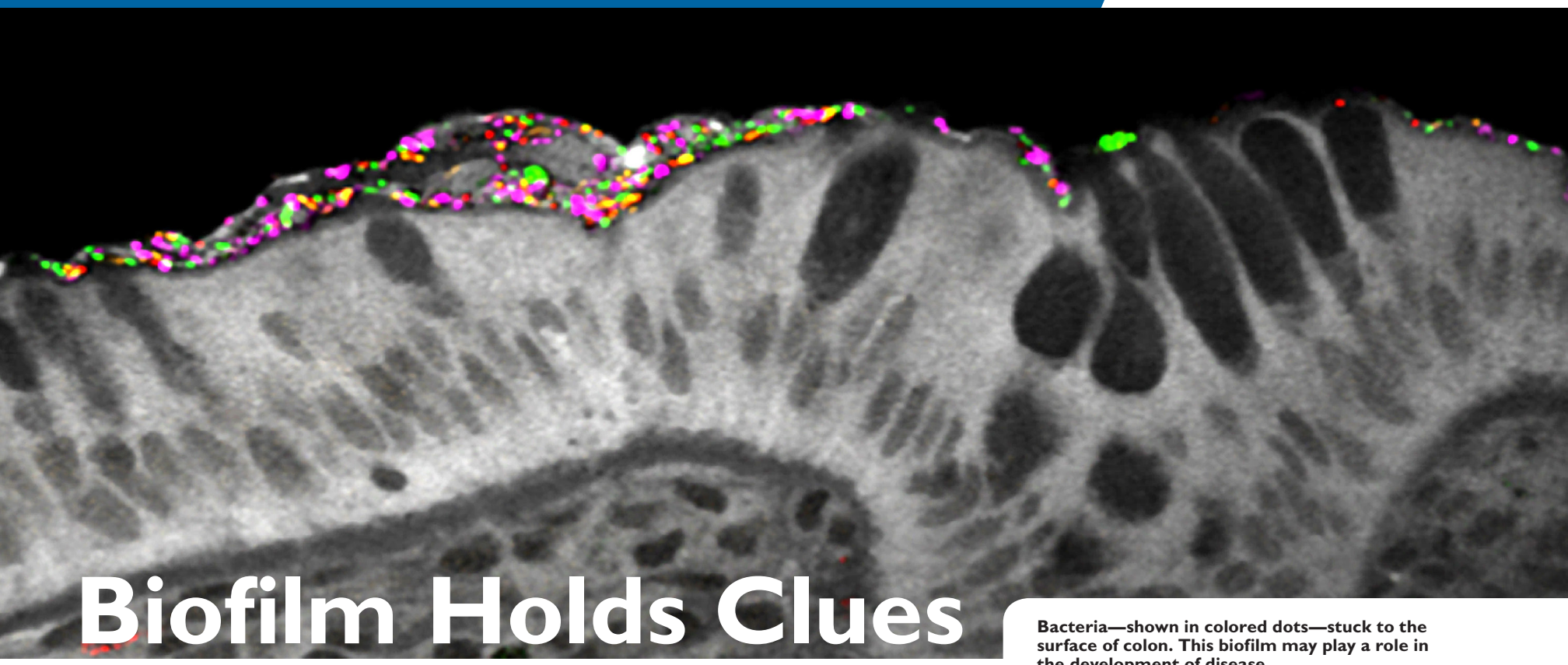
JOHNS HOPKINS
InsideTract

SUMMER 2016

NEWS FROM THE JOHNS HOPKINS
DIVISION OF GASTROENTEROLOGY AND HEPATOLOGY

JOHNS HOPKINS
MEDICINE



Biofilm Holds Clues to Colon Cancer

Bacteria—shown in colored dots—stuck to the surface of colon. This biofilm may play a role in the development of disease.

It's fairly common knowledge that a long-term diet of high-fat red meat and a sedentary lifestyle can be a dependable recipe for colon cancer.

But why? What is it about red meat or a high-fat diet that promotes cancer in the colon? And why is a lack of exercise such a risk?

Francis Giardiello and **Cindy Sears** are taking a look at the microbiome for answers.

"The bacteria in the colon may be influenced by what you eat," Giardiello says, "and these environmental factors can give you certain populations of bacteria that, then, predispose you to colon cancer."

But Giardiello, former director of the Johns Hopkins Division of Gastroenterology, isn't looking at the bacteria that move through the colon; he's looking at the bacteria stuck to the walls—the biofilm. Do the bacteria that adhere to the hollow organ play a role?

THE BACTERIA IN THE COLON MAY BE INFLUENCED BY WHAT YOU EAT AND THESE ENVIRONMENTAL FACTORS CAN GIVE YOU CERTAIN POPULATIONS OF BACTERIA THAT, THEN, PREDISPOSE YOU TO COLON CANCER.

Working with Sears from the Johns Hopkins Division of Infectious Disease, Giardiello is exploring the relationship between biofilm and cancer.

The pair applied for an R1 grant from the National Institutes of Health for what would be the first-ever comprehensive study of its kind.

"We are going to evaluate many patients going through colonscopy," he says, "checking for these biofilms in their colon, and seeing if they associate with colon cancer or polyps."

Giardiello says 141,000 Americans a year get colon cancer. And every year, 50,000 people die in the U.S. die of the disease. He estimates that 70 to 80 percent of colon cancer cases are the result of a poor diet and not enough physical exercise. While genetics and predisposition play a role, they're far less important than the environment created by diet and a lack of exercise, says Giardiello.

Giardiello and Sears also plan to study the biofilm's durability.

"Meaning, if you find it once in, say, January and then rescope the patient in July, are the biofilms still there? And are they the same? Are they durable?" he asks. "If that's the case, this could be a biomarker for risk for colon cancer."

Francis Giardiello

Giardiello cites preliminary data from Sears indicating that the bacteria enterotoxigenic *Bacteroides fragilis* is particularly noxious to the lining of the colon.

"They're causing inflammation," he says. "And that inflammation can lead to cancer." ■

Tony Kalloo

Evolving Approaches

Much of what we see in this edition of *Inside Tract* deals with evolution of one kind or another. Whether it's about bringing medicine and science up to speed with the advances in high-definition images from endoscopic cameras or it's about transforming our transplant medicine program to regularly include patients from further away, we're constantly moving forward in the GI-Hepatology Division at Johns Hopkins.

In the past 10 years, better images from better cameras have changed the field of endoscopy. We can get clear pictures today of things that we only suspected a decade ago.

Mark Lazarev is among the leaders of an international study to bring clinical and diagnostic language into line with what we actually see, rather than default to old terminology.

Similarly, Mouen Khashab now works with Spyglass technology that gives us a clear view of the bile and pancreatic ducts. Prior to high-definition images that guide us into the ducts, we didn't even like to biopsy those areas, since the accuracy of the biopsies wasn't at all reliable.

Now we can see strictures, tumors and other problems for ourselves. It really is a game-changer.

Frank Giardiello is embarking on an important study of the microbiome. But what's different about his study is that he's not studying what's in the colon. He's studying what's *on* it—biofilm.

And finally, Kirti Shetty discusses how we're newly able to bring the Johns Hopkins science, research and medicine that has been for so long associated only with Baltimore to our neighbors in the Washington, DC area. We're thrilled to be able to share our transplant program with our neighbors.

Help Advance IBD Research

IBD research survey

Please take this brief survey designed to strengthen the international collaborative research process by examining variations in diagnosis and treatment of IBD.

Visit expertibd.weebly.com or scan the QR code.

Bringing Bile, Pancreatic Ducts into **Better Focus**

To see a video Q-and-A with Mouen Khashab on the new era of digital cholangioscopy, please visit **bit.ly/next_gen_cholangioscopy**.

For years, many endoscopists have been reluctant to explore bile and pancreatic ducts. In most cases, camera technology to observe the intricate and hard-to-reach duct systems has failed to keep up with other high-definition imaging tools.

Until now.

Mouen Khashab uses a next-generation cholangioscope system to see directly inside the elusive ducts of the pancreas and biliary tree. Khashab and colleagues are among the first clinicians applying the technology in Maryland and the surrounding region.

"Now you can see the bile duct and pancreatic duct the same as you see the esophagus, the colon, the stomach," says Khashab. "So our diagnostics and therapeutics within the pancreatic and biliary systems have gotten much better because of the improvement in the device."

Khashab says the first generation of this scope was fiber optic, which provides a far lower-definition image than the current digital version. "It was much harder to see fine detail," he says, adding that, rather than direct visualization, endoscopists relied on radiography.

> "WE COULDN'T RELY ON THOSE BIOPSIES, SO WE ENDED UP REPEATING THE PROCEDURE AND DOING MORE DIAGNOSTICS. BUT NOW WE CAN ACTUALLY SEE TUMORS." **MOUEN KHASHAB**

"Let's say somebody presented with an indeterminate bile duct stricture or pancreatic duct stricture," Khashab proposes. "We couldn't be sure whether they were benign or malignant." Even biopsies of these areas are only 40 percent accurate, says Khashab.

"So we biopsy this patient and let's say it comes back negative for malignancy. We can't tell him or her 'you have a benign stricture.' We can't rely on those biopsies, so we end up repeating the procedure and doing more diagnostics."

But now, says Khashab, "we can actually see tumors with this new device."

A patient needing a cholangioscopy rests sedated on a table, prepped and ready for endoscopy. Khashab suspects the 43-year-old man with jaundice symptoms has a stricture or a stone. Next to the patient are three high-definition screens: a screen for x-ray guidance, a screen for endoscopy and a screen devoted solely to the new camera.

The scope is inserted through the channel of the standard ERCP scope and guided gently into the bile duct. Images of the tiny duct come to life on the screen, magnified hundreds of times. Irrigation and biopsies are possible, as are laser probes to manage stones.

Khashab found that the patient did indeed have a benign biliary stricture caused by a prior procedure and he inserted a stent into the duct, holding it open for proper function. ■

Normal bile duct

Inflammatory changes of bile duct with underlying malignancy

Liver Care and Transplant for D.C.-Area Patients

Patients in the National Capital Region who need liver transplants needn't make their way to Baltimore for their many workup and evaluation appointments. Instead, Johns Hopkins comes to them.

Hepatologist **Kirti Shetty** has found that many of her patients in the Greater Washington region prefer to stay close to home for their care. "Patients with complex liver disease are pleased to have access to Johns Hopkins specialists right in their own neighborhoods," she says.

As director of hepatology, Shetty leads a Johns Hopkins' regional transplant outreach and care program. The Johns Hopkins transplant program serves patients throughout the National Capital Region. A multidisciplinary team of Johns Hopkins specialists perform evaluations in Bethesda and Frederick, MD. In a single day, patients can consult with members of a diverse group of Johns Hopkins experts which would otherwise only be possible with multiple appointments at different locations." Following the transplant evaluation, we are able to provide ongoing care at the clinic closest to them," she explains. "Through Johns Hopkins Community Physicians, we have clinics all over the region."

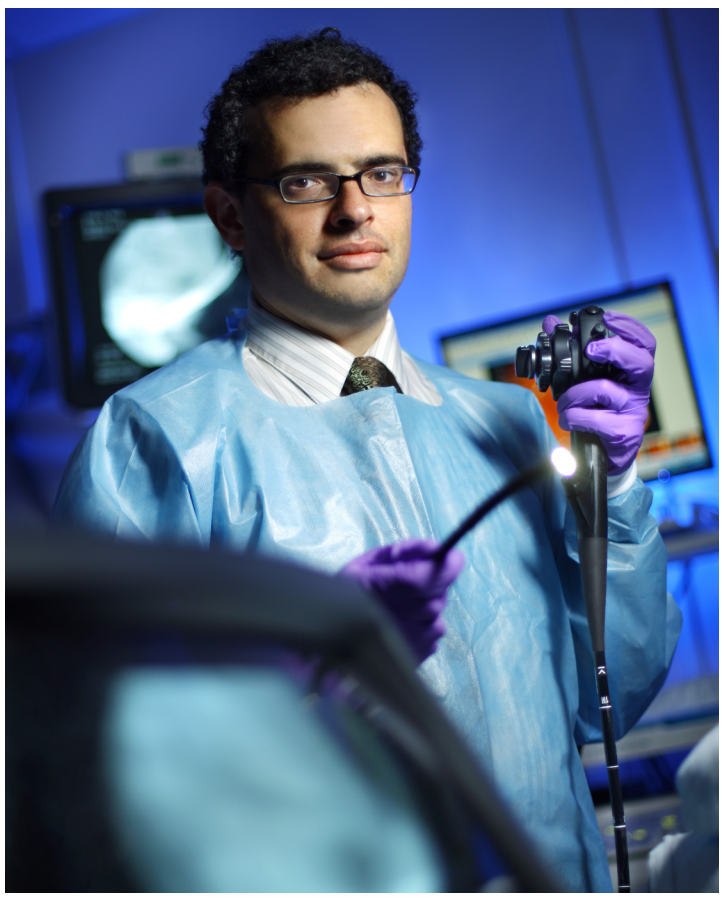
Patients may be hospitalized at the two Johns Hopkins Medicine hospitals within the region, Sibley and Suburban, with the transplant procedure being performed at the The Johns Hopkins Hospital. Patients then transition back to their own communities for follow-up care. "This seamless, integrated system combines the expertise of one of the world's leading transplant programs with the convenience of care close to home," Shetty says. ■

The Johns Hopkins Comprehensive Transplant Center

The Liver Transplant program of the Johns Hopkins Comprehensive Transplant Center has the highest patient survival rate in the mid-Atlantic region and the best one-year patient and graft survival rates in Maryland. With some of the leading liver specialists in the country gathered in one location, this multidisciplinary clinic provides the Washington D.C. area access to the highest quality care and the most up-to-date treatments of advanced liver disease and liver tumors.

Tales from the Crypt

How a group of international researchers aim to redefine mucosal disease



As endoscopy advances through increasingly better imaging, **Mark Lazarev** and colleagues think it's time for diagnosis to catch up with the technology.

Lazarev, a Johns Hopkins gastroentrologist who specializes in inflammatory bowel disease, and researchers from seven other centers globally will soon embark on a study aimed at redefining aspects of mucosal disease.

"Specifically," says Lazarev, "we need to change how we discuss *mild* IBD."

Severe disease is easy to spot, he says. "Even without the latest scopes, we had little trouble identifying and describing cases. But milder forms have given us problems, because there were so many things we couldn't see."

With current high-def microscopy, however, endoscopists can survey the individual intestinal glands called crypts—10 million of which line the epithelial inner surface of the organ. The first signs of disease can be elongation or irregular crypts. Crypt abscesses are also now entirely visible.

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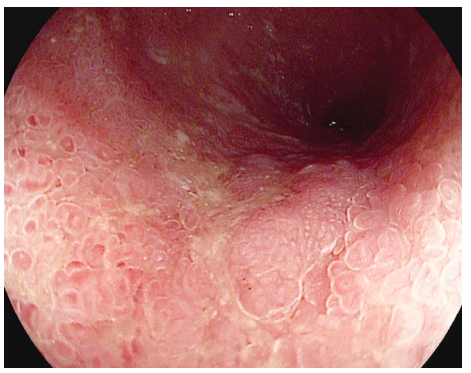

Normal colon under NBI filter showing normal appearing colon crypts

Dilated and elongated crypts associated with active colitis and ulceration

Tales from the Crypt

(continued from page 3)

As just one example of the need to reframe the discussion around IBD, Lazarev points to the common diagnosis of "loss of vasculature." For years, "we thought we were looking at vessels obliterated by disease," he says.

But new cameras have proven there's no loss of vasculature in patients with the disease—merely disrupted vessels. Meanwhile, the language has yet to reflect what endoscopists can now see for themselves.

The first-of-its-kind multicenter study will involve taking videos and pictures within the most diseased segments of the rectum and sigmoid, which will be scored by a number of IBD experts according to a new grading system developed to improve specificity of diagnosis. "We'll also take a biopsy right at the site," says Lazarev, "to further correlate it. ■

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Inside Tract is one of many ways the Johns Hopkins Division of Gastroenterology and Hepatology seeks to recognize and enhance its partnership with its thousands of referring physicians. Comments, questions and thoughts on topics you would like to see covered in upcoming issues are always welcome.

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NEWS FROM THE JOHNS HOPKINS DEPARTMENT OF GASTROENTEROLOGY AND HEPATOLOGY

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