospitals ranking.

Over the past few years, the Division of Gastroenterology & Hepatology has expanded. Several new physician scientists have joined an already exceptional staff of gastroenterologists and hepatologists with the highest level of skills in diagnosis, treatment and research.

Our patients receive expert care from professionals who know their disease inside and out. Through research and collaboration, we are able to give our patients treatment options to fit their needs, improve their health and enhance their quality of life.

2008 Highlights

In this booklet, we summarize some of the many innovations taking place at Johns Hopkins. Examples include:

- *NOTES*, a new approach to performing surgical intervention in the peritoneal cavity. Pioneered at Johns Hopkins, *NOTES* may simplify surgery in the future. (*see page 9*)
- A new method of early diagnosis and treatment of a form of hereditary pancreatic cancer that otherwise may not be treatable. (*see page 30*)
- Using confocal microendoscopy for a real-time look at cells to determine if cancer is present and which therapies could work best. (*see page 11*)

Quality

We have developed ways to improve our quality of care and patient safety. First and foremost, we have established a committee dedicated to developing solutions for safety and quality challenges. Our staff is committed to fostering a culture of safety and innovation. And we continue to improve patient care by translating research to clinical care and better treatments.

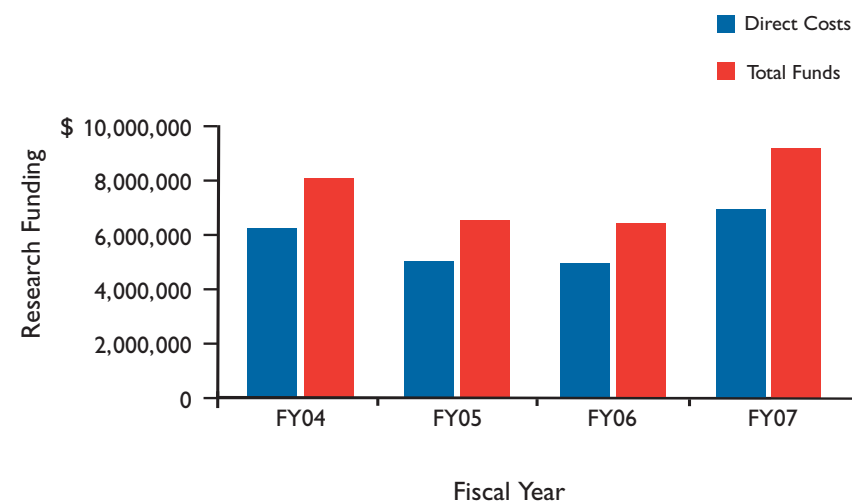
Research

Our scientific investigations continue to bring new hope to patients from around the world.

Recent research includes:

- New insight into the digestion process, as well as into the mechanics underlying the progression of *E. coli*. (*see page 36*)
- A novel way to fight colorectal cancer in development. (*see page 26*)
- The discovery of genetic markers to predict Barrett's esophagus and cancer. (*see page 22*)

Research Funds



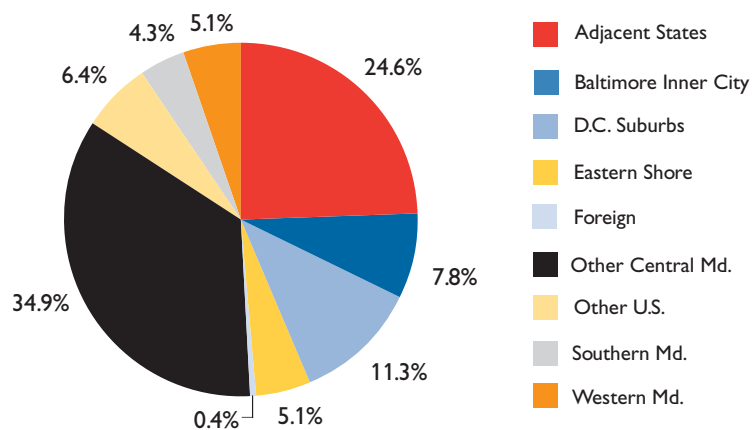
Experience and Outcomes

We see more than 9,000 patients each year and perform nearly 14,000 procedures. Patients travel from within the United States and from all over the world for treatment from our faculty.

2007 Outpatient Visits 8,403

2007 Inpatient Discharges 982

Gastroenterology & Hepatology Patient Origin Adult Inpatients FY05–FY07



“From the moment I arrived at Hopkins in 1988, it was clear that I had landed in the midst of an exceptional group of gastroenterologists and hepatologists—doctors determined to tease out the pathogenesis of the diseases we treat and find better therapies based on new knowledge.”

— Anthony Kalloo, M.D., Chief, Division of Gastroenterology & Hepatology

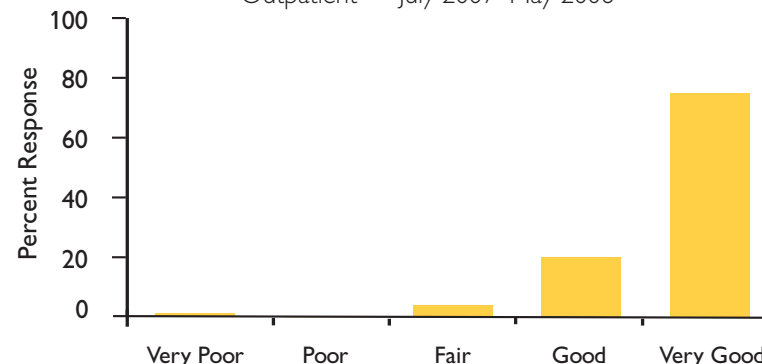
Patient Satisfaction

In our efforts to provide our patients with the best treatment and care, we continually solicit patient feedback and use this information to help improve the patient experience. Results from our most recent

patient satisfaction surveys from July 2007 through May 2008 indicate that over 90 percent of our patients would likely recommend their Hopkins care providers and our practice.

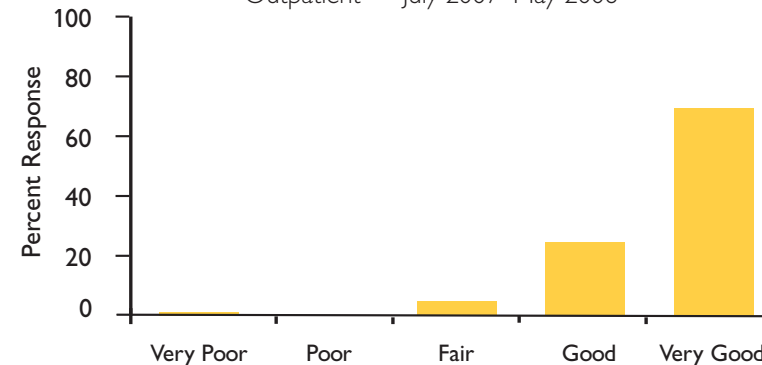
Likelihood to Recommend Practice

Outpatient — July 2007–May 2008



Overall Quality of Care

Outpatient — July 2007–May 2008



Demonstrating Clinical Innovation and New Discoveries

Learn on the following pages how we are breaking new ground in patient care.

Demonstrating Clinical Innovation

- Natural Orifice Transluminal Endoscopic Surgery: Hopkins-Pioneered Notion Taking Off Worldwide
- Endomicroscope Revolutionizing GI Disease Detection
- Endoscopic Ultrasound for Improved Vascular Therapy
- Unique Niche for Failed ERCP Patients
- Innovations in Botulinum Toxin Linked to Hopkins; Obesity Studies Ongoing
- Endoscopic Cryotherapy for the Gastrointestinal Tract
- Bringing Nurse Practitioners Into the Fold

New Discoveries

- Biomarkers for Barrett's Esophagus: Early Predictors Could Save Lives
- Large Study IDs Additional Genetic Regions for Crohn's Disease Using Novel Method
- New Radioactive Agents for Colon Cancer Work Inside Cells
- Research into Preventing Cirrhosis
- Hopkins-Pioneered Pancreas Cancer Screening Saving Lives
- Trial Shows Curcumin (Curry) Treats Polyps With Few Side Effects: Potential Colon Cancer Preventive
- Protein Discovery Aids in Understanding Digestion, Potential Treatments
- Saving Lives with E. Coli Research

Demonstrating Clinical Innovation

Natural Orifice Transluminal Endoscopic Surgery: Hopkins-Pioneered Notion Taking Off Worldwide

Johns Hopkins physicians may have broken through the final roadblock to making natural orifice transluminal endoscopic surgery (NOTES) a reality, says NOTES pioneer **Anthony Kalloo**, director of the Division of Gastroenterology & Hepatology.

The idea of performing gastrointestinal surgery without leaving a trace that surgeons were ever there (for example, removing the gallbladder or performing gastric bypass through a natural orifice, such as the mouth, rectum or vagina), first received laughs but now is garnering serious attention, says Kalloo. Surgeons and gastroenterologists worldwide have joined in the effort to perfect the procedure. A coalition of select scientists, including Kalloo, has formed the Natural Orifice Surgery Consortium for Assessment and Research (www.noscar.org).

"There has been an unbelievable explosion in interest since re-

sults showed this procedure can be safely accomplished," he says. Kalloo and colleagues at Hopkins started work on this innovative concept more than 10 years ago and have overcome challenges, such as preventing infection in the peritoneal cavity and securing closure of the gastrointestinal incisions, by developing new methods and technology.

The final hurdle, ensuring complete sealing of the puncture hole following surgery to prevent infection, proved most difficult. The closure of the gastrointestinal incision has always been challenging. But after hundreds of experiments, Kalloo believes they've found the answer to reliable closure of the incision. These new devices are now undergoing vigorous testing.

"I think we've almost done it," Kalloo says. His quest to perfect NOTES stems from a desire to provide patients with the benefits of safer and less invasive surgeries, including scar-free appendectomies, easier gallbladder removals, better gastric bypasses and

smoother tubal ligations—all with even shorter recoveries, less pain and no external scarring.

Ideal candidates for the procedure include people who are morbidly obese. Hopkins physicians are leading efforts in using NOTES for obesity surgery. So far, three patients have undergone these procedures with no problems or complications.

“We’re taking minimally invasive surgery to a whole new level,” Kalloo says. Currently, researchers at Hopkins have performed several successful hybrid approaches—blending the use of both a laparoscope and a flexible upper endoscope.

“We’re working toward pure natural orifice surgery, to usher in what I believe to be a more ideal kind of GI surgery,” he says.

RESEARCH PUBLISHED:

Kalloo AN, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevoy SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointestinal Endoscopy* 2004;60:114-117.

Giday SA, Kantsevoy SV, Kalloo AN. Current status of natural orifice transluminal surgery. *Gastrointestinal Endoscopy Clinics of North America* 2007;17(3):595-604.

Giday SA, Kantsevoy SV, Kalloo AN. Principle and history of Natural Orifice Transluminal Endoscopic Surgery (NOTES). *Minimally Invasive Therapy & Allied Technologies* 2006;15(6):373-377.

Shih SP, Kantsevoy SV, Kalloo AN, Magno P, Giday SA, Ko CW, Isakovich NV, Meireles O, Hanly EJ, Marohn MR. Hybrid minimally invasive surgery—a bridge between laparoscopic and transluminal surgery. *Surgical Endoscopy* 2007;21(8):1450-1453.

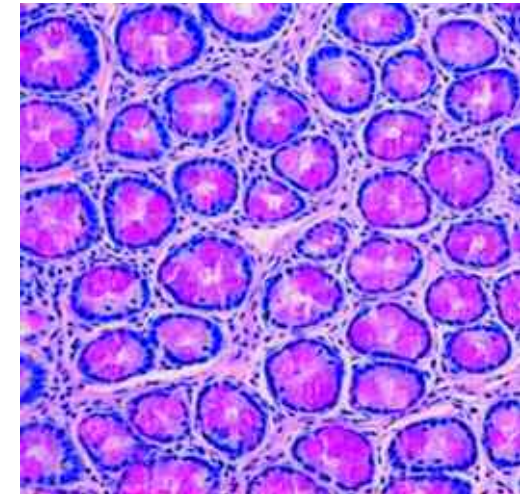
Ko CW, Shin EJ, Buscaglia JM, Clarke JO, Magno P, Giday SA, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Kalloo AN, Kantsevoy SV. Preliminary pneumoperitoneum facilitates transgastric access into the peritoneal cavity for natural orifice transluminal endoscopic surgery: a pilot study in a live porcine model. *Endoscopy* 2007;39(10):849-853.

Endomicroscope Revolutionizing GI Disease Detection

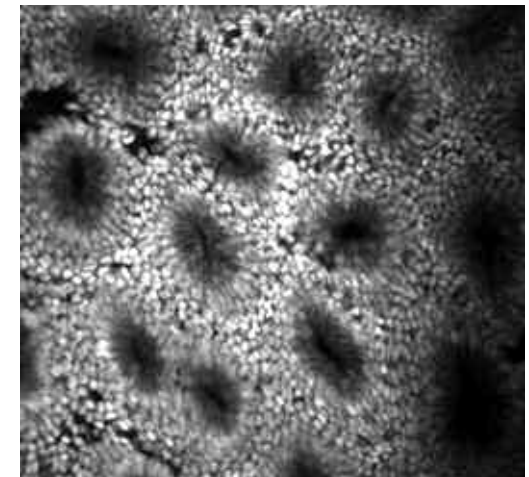
Johns Hopkins physicians, collaborating with researchers at Johannes Gutenberg University in Mainz, Germany, became the first in the United States to use confocal endomicroscopy to instantly diagnose patients with gastrointestinal cancer.

Gastroenterologist **Marcia (Mimi) Canto** is studying the use of the new type of endoscopy to improve diagnosis of diseases of the esophagus and gastrointestinal tract. The confocal endomicroscope includes a miniaturized microscope at the tip of a conventional endoscope to enable physicians to view cellular, vascular and connective structures in detail.

“This tool magnifies the mucosa 1,000 times so microscopic pictures of cells can be obtained,” she says. “In most instances, gradation of cellular changes allows an immediate in vivo diagnosis of gastrointestinal disease.”



Conventional histology—horizontal slice



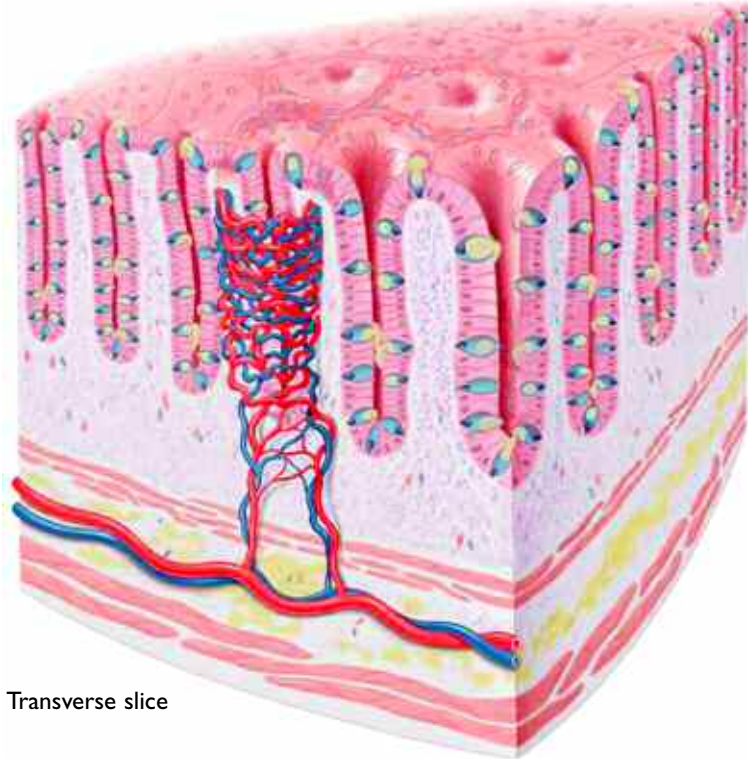
Endomicroscopy—horizontal slice

Images courtesy of PENTAX

Clinical trials with the device are under way to determine its effectiveness at identifying dysplasia and early cancers in patients with Barrett's esophagus. If it proves effective, confocal endomicroscopy could change the way physicians

view and evaluate abnormal lesions during endoscopy procedures, particularly in determining the need for biopsies and potential removal of lesions. Results of the pilot studies are expected within a year.

Horizontal slice



Transverse slice

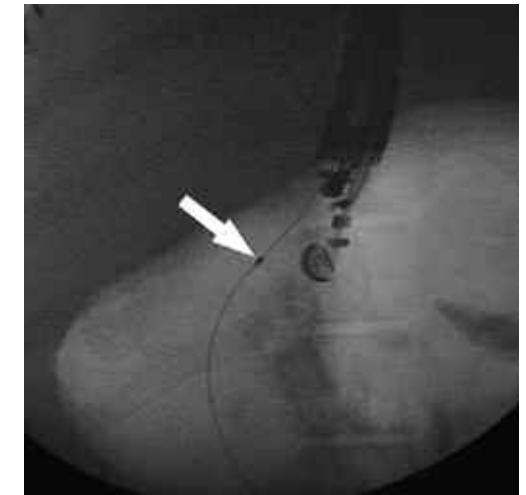
Images courtesy of PENTAX

Endoscopic Ultrasound for Improved Vascular Therapy

Portal hypertension, elevated pressure in the major vascular system of the liver, is difficult to treat. Physicians cannot directly measure or control portal vein pressure because of its location—far away from any peripheral vein through which interventional radiologists normally perform vascular interventions.

But Johns Hopkins gastroenterologists are developing a technique using endoscopic ultrasound (EUS) for direct measurements of portal vein pressure in humans. Such measurements would guide therapy and could save the lives of people with chronic liver disease. With EUS, physicians can monitor the pressure after medication is administered, fine-tuning the dosages for better results.

“EUS provides a stable platform to access the portal vein,” says gastroenterologist **Samuel Giday**. “Using a catheter to administer clot-dissolving drugs will have great impact in patients suffering from vessel blockage.” In addition, chemotherapeutic agents can be



EUS-guided portal vein catheterization

administered using this technique to target the specific feeding portal vessel, which will lessen the systemic side effects in patients, Giday says.

Giday and his team are piloting studies using EUS guidance to reach those vessels. Over the past two years, their studies in animals have shown that EUS-guided portal vein catheterization through the stomach and duodenum is safe and effective for portal angiography and pressure measurements. Human trials are expected to start in the next year.



Portal veinography using a contrast injected through the catheter

RESEARCH PUBLISHED:

Giday SA, Clarke JO, Buscaglia JM, Shin EJ, Ko CW, Magno P, Kantsevov SV. EUS-guided portal vein catheterization: a promising novel approach for portal angiography and portal vein pressure measurements. *Gastrointestinal Endoscopy* 2008;67(2):338-342.

Magno P, Ko CW, Buscaglia JM, Giday SA, Jagannath SB, Clarke JO, Shin EJ, Kantsevov SV. EUS-guided angiography: a novel approach to diagnostic and therapeutic interventions in the vascular system. *Gastrointestinal Endoscopy* 2007;66(3):587-591.

Unique Niche for Failed ERCP Patients

Johns Hopkins' skilled physicians are using new tools in the treatment of patients referred for previously failed access to the pancreatic and bile ducts. They have found that in people with altered anatomy where endoscopic retrograde cholangiopancreatography (ERCP) was previously technically impossible, using single balloon enteroscopy allows the deep access into the small bowel needed to make the procedure feasible.

"The enteroscope allows access to places that would have been otherwise impossible to reach by conventional means due to the complex nature of the anatomy," says **Patrick Okolo**, chief of gastrointestinal endoscopy. He has performed this procedure in more than 100 patients; Hopkins is one of only a few medical centers in the United States that offer it.



Patrick Okolo, chief of gastrointestinal endoscopy

The body relies on the biliary system to eliminate bile acids, cholesterol and bilirubin. Obstruction or a disturbance in the integrity of the bile duct results in many clinical conditions. ERCP is a noninvasive way to provide considerable relief for the patient with minimal inconvenience or risk. In people with anatomic rearrangements, percutaneous procedures or surgery was often used to approach biliary problems. Access to the pancreas is difficult in these patients and often poses a clinical dilemma.

“Now in at least 75 percent of patients where the anatomy is abnormal, we’re able to offer them enteroscopy in lieu of surgery or percutaneous transhepatic procedures,” Okolo says. A growing group of patients who may be candidates are those who have had reconstructive small bowel surgery or gastric bypass surgery.

In the new procedure, the enteroscope is outfitted with a balloon to help pleat the small bowel; this allows for deep intubation of the small intestine, providing access to areas of the small bowel previously inaccessible by endoscopy. A full manuscript detailing the initial Hopkins’ experience using this technique is in preparation; the researchers expect to publish it soon.

RESEARCH PUBLISHED:

Okolo P, Lauder N. Single Balloon Augmented Enteroscopy (SBAE): Initial experience at a single institution. *Gastrointestinal Endoscopy* 2007;65(5):AB341.

Innovations in Botulinum Toxin Linked to Hopkins; Obesity Studies Ongoing

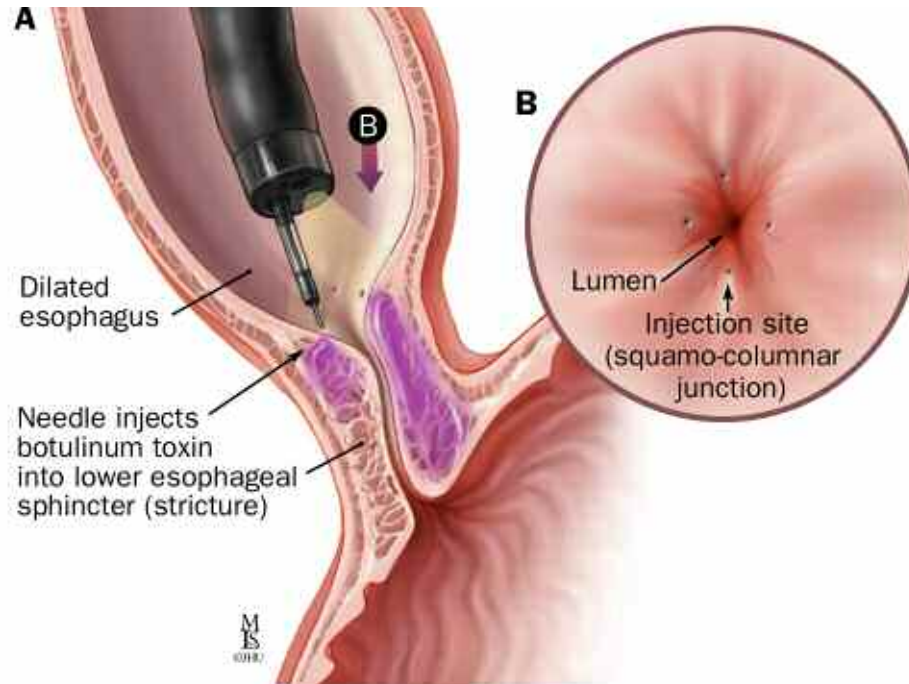
Johns Hopkins researchers pioneered the use of botulinum toxin in gastrointestinal disorders in the 1990s. Today, the use of botulinum toxin for treating GI conditions, including achalasia, gastroparesis, anal fistulas and sphincter of Oddi dysfunction, is widespread, and new studies evaluating further GI uses, including treating obesity, are under way.

“This is a prime example of how research conducted at Hopkins has changed the treatment of disease all over the world,” says **Anthony Kalloo**, chief of the Division of Gastroenterology & Hepatology. “Our animal and human trials involving botulinum toxin led to further research and extensive adoption by gastroenterologists everywhere.”

Botulinum toxin, one of the most lethal poisons in the world, causes the muscles to relax by inhibiting the release of neurotransmitters—essentially leading to paralysis. Several disorders of the gastrointestinal tract are due to muscle spasms and excessive muscular contraction; relaxing the muscles would ease symptoms.

For example, in achalasia the lower esophageal sphincter remains contracted, and the person is unable to swallow. Hopkins researchers found that after they injected botulinum toxin into the area, the muscle relaxed, allowing the person to swallow again.

Researchers at Hopkins now are studying using the toxin to help obese people lose weight. By injecting botulinum toxin into the stomach muscle, they aim to induce a feeling of prolonged satiety. Clinical trials are ongoing.



Technique for intrasphincteric injection of botulinum toxin for achalasia

RESEARCH PUBLISHED:

Pasricha PJ, Ravich WJ, Hendrix TR, Sostre S, Jones B, Kalloo AN. Intrasphincteric botulinum toxin for the treatment of achalasia. *New England Journal of Medicine* 1995;332(12):774-778.

Pasricha PJ, Miskovsky EP, Kalloo AN. Intrasphincteric injection of botulinum toxin for suspected sphincter of Oddi dysfunction. *Gut* 1994;35(9):1319-1321.

Endoscopic Cryotherapy for the Gastrointestinal Tract

For years, thermal therapy was the cornerstone of endoscopic treatment of bleeding mucosal lesions in the gastrointestinal tract, even though it has a 20 percent failure rate. Cryotherapy (freezing therapy) was not an option because no device could deliver the cryotherapy through an endoscope.

But 10 years ago, Johns Hopkins physicians developed such a device, which uses nitrous oxide to deliver a freezing spray, and studies

have shown it to be highly effective for Barrett's esophagus and for gastrointestinal lesions caused by superficial mucosal disease.

"We engineered a way of using compressed gas to freeze gastrointestinal tissue," says **Marcia (Mimi) Canto**, associate professor of medicine and oncology.

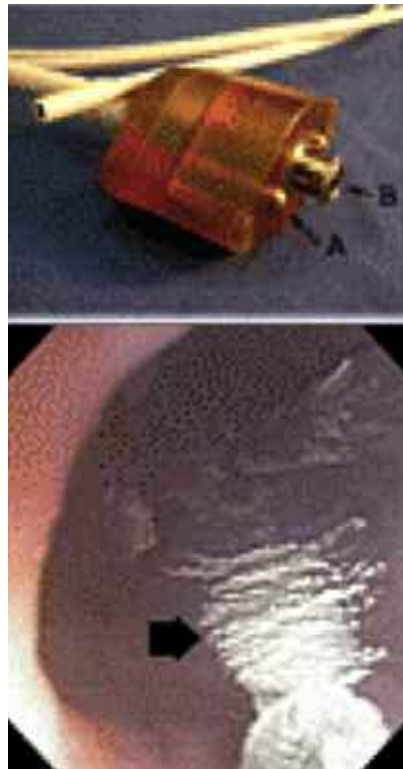
Today, Canto and her colleagues are testing an improved device that uses carbon dioxide. The device showed promising results in animal studies, says Canto, who is leading the ongoing patient trials.



Barrett's esophagus



Two days post-cryotherapy



Cryotherapy—liquid nitrogen

The CO2 device is simple, portable and relatively inexpensive. It requires no diet change or additional medications for the patient and causes minimal to no post-procedure symptoms, Canto says.

“It is a novel, promising mucosal ablative therapy,” she says.



RESEARCH PUBLISHED:

Kantsevov SV, Cruz-Correa MR, Vaughn CA, Jagannath SB, Pasricha PJ, Kalloo AN. Endoscopic cryotherapy for the treatment of bleeding mucosal vascular lesions of the GI tract: a pilot study. *Gastrointestinal Endoscopy* 2003;57(3):403-406.

Bringing Nurse Practitioners Into the Fold

Prompted by the nationwide shortage of gastroenterologists, Johns Hopkins has launched the country’s first program to prepare nurse practitioners to help fill the gap and improve patient access. The Johns Hopkins Nurse Practitioner Fellowship in Gastroenterology and Hepatology, an intensive, 12-month program, combines advanced didactic education with focused, inpatient and ambulatory clinical experience.

In addition to attending weekly conferences, monthly grand rounds, and morbidity and mortality conferences, nurse practitioners in the program also complete a course in evidence-based practice or outcomes and are exposed to multiple specialty areas, including integrative nutrition, gastrointestinal oncology, and biliary and pancreatic disorders. As a result, graduates develop the skills and knowledge to provide high-quality gastroenterology and hepatology care in any setting.

“This program is unique,” says co-director **Sharon Dudley-Brown**, “in that it’s integrated with our traditional gastroenterology and hepatology fellowship, so both NP and first-year GI fellows receive comparable training experiences.”



Gerard Mullin and Sharon Dudley-Brown, co-directors of the Johns Hopkins Nurse Practitioner Fellowship in Gastroenterology and Hepatology

New Discoveries

Biomarkers for Barrett's Esophagus: Early Predictors Could Save Lives

Esophageal cancer is one of the leading causes of cancer death worldwide. Barrett's esophagus (BE) almost always precedes one type of this cancer, esophageal adenocarcinoma (EAC). But if only one in 200 BE patients per year develops EAC, how can you most efficiently screen to find that one? Genetic biomarkers recently discovered by Hopkins researchers may be the answer.

"Current surveillance methods, such as endoscopy and biopsy, don't allow us to focus on the very few patients who are truly in danger of developing EAC," says gastroenterologist **Stephen Meltzer**. And by the time most esophageal cancers are detected, it is too late for treatment to be effective, says gastroenterologist **Jean Wang**. "Earlier detection of this cancer has been shown to make a significant impact on patient outcomes," she says.

Meltzer, Wang and their team are investigating genetic biomarkers to find better ways of detecting Barrett's esophagus and predicting which patients are at highest risk for developing EAC.

By studying cells of patients with BE who later progressed to EAC, they have found eight tumor suppressor genes that were "disabled" early on in BE by DNA methylation (which turns the tumor suppressor genes off). By studying these genes, they found that this tell-tale DNA methylation is detectable before any other changes.

Their goal now is to validate the classification of patients into high-, normal- and low-risk groups based on these gene predictors.

"We hope the results of a large-scale validation study will finally help clinicians know which BE patients need intensive surveillance and which ones don't," Meltzer says.

RESEARCH PUBLISHED:

Jin Z, Hamilton JP, Oлару A, Sato F, Yang J, Ito T, Kan T, Agarwal R, Meltzer SJ. Hypermethylation of the somatostatin promoter is a common, early event in human esophageal carcinogenesis. *Cancer* 2008;112(1):43-49.

Jin Z, Hamilton JP, Yang J, Mori Y, Oлару A, Sato F, Ito T, Kan T, Cheng Y, Paun B, David S, Agarwal R, Abraham JM, Meltzer SJ. Hypermethylation of the AKAP12 promoter is a potential biomarker of Barrett's-associated esophageal neoplastic progression. *Cancer Epidemiology, Biomarkers & Prevention* 2008;17(1):111-117.

Jin Z, Oлару A, Yang J, Sato F, Cheng Y, Kan T, Mori Y, Mantzur C, Paun B, Hamilton JP, Ito T, Wang S, David S, Agarwal R, Beer DG, Abraham JM, Meltzer SJ. Hypermethylation of tachykinin-1 is a potential biomarker in human esophageal cancer. *Clinical Cancer Research* 2007;13(21):6293-6300.

Hamilton JP, Sato F, Jin Z, Greenwald BD, Ito T, Mori Y, Paun BC, Kan T, Cheng Y, Wang S, Yang J, Abraham JM, Meltzer SJ. Reprimo methylation is a potential biomarker of Barrett's-associated esophageal neoplastic progression. *Clinical Cancer Research* 2006;12(22):6637-6642.

Mori Y, Cai K, Cheng Y, Wang S, Paun B, Hamilton JP, Jin Z, Sato F, Berki AT, Kan T, Ito T, Mantzur C, Abraham JM, Meltzer SJ. A genome-wide search identifies epigenetic silencing of somatostatin, tachykinin-1, and five other genes in colon cancer. *Gastroenterology* 2006;131(3):797-808.

Schulmann K, Sterian A, Berki A, Yin J, Sato F, Xu Y, Oлару A, Wang S, Mori Y, Deacu E, Hamilton J, Kan T, Krasna MJ, Beer DG, Pepe MS, Abraham JM, Feng Z, Schmiegel W, Greenwald BD, Meltzer SJ. Inactivation of p16, RUNX3, and HPP1 occurs early in Barrett's-associated neoplastic progression and predicts progression risk. *Oncogene* 2005;24(25):4138-4148.

Large Study IDs Additional Genetic Regions for Crohn's Disease Using Novel Method

Johns Hopkins researchers recently published results from the largest study performed to date (nearly 1,000 families) that identified additional chromosomal regions responsible for Crohn's disease and ulcerative colitis (UC) in families. Particularly important was the inclusion of a large sample of the Jewish population (25 percent of study families), which has two to nine times greater risk of inflammatory bowel disease (IBD) than other patient groups, says study leader **Steven Brant**, director of the Meyerhoff IBD Genetics Laboratory. Brant works with other researchers in the NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases) IBD Genetics Consortium.

The teams in the consortium identified a new region for familial Crohn's disease on chromosome 13 as well as two regions important in Crohn's among Jewish families on chromosomes 1 and 3. Previous studies have identified regions for familial Crohn's disease and ulcerative colitis, but those studies were much smaller and used "low-density" microsatellite markers, which means only one marker for every 10 million base pairs of DNA, to identify the Crohn's disease familial gene regions.

Brant's team performed a genome-wide linkage scan and was the first in the field of IBD genetics to use high-density single-nucleotide polymorphism (SNP)-based markers, more than 10 times the number of markers of any previous study, he says.

"We used more markers to track the chromosomal segments inherited in families to determine risk of inheriting IBD," Brant says. The higher density SNP markers confirmed previously identified regions for familial IBD genes as well as finding more regions.

IBD is a complex genetic disorder; more than 25 percent of people with IBD have a familial form of the disease. Brant's next steps include identifying the specific genes present at these locations that cause familial IBD.

RESEARCH PUBLISHED:

Shugart YY, Silverberg MS, Duerr RH, Taylor KD, Wang MH, Zarfes K, Schumm LP, Bromfield G, Steinhart AH, Griffiths AM, Kane SV, Barmada MM, Rotter JI, Mei L, Bernstein CN, Bayless TM, Langelier D, Cohen A, Bitton A, Rioux JD, Cho JH, Brant SR. An SNP linkage scan identifies significant Crohn's disease loci on chromosomes 13q13.3 and, in Jewish families, on 1p35.2 and 3q29. *Genes and Immunity* 2008; Jan 31 [Epub ahead of print].



Steven Brant, director of the Meyerhoff IBD Genetics Laboratory

New Radioactive Agents for Colon Cancer Work Inside Cells

Johns Hopkins scientists are developing a novel way to fight colorectal cancer using tiny molecules to deliver a barrage of radiation inside cancer cells.

Current treatments bind to the surface of cells and are difficult for the body to excrete, causing unwanted damage to other organs. In



Steve Meltzer, professor of medicine and oncology

pivotal studies, a new radiation delivery system effectively targeted colon cancer cells without binding to normal cells, say colorectal cancer specialists **John Abraham** and **Steve Meltzer**.

Antitumor antibodies used to deliver radiation or chemicals to tumors can be more than 1,000 amino acids long. In contrast, Abraham's and Meltzer's peptide is only 10 amino acids long. Using radioactive phosphorous (P32) to test the result, the researchers were surprised when the cells bound and ingested the peptides, transferring the radiation inside. This radiation could potentially kill the tumor cells by damaging their DNA and proteins.

"P32 or other types of radioactively tagged peptides can penetrate through large, thick colon cancer tumors where other drugs may not," says Meltzer. In addition, these peptides may be able to find and help diagnose metastases or recurrences of colon tumors while they are still small enough to treat. Im-

ages can be taken of the labeled peptides in the body as they bind, revealing where stray tumor cells may be nesting.

Abraham, Meltzer and their team continue designing and testing peptides on human cell samples, as well as in animal models of colon cancer.

"We're quite excited about the potential impact that peptide binding therapy could have on the many patients suffering from colorectal cancer," Meltzer says.

RESEARCH PUBLISHED:

Abraham JM, Sato F, Cheng Y, Paun B, Kan T, Oлару A, Jin Z, Yang J, Agarwal R, David S, Hamilton JP, Ito T, Mori Y, Meltzer SJ. Novel decapeptides that bind avidly and deliver radioisotope to colon cancer cells. *Public Library of Science ONE* 2007;2(10):e964.



Steve Meltzer and John Abraham

Research into Preventing Cirrhosis

Cirrhosis is the 12th leading cause of death by disease, killing 26,000 people in the United States each year. Alcoholism is a common cause of cirrhosis. In the liver, alcohol converts to toxic metabolites such as acetaldehyde (AcH), which triggers reactive oxygen species (ROS, byproducts of the metabo-

lism of oxygen) to activate stellate cells, the main source of collagen that leads to fibrosis and cirrhosis.

Esteban (Steve) Mezey leads Johns Hopkins' research into the progression of cell changes during oxidation that lead to cirrhosis. Mezey aims to find potential therapies to prevent or reverse the fibrosis (scarring) that precedes cirrhosis and, ultimately, end-stage

liver disease. One area of his research is in vivo studies in mice to determine the effects of enzymes (specifically, NADPH oxidase, which increases oxidation) on fibrotic development.

"We're hoping to find that we'll be able to decrease the chances of scarring by feeding the mice antioxidants," he says.

Researchers also are studying culture cells injected with collagen that has been exposed to various compounds to determine the specific mechanisms by which each stimuli affects the fibrosis. Knowing these differences could help them find more ways to block the development of fibrosis.

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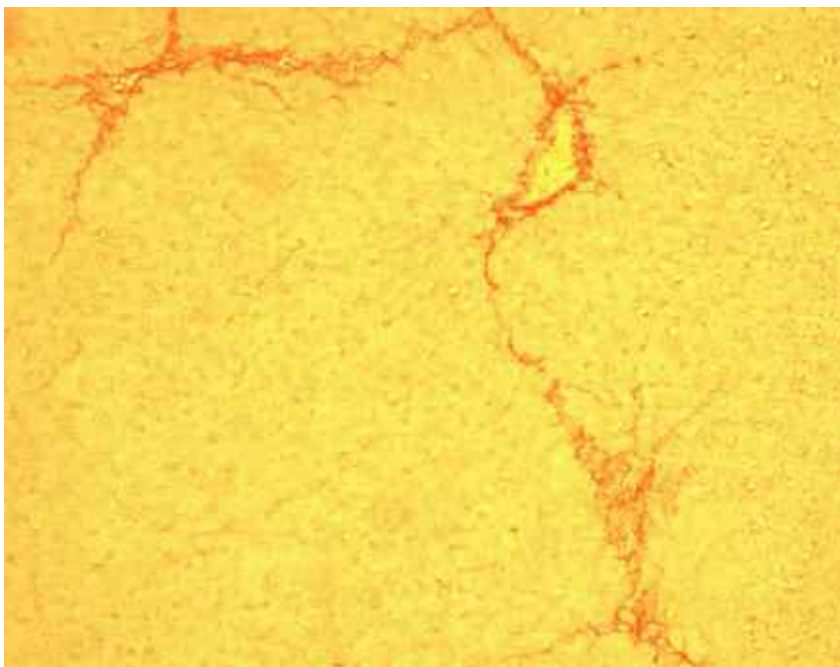
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Potter JJ, Mezey E. Acetaldehyde increases endogenous adiponectin and fibrogenesis in hepatic stellate cells but exogenous adiponectin inhibits fibrogenesis *Alcoholism: Clinical and Experimental Research* 2007;31:2092-2100.



This liver section shows fibrosis (in red) with the development of early cirrhosis (red surrounding the liver lobule with the formation of a nodule) caused experimentally in mice after chronic carbon tetrachloride administration.

Hopkins-Pioneered Pancreas Cancer Screening Saving Lives

Detecting pancreatic cancer early offers the best chance of prolonged survival, because symptoms appear only in the late stages and the tumors often are resistant to chemotherapy and radiation. The American Cancer Society estimates that 37,170 people in the United States will be diagnosed with pancreatic cancer this year, and 33,370 will die of it. Most people who have pancreatic cancer will die within five years of being diagnosed.

About one in 10 pancreatic cancer patients has a family history of the cancer. Using this knowledge, Hopkins gastroenterologist **Marcia (Mimi) Canto** has pioneered cancer of the pancreas screening (CAPS), an early detection test that studies show may save lives.

“The knowledge that pancreatic cancers run in families provides a unique opportunity to prevent the development, identify early and treat precancer of the pancreas, and advance our research of the genetic basis for the development of all forms,” Canto says.

In a multi-center study, Canto and her team screen people at high risk (those with a strong family history) for early pancreatic tumor growths using endoscopic ultrasound (EUS), computed tomography (CT scan) and magnetic resonance imaging (MRI), and test a panel of candidate biomarkers. If they find abnormalities, they recommend pancreatic surgery—a major intervention.

“The resection of noninvasive precancers will cure these lesions before they have the opportunity to spread and metastasize,” Canto says.

A potential side effect of the surgery is the development of diabetes, but high-risk patients seem to be willing to make that trade. “Pancreatic cancer is devastating to families, and this approach helps us save lives,” explains Canto.

Canto recently received funding to continue her work in CAPS4. In addition, translational studies are under way at Hopkins to discover novel biomarkers for the genes in families that develop the disease.

RESEARCH PUBLISHED:

Abe T, Fukushima N, Brune K, Boehm C, Sato N, Matsubayashi H, Canto M, Petersen GM, Hruban RH, Goggins M. Genome-wide allelotypes of familial pancreatic adenocarcinomas and familial and sporadic intraductal papillary mucinous neoplasms. *Clinical Cancer Research* 2007;13(20):6019-6025.

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Mimi Canto uses endoscopic ultrasonography to visualize tiny lesions.

Trial Shows Curcumin (Curry) Treats Polyps With Few Side Effects; Potential Colon Cancer Preventive

A small Hopkins study recently found that a pill form of curcumin, the main spice found in curry, reduced the size and incidence of polyps in familial adenomatous polyposis (FAP), an inherited form of colon cancer. Now, researchers are enrolling patients in a larger,

double-blind, placebo-controlled, randomized trial that is under way at two sites to see if they can reproduce their findings.

“Initial studies show that this nutrient may have the ability to regress these adenomas in a way that doesn’t cause side effects,” says gastroenterologist **Frank Giardiello**.

FAP is characterized by the development of hundreds to thousands of colorectal adenomas (polyps) and

eventual colon cancer, often at a young age. Giardiello has been searching for ways to slow or stop the ongoing production of these aggressive adenomas for years. His research led to the use of nonsteroidal anti-inflammatory drugs as a possible way to manage polyps, but the drugs cause significant side effects, including gastrointestinal ulcerations and bleeding.

After recent studies reported that curcumin may prevent the progression of some cancers—along with findings that people who eat large amounts of curry have a lower rate of colon cancer—Giardiello and colleague Maria Cruz-Correa of the University of Puerto Rico Cancer Center wanted to know more.

They recruited five patients for a nine-month trial taking curcumin in a dose well above the amount that could be consumed in food. At the end, the average number of polyps dropped 60.4 percent, and the average size dropped by 50.9 percent.

Most importantly, in all patients, side effects were minimal and short-lived. The researchers hope the larger trial replicates these results.

“We could go a long way in preventing and managing polyps and colon cancer in high-risk populations,” says Cruz-Correa.

FARR Laboratories (Santa Monica, Calif.) is providing all active and placebo curcumin formulations (Calcumin) for the study free of charge.

RESEARCH PUBLISHED:

Cruz-Correa M, Shoskes DA, Sanchez P, Zhao R, Hyland LM, Wexner SD, Giardiello FM. Combination treatment with curcumin and quercetin of adenomas in familial adenomatous polyposis. *Clinical Gastroenterology and Hepatology* 2006;4(8):1035-1038.



Frank Giardiello and *Curcuma longa*

Protein Discovery Aids in Understanding Digestion, Potential Treatments

Research led by **Mark Donowitz**, LeBoff Professor of Medicine and director of the Hopkins Center for Epithelial Disorders, may lead to improved treatment of diarrheal disease by studying how a protein functions and undergoes changes in activity as part of digestion.

The protein, sodium/hydrogen exchanger 3 (NHE3), is the major protein responsible for intestinal salt absorption. The Donowitz laboratory previously showed that this protein has two parts: a part that moves the sodium across the intestinal membrane, and an attached part that sticks into the inside of the cell and accounts for the changes in the protein's function that occur with normal digestion. This protein also explains how diarrheal disease occurs, where viruses or bacterial products cause the same type of NHE3 inhibition that happens in digestion but with larger and longer effects.



Mark Donowitz, LeBoff Professor for Research in Digestive Diseases

The lab's recent work has shown that the intracellular part of NHE3 acts to form large complexes with other proteins by using itself as a scaffold to create groups of proteins working together to regulate it. Until now, it was thought that the formation of signaling complexes was a random process

and that proteins binding to NHE3 did so with no particular organization.

"We've found that instead of random binding, clusters of signaling molecules are formed at certain sites in the intracellular part of NHE3 and they change as part of the control of NHE3 activity," he says. "This indicates that the intracellular part of NHE3 organizes its own regulation and brings together all the partners that take part in its regulation, like an orchestra leader brings together all the parts of the symphony."

Donowitz, a past president of the American Gastroenterological Association, hopes this discovery will lead to the development of drugs to treat diarrheal diseases. Many diarrheal diseases, especially those associated with intestinal inflammation, have changes in NHE3 as the major contributor.

RESEARCH PUBLISHED:

Cha B, Kenworthy A, Murtazina R, and Donowitz M. The lateral mobility of NHE3 on the apical membrane of renal epithelial OK cells is limited by the PDZ domain proteins NHERF1/2, but is dependent on an intact actin cytoskeleton as determined by FRAP. *Journal of Cell Science* 2004;117:3353-3365.

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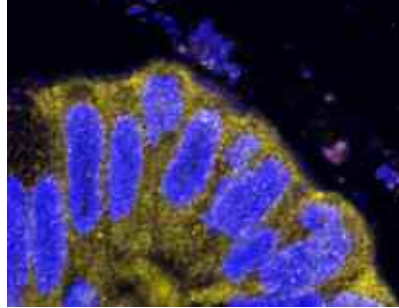
For more information about our published research, visit PubMed at www.pubmed.gov. Articles and abstracts are indexed by author, topic or journal.

Saving Lives with E. Coli Research

In the United States, more than 20,000 infections and 250 deaths occur each year from the enterohemorrhagic *Escherichia coli* bacteria strains that, when ingested via contaminated food or water, colonize the intestine and produce Shiga toxins in the intestinal lumen. Shiga toxins can be deadly because they are able to cross the intestinal wall, spread systemically and cause blood clots to form in the kidney. That leads to kidney failure, which is fatal in 10 percent of cases (primarily in young children).

There is no treatment for Shiga-producing toxin, says Hopkins researcher **Olga Kovbasnjuk**. In fact, antibiotics may increase the risk of kidney complications from Shiga toxins by up to 50 percent.

Normal human intestinal epithelial cells do not have the receptor for Shiga toxins, so it was not clear how the toxins got into the bloodstream. Kovbasnjuk recently has discovered and described a method of macropinocytosis, a process that allows the toxins into the bloodstream. She and her team are studying tissue of patients made ill in the



This human colonic tissue is from a patient infected with Shiga toxin producing *E. coli* (EHEC) bacteria. Blue - bacteria and nuclei of human colonic epithelial cells; red - Shiga toxin 1; and green - Shiga toxin 2 taken up by human colonic epithelial cells

recent outbreaks of *E. coli* to further define the intestinal sites of bacterial colonization and its process.

“If we better understand the molecular mechanism of Shiga toxin macropinocytosis, we can see how to inhibit the toxin uptake to reduce the chance of systemic complications,” she says. “Eventually, each step in the process can be targeted with drugs to prevent kidney damage and save lives.”

RESEARCH PUBLISHED:

Maluykova I, Gutsal O, Laiko M, Kane A, Donowitz M, Kovbasnjuk O. Latrunculin B facilitates Shiga toxin 1 transcellular transcytosis across T84 intestinal epithelial cells. *Biochimica et Biophysica Acta*. In process.

Kovbasnjuk O. New insights into the role of Shiga toxins in intestinal disease. *Gastroenterology* 2005;129(4):1354-1355.

Patient Safety and Quality Measures

Improving Quality of Life for Patients with Liver Cancer

Hepatocellular carcinoma (liver cancer) is responsible for more than 16,500 deaths a year in the United States and is one of the most common malignancies in adults who have cirrhosis. Although potentially curable by surgical resection (removing the part of the liver containing the tumor), only patients with localized disease and normal liver function are surgical candidates.

At Johns Hopkins, members of an active liver tumor board work to improve the quality of life for patients with both operable and inoperable cancers of the liver. Hopkins physicians perform 20 liver transplants each year for cancer, but see more than three times that volume in patients who are not candidates for transplant or surgical resection (usually because of the tumor’s increased size or progression beyond the liver).

“We treat patients at all stages



James Hamilton, Ayman Koteish, and Zhiping Li

with chemoembolization or radiofrequency ablation to minimize tumor growth and, in some cases, shrink tumors, to increase their survival,” says gastroenterologist **James Hamilton**.

Chemoembolization arrests blood flow and delivers highly concentrated drugs directly to the tumor via a catheter. It offers 10 to 25 times better saturation than systemic infusion alone. This treatment has shown positive results in preventing the tumor from growing or metastasizing throughout the body, and in some cases has resulted in significant tumor shrinkage. A second therapeutic option, still experimental, is placing radioactive seeds into the tumor. Both of these treatments are generally well tolerated, cause little systemic side effects and rarely cause a worsening of liver function.

Trials will soon be under way to study the effects of the

chemoembolization or surgical resection coupled with a new anti-cancer agent called Nexavar (sorafenib), Hamilton says. This promising agent also will be studied in patients with large tumors before and after transplant.

Someday, molecular-based diagnostic tests for early detection, gene therapy and immunotherapy may become available for the management of hepatocellular carcinoma. Currently, Hamilton and a multidisciplinary team of researchers are investigating the early genetic changes that predict the development of cancer in patients with chronic liver disease.

RESEARCH PUBLISHED:

Liapi E, Georgiades CC, Hong K, Geschwind JF. Transcatheter arterial chemoembolization: current technique and future promise. *Techniques of Vascular and Interventional Radiology* 2007;10(1):2-11.



Nurse manager Christine Smith confers with colleagues Lori Wroblewski and Angela Palmer.

Safety Program Improves Communications, Work Solutions

Physicians, nurses and staff in the Division of Gastroenterology & Hepatology collaborate to identify and improve safety issues for patients and health care providers. The department's Comprehensive Unit-based Safety Program (CUSP), started two years ago, is part of their effort to create a culture that targets system challenges without pointing to individual fault.

“We meet monthly to review potential hazards and identify concerns, and then brainstorm for solutions,” says nurse manager **Christine Smith**. “The goal is to make the environment safer for everyone and provide a no-fault forum for open discussion.”

For example, nurses saw a need for advanced training in the use of anesthesia because an increasing number of patients in the recovery room were under anesthesia. The nurses worked with educators and

the department of anesthesiology to develop a training program for nurses in the critical care areas. Now, all new nurses are required to complete additional training before starting on the unit and existing staff are going through the same training.

“In this instance, we received the support and training we needed by outlining the solution and working with our anesthesia colleagues as part of this safety initiative,” Smith says.

Smith says she regularly receives ideas to add to the monthly meeting agenda. “We’re creating a blame-free atmosphere where people aren’t afraid to bring up issues,” she says. Many ideas originate from near misses—cases where errors or complications are averted at the last minute. Staff members use the CUSP forum to dissect the incident and create formal protocols to prevent the problem from recurring.

“As we share information, it is an opportunity for all of us to learn,” she says. “We’re keeping others from repeating close calls and ensuring the safety of our patients and staff alike.”

A Broader Approach: Integrative Medicine Has a Role in Chronic GI Conditions

Gastroenterologists are often facing off against the persnickety nature of chronic digestive diseases, particularly where treatments are concerned.

“It’s been our challenge that one patient will respond completely differently to a specific treatment than another patient with the same condition and symptoms,” says gastroenterologist **Linda Lee**, clinical director of outpatient services. “Or that a treatment becomes ineffective or less desirable because of untoward side effects.”

Typically, those treatments are focused on pharmacologic solutions. But, for chronic GI conditions like gastroparesis, dyspepsia and irritable bowel syndrome (IBS), for example, sustained answers are as complex as the human body itself.

“We often assume good medicine means using a hi-tech approach,” says Lee. “But, it’s not always just about prescribing a drug or scheduling a procedure—and it’s definitely not about using the same approach for every patient.”

Lee—a conventionally trained gastroenterologist—heads a new initiative, the Johns Hopkins Digestive Center and Integrative Medicine, that draws on the expertise of both allopathic (or conventional) and complementary medicine specialists in a single location. Integrating these two perspectives by offering a choice of the best therapies each approach has to offer, is a powerful resource for patients who struggle with chronic GI conditions, says Lee. The center also emphasizes the critical role of good nutrition in managing digestive symptoms.

Women outnumber men when it comes to conditions like IBS and gastroparesis, and the center focuses on those gender susceptibilities. Gastroparesis—a delayed emptying of the stomach that causes such frustrating and even debilitating symptoms as nausea, vomiting and



bloating—is a classic example of a condition that affects primarily women and for which physicians may reach first for the pharmacologic solution.

“The problem,” says Lee, “is that the only FDA-approved drug for gastroparesis may cause terrible side effects. So, in this case as in so many other GI illnesses, we really need to be thinking more broadly about how we can help patients achieve a sense of wellness and improve quality of life despite their chronic conditions.”

And, what this new center has immediate access to is the kind of Hopkins-based research into digestive diseases that can have an impact of those treatments—whether it’s molecular and cellular, physiological or behavioral.

Lee says it’s not about eschewing pharmacology and surgical interventions, but rather about broadening the treatment approach and taking a much closer look at patients and their lives.

“We really want to try to control their symptoms in a different way—through more choices that are wellness-based,” she says.

The Patient Experience

Pregnancy and IBD: Careful Planning, Close Monitoring Key

Meredith Berlin, now 33, recently gave birth to her third child, a girl named Ellie. Thanks to the careful management of her ulcerative colitis (UC), the Maryland resident felt great throughout her pregnancy.

That wasn't the case in earlier years.

Only 9 when she was diagnosed with UC, Berlin has lived with

flare-ups most of her life. In remission for years before her first pregnancy (Jake, now 6), she said her UC wasn't a problem—until her second pregnancy ended in miscarriage and a long bout of symptoms that lasted for more than a year and a half.

She wasn't in total remission when she got pregnant for the third time, and "it was a lousy

pregnancy," she recalls. Immediately after the birth of her second boy (Mason, now 3 1/2), who was almost two months early, she started IV drug therapy with infliximab at the Meyerhoff IBD Center. The center, headed by **Theodore Bayless**, has treated challenging patients with inflammatory bowel disease for decades.

The treatment changed her life. "I went in thinking surgery was my only option, but now I wish I had started it [the therapy] sooner," she says.

Infliximab is often used to treat cases of UC and Crohn's disease that have not responded well to traditional therapies, according to **Steven Brant**, associate professor of gastroenterology. For Berlin, flare-up symptoms include frequent trips to the bathroom, discomfort, stomach pains and exhaustion. Since starting treatment with infliximab, her symptoms have ceased.

When she was ready to try for her third, and probably final, child, Berlin first consulted her physician. "I was in remission and on the therapy, and it was a good time to do it," she says. She remained on the medication with close monitoring, had an uneventful pregnancy and stayed in remission.

Berlin receives the infliximab infusions in a two-hour appointment every eight weeks. She also takes pills two times a day. Since her second child was born prematurely, she says, she was very careful throughout her last pregnancy. Berlin credits her husband, Mitchell, for being an invaluable source of support. Her sons show no signs of the disease.

Berlin advises other women with UC who want to get pregnant to stay on top of symptoms and learn about the disease. At the first sign of a possible symptom, she phones her doctor for advice and a possible increased dosage if warranted.

"With diligence and planning, it's very possible to have a successful pregnancy with UC," she says.



Meredith Berlin with children Ellie, Mason and Jake

Our Faculty

Anthony Kalloo is a professor of medicine and director of the Division of Gastroenterology & Hepatology at the Johns Hopkins University School of Medicine.

Kaloo graduated from the University of the West Indies Medical School and completed internships at Port of Spain General Hospital in Trinidad and Howard University Hospital in Washington, D.C. He completed his fellowship training program in the combined Georgetown University, VA Medical Center and NIH program. He also served as an instructor in medicine at Georgetown University before joining the faculty at Johns Hopkins in 1988.

A former associate editor of the peer-reviewed journal *Gastrointestinal Endoscopy*, Kalloo is the founder and immediate past medical director of The Johns Hopkins Gastroenterology & Hepatology Resource Center (www.hopkins-gi.org), a 3,000-page multilingual Web resource for patients and physicians. He is a past panel chair for gastroenterology and urology devices with the United States

Food and Drug Administration. Kalloo is also a member of the Apollo group, a think-tank endoscopy group.

His special interests include therapeutic endoscopy, pancreatitis, sphincter of Oddi dysfunction and abdominal pain. Dr. Kalloo pioneered natural orifice transluminal endoscopic surgery (NOTES), a technique to enable abdominal surgery without the use of incisions. In addition to authoring multiple scientific papers and book chapters, he has been granted several patents for his work, including the use of botulinum toxin in the gastrointestinal tract, endoscopic cryotherapy and the winged biliary/pancreatic stent. He is board-certified in internal medicine and gastroenterology.

The Johns Hopkins Division of Gastroenterology & Hepatology

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Marcia Canto, M.D., M.H.S.
Francis Giardiello, M.D.
Stephen J. Meltzer, M.D.

General

Mark Donowitz, M.D.
Francis Giardiello, M.D.
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Zhiping Li, M.D.
Esteban Mezey, M.D.

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Sharon Dudley-Brown, Ph.D.
John Kwon, M.D., Ph.D.

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James Potter, B.S.
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Fumiaki Sato, Ph.D.
Cynthia Sears, M.D.
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Lan Wang, M.D., Ph.D.

Therapeutic Endoscopy, Barrett's Esophagus and Pancreatic Cancer

Marcia Canto, M.D., M.H.S.
Kerry Dunbar, M.D.
Samuel A. Giday, M.D.
Sanjay Jagannath, M.D.
Anthony N. Kalloo, M.D.
Patrick I. Okolo III, M.D., M.P.H.

Women's Digestive Health

Linda Lee, M.D.

How to Refer a Patient

The Johns Hopkins Hospital Division of Gastroenterology & Hepatology welcomes referrals of new patients. We look forward to working with you to determine the most appropriate care for your patients.

There are several ways to refer a patient. For urgent physician-to-physician referrals or consultation, please call the Hopkins Access Line (HAL) at **1-800-765-5447**.

You also may refer patients to any of the Johns Hopkins Gastroenterology & Hepatology faculty by calling **410-955-4166**.

To refer a patient to the Johns Hopkins Digestive Center and Integrative Medicine, please call **410-321-1082**.

For more information about the Johns Hopkins Hospital Division of Gastroenterology & Hepatology, visit our Web site at www.hopkins-gi.org.

Locations

Patient consultations are offered in offices throughout the Baltimore metropolitan area, including the Out-patient Center at The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center and ambulatory out-patient centers at Green Spring Station in Lutherville, White Marsh and Johns Hopkins at Cedar Lane in Howard County. For directions and maps, please visit our web site at www.hopkinsmedicine.org/directions.

Remote Second Opinion Program

For patients who seek a second medical opinion for their digestive or liver disease but are unable to travel, Johns Hopkins Gastroenterology & Hepatology offers a remote second opinion program. This program provides timely recommendations from our physicians for patients who may need help in selecting their best treatment option or want a confirmation of their initial diagnosis. This service is not available for patients residing in Iowa, Louisiana or Maine. For more information, please visit our Web site at www.hopkins-gi.org/secondopinion.

Referral Assistance

Johns Hopkins USA

Johns Hopkins USA provides one point of contact for our out-of-town patients. Our staff can help patients identify appropriate physicians or specialists, coordinate multiple medical appointments, arrange second opinions, and obtain general information on Johns Hopkins' numerous services. In addition, Johns Hopkins USA staff can provide information regarding transportation, lodging and other travel needs. Call **410-735-HUSA (4872)** to talk with Hopkins USA. For family accommodations on the patient floor, see information regarding the Marburg Pavilion on page 48.

Johns Hopkins Medicine International

The professional staff of Johns Hopkins Medicine International coordinates all aspects of international patients' medical care, paying special attention to personal, cultural and travel-related needs. The staff will arrange consultations, second opinions or treatments, and will coordinate appointments in a time-efficient manner. The staff also provides medical records reviews

before the patient travels to the United States, language interpreters, cost estimates and assistance with travel arrangements.

For more information, call **+1-410-955-8032** or visit the Web site at www.jhintl.net.

Accommodations Assistance

Accommodations Office

The Johns Hopkins Hospital has arranged special rates (and shuttle service in some instances) at local hotels for patients and their families. A full-service travel agency is available to help patients and their families with air, hotel or other accommodations. It is open Monday through Friday, 8:30 a.m. to 5 p.m. Please call **1-800-225-2201** or **410-614-1911** for assistance.

Marburg Pavilion

Located in the historic Marburg Building, the Marburg Pavilion offers deluxe accommodations for adult patients. A limited number of private rooms and two-room suites are available for an additional charge and feature fine wood furniture, private baths, entertainment centers and an array of services, such as expanded dining menus and overnight sleeping accommodations for family members. For more information, call **410-614-4777**.

Patient Relations

Patient representatives are available to help resolve any concerns about patient care, interpret the policies and procedures of the hospital, and arrange for services patients may need. At The Johns Hopkins Hospital, call **410-955-CARE (2273)** to speak with a patient representative. Hours are 8:30 a.m. to 5 p.m. and the office is located in the hospital at Carnegie 100.

At Johns Hopkins Bayview Medical Center, call **410-550-0626**

to speak with a patient representative about any patient care concerns. Hours are 8:30 a.m. to 5 p.m. The office is located in the Bayview Medical Office on the main level.

Sign Language

Deaf and hearing-impaired patients can arrange for interpreters or use the TTY in the patient relations offices at both The Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center. For more information, call **410-955-2273** at JHH or **410-550-0626** at Bayview.

For more information, please visit The Johns Hopkins Hospital Web site at www.hopkinsmedicine.org or the Johns Hopkins Bayview Medical Center Web site at www.hopkinsbayview.org

For patient information and a visitor's guide to The Johns Hopkins Hospital, visit www.hopkinshospital.org/patients

Johns Hopkins Medicine Overview

Johns Hopkins Medicine—established in 1995 to unite Hopkins biomedical research, clinical teaching and business enterprises—brings together the Johns Hopkins University School of Medicine and its faculty with the facilities and programs of the Johns Hopkins Health System. The Health System, which has its origins in the founding of the world famous Johns Hopkins Hospital, now comprises three hospitals as well

as other elements of an integrated system, from a community physicians group to home care. The components of Johns Hopkins Medicine are consistently named at the top of national rankings for best hospital and best school of medicine, and its faculty consistently wins the largest share of NIH research funds. Results of this research continue to advance efforts to diagnose, treat and prevent many diseases.



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Division of Gastroenterology and Hepatology
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