

# PHYSICIAN

**Update**

FOR HOPKINS CLINICAL FACULTY AND REFERRING PHYSICIANS

## To Ferret Out Early Pancreatic Cancer

**W**hat makes pancreatic cancer so deadly is its stealth: Symptoms rarely emerge until the disease is nearly impossible to eradicate.

And though pancreatic cancer is the fifth leading cause of U.S. cancer death, its low annual incidence (about 14,000 people) has made finding a reliable early screening tool about as simple as decoding ancient runes. But for gastroenterologist **Mimi Canto**, pancreatic cancer's Rosetta stone may lie with people known to be at substantially increased risk: those with two or more diagnosed relatives.

Canto is highly experienced in endoscopic ultrasonography, a technique that can detect pancreatic lesions as small as 2 millimeters because it produces images from the inside out. In 1998, she launched a prospective evaluation to determine if EUS could indeed be the basis of an early warning system. The study's pilot phase drew asymptomatic participants from the National Familial Pancreas Tumor Registry, established here in 1994 to track pancreatic cancer patients and their relatives. Among Canto's first tasks was finding out if at-risk people even *wanted* to be screened, an answer that turned out to be a resounding yes. Of those invited to participate, 90 percent were interested, and many spent their own money to fly here.

In a second prospective study (called CAPS 2 or Cancer of the Pancreas Screening), eight of 78 high-risk people she examined with EUS had precancerous lesions suspicious enough to warrant removal. "Compared with other screening tools," Canto says, "that's a high yield."

Seven patients successfully underwent surgery at Hopkins, offering pathologist **Ralph Hruban** an opportunity to study the resected tissue. "We learned," says



**Marcia Canto uses endoscopic ultrasonography to visualize tiny pancreatic lesions.**

Canto, "that there are pancreatic cancer precursor lesions in large and small ducts that cause chronic pancreatitis, even in patients with no history of alcoholism or similar risk factors. This explains why we see chronic pancreatitis-like changes during screening tests so commonly." The study has also provided specimens for biomarker research being conducted by Canto's co-principal investigator, pathologist **Michael Goggins**.

Now, Canto is planning a multicenter study called CAPS 3 to further refine ways of predicting risk.

"When we began," she says, "we didn't know what pancreatic precursor lesions were. Now we know what to look for so we can intervene."

Here, that doesn't mean an immediate trip to the operating room. "With EUS, it's not only a matter of interpretation but feeling comfortable making a clinical

### The Vaccine Gurus

In the latest trial of a vaccine to halt pancreatic cancer, two scientists here have achieved striking results. A year ago, oncologists Liz Jaffee and Daniel Laheru announced that three of 14 patients who'd received their vaccine as an adjuvant treatment were alive and cancer-free seven years later. Now, they've reported on the first two years of a three-year study of 60 men and women who'd gotten the immune-boosting vaccine as a follow-up to surgery and traditional postoperative chemotherapy and radiation. They found 88 percent survival at one year and 76 percent after two, compared to the usual one- and two-year rates of 63 percent and 42 percent.

A result of hundreds of hours in the lab, the vaccine has had considerable fine-tuning, first by Jaffee and then, more recently, when Laheru joined in. The stumbling block was finding the right antigen on cultured tumor cells to cultivate as a lure for patients' immune systems—something that would derive a walloping response against the malignancy. Finally, the researchers tried GM-CSF, an immune-stimulating protein not inherent in the tumor cells. By irradiating the cells enough to render them harmless, and genetically engineering them with the GM-CSF gene, they've created an apparently potent vaccine and expect to begin multicenter trials in two years. "We're hopeful," says Jaffee, "that these early results will hold true."

☎ 410-955-8974 to learn more. ■

recommendation," Canto says. "We're currently not recommending prophylactic total pancreatectomy. We offer all [out-of-town] patients referral to a local center of excellence or to return here for ongoing follow-up. As long as they're being watched, they feel better about their risk."

☎ 410-614-0420 to learn more. ■

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# A Newscaster Rejoins the Hearing World

For more than a decade, longtime Baltimore newscaster Bob Turk battled in private with his relentlessly worsening hearing. At first, he managed with hearing aids. But by late 2004, even the most expensive models were failing him: Hearing in his right ear had plummeted to less than 15 percent, and what speech he caught in his left ear kept breaking up. On the air, he mispronounced words, garbled his intonations, no longer always understood the news anchors.

Although Turk had been getting his audiological care at Hopkins for years, it wasn't until he went public about his hearing loss during a spring 2005 broadcast—and his coworker asked when he planned to do something about it—that he committed to moving forward with a cochlear implant.

Unlike hearing aids, which merely amplify sound, cochlear implants bypass impaired inner-ear structures and instead stimulate the auditory nerve directly via an electrode array surgically embedded in the cochlea. Particularly in recent years, their use in children has been well publicized, yet it is adults with acquired deafness who account for about half the people annually receiving a cochlear



Before receiving a cochlear implant, says Bob Turk, "I was only hearing highs and lows, things like sirens, dogs barking, kids screaming. I had nightmares about waking up totally deaf."

implant at Hopkins.

"There is no age limit," says **John Niparko**, director of otology and neurotology and head of Hopkins' Listening Center. "The desire to maintain connections with those around you is an important factor in maintaining life skills. There is now a wealth of research to indicate that putting one's social interactions out to pasture is unhealthy, physically as well as emotionally."

One reason adults who are no longer

able to hear more than half of amplified words can do well with a cochlear implant is that they have what Niparko calls an existing auditory foundation—an established and secured ability to comprehend the complex signals contained in speech. This is important because the perception of sound that occurs when an implant is first activated a few weeks after surgery isn't automatically understandable. Not only do the external components of the device—a sound processor,

microphone and transmitter—have to be individually mapped and periodically fine-tuned, but the person must be highly motivated to relearn how to interpret the incoming signals. "There's a difference," says Niparko, "between having your sound sensitivity restored and being able to listen effectively. While information processing has made giant leaps forward to improve the quality of the sound signal, the implant listener's drive is key to weaving this technology into daily life. Bob Turk's courage in meeting this challenge daily, with thousands of people watching, is remarkable."

To that end, Niparko's group has created one of the most comprehensive implant centers in the United States. In addition to ear surgeons, the staff includes educators, engineers, audiologists, speech-language pathologists, psychologists, imaging technologists—even cellular biologists. All implant candidates are thoroughly screened, physically, emotionally and psychologically, then closely followed and supported after the procedure, including training to understand speech in such challenging situations as a noisy restaurant.

Still, Bob Turk surprised nearly everyone. "The minute my implant was activated last August, it was like I was in a radio booth with a headset and mike," he says. "I immediately understood what was being said. The next week, I was back on the air. If I were a member of the Listening Center team, I'd be really proud. They're miracle workers."

☎ 410-955-9793 to learn more. ■

## HEMATOLOGY

### The Brodsky Approach to Severe Aplastic Anemia

In June 1999, Mark Strome felt like one lucky guy. All the leading financial publications had recently touted his skill in creating one of the world's most successful hedge funds. And he'd just built a family retreat in Telluride, where he had plans to spend weekends scaling Colorado's 14,000-foot peaks and skiing black-flag slopes. Then the Los Angeles financier woke to the first signal that his future may have hit a roadblock—a nosebleed that wouldn't stop.

Strome drove straight to his physician, who cauterized his nose. When the bleeding kept on, the doctor ordered tests and found that Strome's platelet count was 1,000. "Go immediately to the hospital," he directed. "And don't bump your head or you'll die." A week later, Strome learned he had severe aplastic anemia (SAA). With the immune system rendering stem cells incapable of producing red and white blood cells

and platelets, death usually comes in one to two years.

Strome's L.A. hematologist suggested the standard treatments—bone marrow transplant or the "gold-standard," antihymocyte globulin (ATG). In Strome's case, there was no suitable bone marrow donor, so he went on the drug. But ATG leaves patients wide open to side effects like infection, hormonal imbalance and osteoporosis. Up to half also have a relapse or develop some type of malignant blood disease. Strome followed the script, improving initially but then relapsing. In August 2000, just when he'd run out of options, a friend surfing the Web discovered Johns Hopkins hematologist **Rob Brodsky**.

Brodsky has been achieving extraordinary results treating SAA patients with massive doses of the immunosuppressant cyclophosphamide, which stuns the bone marrow and sends already low blood counts plummeting to zero. Then, he waits as

patients' decimated immune systems begin "rebooting" and return to what Brodsky describes as a "healthy, virgin state, like that of a newborn child." Once that happens, the person's chance of developing SAA again becomes remote.

Two weeks later, Strome was in Brodsky's office hearing that the likelihood he could be cured was about 70 percent. But he would need to endure a lot: 4 consecutive days of drug infusions, nausea, hair loss and risks of infection. His treatments began the next week, followed by terrible nausea and a lung infection. But by the end of October, he was back in L.A., working out five times a week. Today, he's completely healthy.

"I used to be the Lone Ranger," Strome says. "I thought I could solve everything by myself. Now, I'm alive, but the Lone Ranger is dead."

☎ 410-502-2546 to learn more. ■

## On the Road to Treatment for Failing Lungs

**O**ne diagnosis no physician wants to make is interstitial lung disease. This group of more than 130 disorders, which carry the common hallmark of scarring in the tissue between the lung's air sacs, are unpredictable, irreversible and responsive to no known treatments short of lung transplantation. Launched by infections, drug toxicities, exposure to occupational or environmental toxins, an autoimmune system gone haywire, or no identifiable cause at all, their seemingly innocuous early symptoms—shortness of breath, dry cough—turn deadly, leaving patients with an average survival of expectancy of three to four years. Typical medical approaches target lung inflammation with such corticosteroid drugs as prednisone or immune-system-controlling medications like cyclophosphamide. Yet for the majority of these diseases, no therapy has yet been proven to stop or cure them—a situation that pulmonologists **Sonye Danoff** and **Maureen Horton** are bent on changing.

As co-directors of Hopkins' Interstitial Lung Disease Initiative, one of a mere handful of ILD centers around the country, Danoff and Horton provide up-to-the-minute clinical care and second opinions for patients from



**Maureen Horton and Sonye Danoff are taking on "the common final pathway of a thousand diseases."**

around the corner and as far away as Europe and South America. They're also knee-deep in research aimed at

finding new therapies and improving clinical guidelines.

Horton, for example, is the princi-

pal investigator of a Phase II trial of thalidomide for idiopathic pulmonary fibrosis, the most common of the ILDs, which usually shows up in patients over 60 and is often attributed to simply getting older. The thalidomide study, Horton says, grew out of lab work here showing that the once-abandoned drug may prevent progressive lung scarring. Danoff and Horton also are leading Hopkins' participation in a second multicenter look at interferon-gamma-1b (Actimmune), which may prolong survival.

Actively seeking ILD causes, the two recognized a couple of years ago a distinct subset of patients, often in their 30s, who have the rheumatologic condition known as myositis. Although ILD associated with this type of muscle inflammation is considered uncommon, Danoff and Horton now think otherwise and have teamed up with rheumatologist **Lisa Christopher-Stine** to not only integrate clinical care but look for clues to the origins of other ILDs.

"We walk these patients through their lives," says Danoff. "Sometimes we walk them to the end of their lives. Our goal is to keep them healthy as long as possible and ultimately find an early intervention to catch ILDs before they proceed to the end stage."

☎ 410-955-3467 to learn more. ■

## DERMATOLOGY

### A Simple Test to Spot Anal Cancer's Precursors



**Ciro Martins uses high-resolution anoscopy to examine suspicious lesions.**

**I**n the anal dysplasia clinic, where dermatologist **Ciro Martins** spends three half-days each week seeing patients and evaluating patients with abnormal anal Pap smears, he keeps a postcard that could be his mantra. It reads: Every person has a rectum, and any doctor can examine it. And for Martins, who's also an HIV expert, that means going one remarkably easy step beyond the typical digital exam.

Just as several types of sexually transmitted human papilloma virus are well known for their association with invasive cervical cancer, there's strong though still indirect evidence linking HPV infection with anal cancer. What isn't well appreciated, says Martins, is that anal Pap smears can not only detect early HPV-induced precancer lesions but also provide the basis for ongoing follow-up and, if necessary, early treatment.

Although in the general population anal cancer annually strikes less than one person in 100,000, the incidence rises substantially among certain subgroups. The best known may be HIV-positive men, but, Martins cautions, the risk goes well beyond gay men who have

receptive anal sex with men: "Physicians who treat HIV are seeing more and more anal cancer, especially in women."

And being HIV positive isn't the only factor contributing to increased vulnerability, he says. Also in this category are HIV-negative men and women with a history of receptive anal intercourse or anal warts, HIV-negative women who've had an abnormal cervical Pap smear, and anyone who is immunosuppressed by other causes, such as transplant patients.

To help prove that anal dysplasia indeed leads to anal cancer, Martins will be heading Hopkins' participation in a multicenter, five- to seven-year study enrolling 12,000 people that will be part of the National Institutes of Health-funded AIDS Malignancy Consortium. Meanwhile, for the uninitiated, he's produced a CD demonstrating how to do an anal Pap smear.

"So many people think you need special equipment," he says. "Not so. It's Q-Tip in, Q-Tip out, done—in less than a minute."

☎ 410-955-3865 to learn more. ■

## Resuscitation from Right Ventricular Infarction

**B**y November 2005, interventional cardiologist **Alan Heldman** was down to a last-ditch option for 86-year-old Pauline Eichen. In the decade since Eichen had had her first heart attack, her right coronary artery seemed determined to narrow—despite repeated dilation and stenting to keep the vessel open. When Eichen arrived at the hospital last fall with chest pain, Heldman again used a drug-eluting stent to widen her artery. But within days, her chest pain returned, and this time, the artery was occluded. What's more, her stunned right ventricle was barely pumping, launching a cascade of shock, kidney failure and plummeting blood pressure unresponsive to four vasopressors given simultaneously.

Fortunately for Eichen—who was deemed unable to withstand the open-chest surgery required to implant a right ventricular assist device—Heldman had another solution. For months, he'd been discussing with cardiac surgeon **John Conte** and coronary care unit director **Steven Schulman** a novel role for a new left ven-

tricular assist. These VADs, which don't require surgical implantation, take over for the heart's main pumping chamber, extracting blood from the left atrium and sending it on to the rest of the body. Normally, the device is connected to the heart via two canulae: one tube threaded into the left atrium; the other, placed in the iliac artery.

But Eichen's deterioration was a result of *right* heart failure. So, catheterizing both femoral veins, Heldman advanced the cannulae to her right atrium and right pulmonary artery and connected them to the VAD. "The results," he says, "were dramatic. Within 10 minutes, her blood pressure went up by 20 points, we could wean off the four vasopressors, and her urine output resumed."

After three days, Aiken's right ventricle was clearly recovering from its infarction, and the VAD was disconnected. The intervention, Heldman says, allowed Eichen to survive a heart attack that was otherwise unsurvivable. ■

## REPRODUCTIVE ENDOCRINOLOGY

### Preimplant Diagnosis Minus the Guesswork

**A**s recently as fifteen years ago, couples at risk for passing on a severe genetic disorder had two ways to discover early on whether they'd conceived a child with the disease—chorionic villus sampling or amniocentesis. These tests, performed at 10 and 16 weeks' gestation, respectively, could either give peace of mind or present two nerve-racking options: continue the pregnancy or terminate it.

Then, preimplantation genetic diagnosis brought promise of a way to better the odds. With PGD, one or two cells are removed from each of a woman's in vitro fertilized eggs at the eight-cell stage. Each extracted cell is analyzed for the presence of a specific abnormality, such as cystic fibrosis. An embryo not found to have the genetic defect can then be implanted in the woman's uterus.

But what's made PGD iffy, says geneticist

**Garry Cutting**, has been knowing whether you've nailed the single cell's two potentially defective genes for a disorder. "Unlike chorionic villus sampling, which provides millions of testing targets, in PGD you've got only one chance to hit both of those genes," he explains. "If there's any contamination, if you're not working with the cell you think you're working with, you'll get an inaccurate or incomplete diagnosis." As a backup, women are usually encouraged to also undergo CVS or amniocentesis.

To push beyond these sometimes risky checks on accuracy—the very tests PGD should supplant—**Howard Zacur**, director of reproductive endocrinology, and **Jairo Garcia**, head of in vitro fertilization, enlisted Cutting's genetic know-how. Cutting—director of the DNA diagnostic laboratory—and his colleagues spent more than five years collaborating with their IVF counterparts. With the assistance of IVF lab direc-

tor **Yulian Zhao**, they performed over 1,000 assays to validate the lab procedures that would prevent contamination and produce clinically reliable results.

"We were," says Cutting, "rather compulsive about this." As a result, they've whittled their error rate to less than 1 percent, creating the first method to be posted as a clinical, not a laboratory, test on the medical genetics information resource GeneTests. Even more gratifying, says Cutting, was their first case—a baby born without cystic fibrosis to parents carrying the CFTR gene: "All the genetic markers we predicted were there."

Now, they're expanding the test to diagnose virtually any inherited genetic disease. "This is taking translation of genetic discoveries to the next level," Cutting says. "We can avoid having to tell parents that their fetus has a life-limiting disorder."

☎ 410-583-2753 to learn more. ■

## Those Vital Links

Johns Hopkins Medicine offers the following links to physicians in the surrounding community. It also urges M.D.'s to use its Physician Liaison Service to offer suggestions and comments. Good communication, we believe, is vital.

### Resources for Referring Physicians

#### Hopkins Access Line (HAL):

#### Physician-Only Line for Consultations, Referrals and Patient Transfers

1-800-765-5447 (Continental United States)

410-955-9444 (Baltimore area and international calls)

#### Online Referral Directory

[www.hopkinsmedicine.org](http://www.hopkinsmedicine.org)

#### Physician Liaison Service: Concerns or Suggestions for Hopkins Medicine

1-800-759-7734 (Continental United States)

410-502-2737 (Baltimore area and international calls) [jhmcares@jhmi.edu](mailto:jhmcares@jhmi.edu)

#### For Updated CME Program Information

[www.hopkinscme.org](http://www.hopkinscme.org)  
Information: 410-955-3169

Fax registration: 410-955-0807

E-mail: [cmenet@jhmi.edu](mailto:cmenet@jhmi.edu)

#### Johns Hopkins USA: For Out-of-Town Patients

410-955-8032. Ask for Hopkins USA: [HUSA@jhmi.edu](mailto:HUSA@jhmi.edu)

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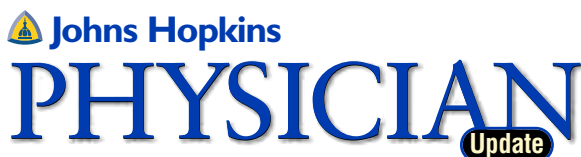
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#### Johns Hopkins Medicine Clinical Trials Information

<http://www.hopkinsclinicaltrials.com/>

#### Kimmel Cancer Center Clinical Trials

<http://www.hopkinskimmelcancercenter.org/clinicaltrials/index/cfm>



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