

PhysicianUpdate

NEWS FOR PHYSICIANS FROM JOHNS HOPKINS MEDICINE

SUMMER 2013



Two New Hands + Two New Arms = A Hopkins First

Last December, 26-year-old infantryman Brendan Marrocco became the only patient at Johns Hopkins to undergo a bilateral arm transplant. While surgeon **W.P. Andrew Lee** and team have performed other radical surgeries involving hands and arms, the complexity of the 13-hour procedure, plus Marrocco's healthy response to it, likely mark a turning point.

The experience raises the likelihood that vascularized composite allografts—multiple-tissue transplants such as those of the arms and hands—will become standard, or close to it, in the near future. “We

see a great psychological as well as physical advantage in a patient to be restored whole,” Lee told a reporter.

The day of the procedure, 16 plastic, orthopedic and microvascular surgeons from Hopkins and other major centers formed two surgical teams for each arm. Earlier, a fifth team had flown out of state to procure the donor's arms and vertebral bodies, the latter of which were for a later marrow infusion.

The result was an above-elbow transplant on Marrocco's right side—joining bone, muscle, vessels, nerves and skin. The left side was more complicated, Lee says, even with the elbow still intact. “We

Teams of surgeons from Johns Hopkins, Walter Reed, UCLA, the Curtis National Hand Center in Baltimore and the University of Pittsburgh rehearsed multiple times, using cadaver arms, for Johns Hopkins' first double arm transplant. The pictured dual team for one arm includes leader **W.P. Andrew Lee** (second from left), who performed the first U.S. double hand transplant in 2009.

designed a way to transplant all of the donor's forearm muscles on top of the remaining recipient muscles and supply them with rerouted recipient nerves.” Usually, recipient nerves are cut at the amputation level. The new way should speed the young man's use of his arm.

Rehab for Marrocco will take several years. Though it's unlikely that he'll see 100 percent restored use, previous patients have motor movement fine enough, say, to tie shoes. “The outcome,” says Lee, “is well worth the effort.” ■

☎ 443-997-1583 for information.

The Sweet Success of Suppression (So Far)

On the day of the transplant, Brendan Marrocco's new hands and forearm came to him courtesy of a donor's kind family and extraordinary surgery. But what lets Marrocco keep his limbs is no less of a phenomenon. The young man underwent a program of “immune modulation” during and around the time of his surgery that not only lowers rejection risk but also cuts down suppressive medication. The approach overturns the status quo.

“The protocol we use to safeguard these composite tissue grafts is unique,” says transplant surgeon **Gerald Brandacher**. Developed by the Johns Hopkins team, it has two goals: Keep patients from rejecting complex transplants. Let patients enjoy a near-normal quality of life.

Hands are targets for rejection, Brandacher says, with their skin and blood vessels bringing “an immunological challenge.” Of necessity, then, standard tactics for hand allograft recipients have included a conservative, lifetime cocktail of three highly immunosuppressive drugs. Toxicity and infection, however, are a constant concern.

Marrocco's treatment underscores the difference. On transplant day, under the new protocol, he received both antibodies and a single immunosuppressant, tacrolimus, to lessen his potential scorched-earth immune response to the graft. Two weeks later, he was infused with donor bone marrow.

“It's not a bone marrow transplant, where you replace the recipient's immune system,” Brandacher says. In Marrocco's case, the goal was to set a fine balance between recipient and donor immune cells. In ways not well understood, the injection reprograms immune response. Recipients' T cells newly tolerate donor tissue as well as their own. The beauty of that? Marrocco should need only mild medication for life, and steroids only rarely.

How Islets Stopped the Pain and Returned One Life to Normal

Alison Sarver had dealt with gastrointestinal problems since she was 18, but it wasn't until March 2012 that the Pittsburgh, Pa., native got a diagnosis—pancreatitis—and with it, hope for a potential recovery.

It started when her mother learned of The Johns Hopkins Hospital Pancreatitis Center, which houses a team of chronic pain physicians, gastroenterologists, pancreatic surgeons, radiologists and pathologists. There, Sarver met with center director **Vikesh Singh**, who recommended that she meet pancreatic surgeon **Martin Makary**.

At this point, Sarver was in constant pain and unable to eat. Her gallbladder had been removed and she relied on a j-tube for sustenance, and she was gradually growing unable to tolerate even that. Surgery, Makary says, was her best option if she ever wanted to live pain-free.

Makary recommended a pancreatic islet transplant—a procedure during which the pancreas is removed and clusters of cells called islets, which are responsible for maintaining healthy blood sugar levels and digestion, are isolated and injected into the liver, where they begin to create insulin.

With the pancreas gone, so is the pain and discomfort. The drawback is that minus a pancreas, patients are unable to produce necessary digestive enzymes and instead have to take them as supplements

with meals. Patients also have an increased risk of diabetes and may eventually have to take insulin.

“The patients we operate on are more than willing to trade acquiring diabetes in hopes of getting rid of chronic pain,” Makary says. “A lot of times there is no other option. They're completely debilitated.”

Sarver underwent the 10-hour operation in November. Her recovery went smoothly, minus a few weeks spent struggling to reintroduce real food to her diet. Today, she says, her life has completely turned around.

“The year before my surgery was one of the worst of my life,” she explains. “Now, I feel like a normal person. I eat without pain. I can support myself, and I'm able to go out and be social. All these are things I never thought would be possible.”

“At Johns Hopkins, the method that we use for pancreatic islet transplantation is unusual in that it involves only a single surgery,” Makary says. “Often, patients must first undergo a separate pancreatectomy, wait for their organ to be processed by an outside laboratory, and then return for a second operation to



By performing necessary lab work during the procedure, Martin Makary says, Johns Hopkins can perform pancreatic islet transplants with one operation instead of the usual two.

transplant the cells. We instead perform all of the lab work in the operating room during the same procedure, saving our patients the frustration, anxiety and pain of having to undergo two separate surgeries for the same outcome.”

“Of the many different kinds of surgery I perform in my practice, the islet transplantation is by far the most dramatic and life-changing,” he says. “People go from being completely disabled and in intense pain to having a normal life restored.” ■

☎ 443-287-3061 for information.



Chris Wolfgang and Anne Marie Lennon are part of Johns Hopkins' multidisciplinary team formed specifically to diagnose, study and treat pancreatic cysts.

Tackling the Pancreatic Cyst

In some cases, a pancreatic cyst can be completely benign. In others, it can be a precursor to cancer. The problem, says pancreatic surgeon **Chris Wolfgang**, is figuring out which is which.

The discovery of a pancreatic cyst is often unintentional—the result, perhaps, of a CT scan or MRI ordered for unrelated reasons, such as to uncover the cause of abdominal pain. From there begins the journey to determine whether the cyst is dangerous or benign.

The Multidisciplinary Pancreatic Cyst Team at The Johns Hopkins Hospital was formed to do exactly that. With six surgeons, a gastroenterologist and experts in imaging and pathology, the team is among the first in the country assembled specifically to diagnose, study and treat pancreatic cysts. “Since 1996, we've learned a lot about the different kinds of cysts,” says Wolfgang. “They're not all the same. There's a certain category of cyst that can be a precursor to benign carcinoma. Intraductal papillary mucinous neoplasms, or IPMNs, for example, carry a 45 to 70 percent risk of becoming cancer.”

“If we know that a patient has a precancerous cyst,” says team member and gastroenterologist **Anne Marie Lennon**, “we'll try to work out exactly what kind it is, how high the risk of cancer is and whether the patient should undergo surgery.”

With advancements in CT and MRI technology, physicians have recognized that pancreatic cysts are more common than ever before realized—they were just harder to find and, thus, less frequently diagnosed. While the increased awareness leads to better detection, the next determination to be made is whether to wait and see what happens or to undergo an extremely invasive operation.

The Multidisciplinary Pancreatic Cyst Team's goal is to ensure that the decision is made with a number of experts who can collectively help determine the best and safest course. “We discuss every case together, which allows the entire group to weigh in,” Lennon says. “The patient is offered a much greater breadth of experience than any one of us alone could offer.” ■

☎ 410-955-5800 for information.

Women and COPD: Suddenly Epidemic but Largely Underdiagnosed

Until a few years ago, chronic obstructive pulmonary disease (COPD) was thought of only as a disease of middle-aged men. Literature reports of the progressive lung disease most often caused by cigarette smoking were exclusively done in males, and physicians trained into the 1990s were taught that it largely affected men.

But over the last 10 to 15 years, the number of women presenting with COPD has sharply increased, says pulmonologist **Enid Neptune**. Today, about 60 percent of COPD patients seen at Johns Hopkins and other centers are women.

This rise reflects the large number of women who began smoking during the women's movement, peaking in the 1980s, says Neptune. COPD is one of several consequences, along with lung cancer and cardiovascular problems, that would present 20 to 30 years later.

Thanks to history, however, "physicians are much less likely to

make the COPD diagnosis in women," Neptune says. "We want to make sure the pulmonary community understands this is an epidemic."

Compounding the problem, COPD research has been underfunded, says pulmonologist **Robert Wise**, head of Hopkins' COPD program.

"There has been very little interest from the public in COPD as a women's disease," he says, "even though more women die from COPD than from breast cancer."

With no cure for COPD, Hopkins investigators have taken on a few research projects to better understand the condition. Wise is the principal investigator for two clinical trials, one of which is evaluating the antihypertensive drug losartan as a way to stabilize or improve lung function in people with COPD. In a previous study in mice, led by Neptune, the drug helped prevent or reverse inflammation and lung damage.

Another trial is testing the potential of the broccoli sprout extract



Robert Wise and Enid Neptune are working to raise awareness of the tremendous rise of COPD in women while seeking better treatments for patients with the disease.

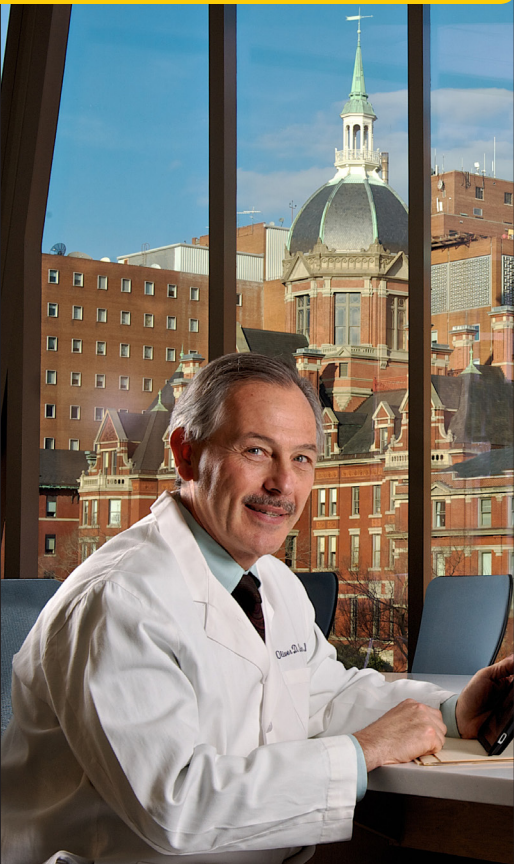
sulforaphane to stimulate Nrf2, a molecule that turns on numerous antioxidant and pollutant-detoxifying genes to protect the lungs from cigarette smoke. COPD patients have significantly lower levels of Nrf2 than nonsmokers. Additional studies are planned to explore the mechanisms of sulforaphane to increase bacterial clearance and restore steroid sensitivity in COPD lung cells.

On the basic science side, Neptune wants to model the effects of cigarette smoking in women in an animal

model, to identify affected pathways and help with more targeted drug development or smoking cessation programs for women.

Studies have shown that women have a harder time quitting smoking, but when they do, they have greater recovery of lung function. And, says Neptune, "There is no point in time in which you don't get a life expectancy benefit from stopping smoking." ■

☎ 410-550-5864 for information.



"Patients typically improve two to three lines on the vision chart with the implantable telescope," says Oliver Schein. "And while nothing yet restores reading and driving ability at this stage of macular degeneration, he says, "we've seen a jump in patients' quality of life."

Putting the Telescope Where?

New help for patients with advanced macular degeneration

It's a bit like the "give me your tired" inscription on the Statue of Liberty, only with an ophthalmic twist. Johns Hopkins now offers an implantable miniature telescope (IMT) to appropriate older patients with end-stage age-related macular degeneration, but, says ophthalmologist **Oliver Schein**, many have not heard about it.

"I know a lot of perfect candidates are out there," he says—patients whose lives would greatly improve with the IMT but who feel sure that nothing can help their vision." As more connect with it, he says, that will change.

Schein, who directs the Wilmer Eye Institute's Comprehensive Eye Service, is Johns Hopkins' expert on the tiny magnifier, federally approved in 2010. He led Wilmer's participation in clinical trials that fed into studies at 20 sites nationwide. And now he's medical monitor for its several-year follow-up surveillance study.

"An implanted telescope obviously can't reverse macular degeneration,"

he says, "but it helps patients resume many favorite activities. It returns a measure of independence."

At 4.4 millimeters in length, the IMT is a telescope that replaces the lens in one eye. It channels incoming light to a remaining healthy but narrow retinal margin outside the damaged macula. Patients still have blacked-out central vision, but gain clarity—through magnification—for the immediately off-center.

Magnification for patients with the condition isn't new. Glasses with a fixed external telescope, for example, are a staple of low-vision care. "But the IMT can be a much more effective way to deliver magnification," Schein says.

"Having the telescope inside the eye increases the width of the visible field three or four times that of the external, fixed version," he says. Tracking is also significantly better. "Since the IMT is within the eye, patients can track objects, despite their head or eye movements."

Schein doesn't discount the anti-stigma benefit of the implant. Patients value their normal appearance and the ability to make eye contact.

While being cleared for the implant, besides an FDA age 75 requirement, there's an in-depth evaluation to rule out precluding health conditions, as well as testing to assure benefit from the IMT. Patients are also coached on what to expect after surgery. Surgical recovery is fast. However, training the brain to coordinate sight from the implanted eye, which loses peripheral vision, and the nontelescopic eye that sees only peripherally takes months of training from experts in low-vision rehab.

So far, patient response is enthusiastic, Schein says. And there's a real plus: Medicare covers the IMT. ■

☎ 410-955-0580 for information.

Johns Hopkins CareLink

Johns Hopkins Medicine is pleased to introduce Johns Hopkins CareLink, a free Web-based portal that enables you to have real-time access to your patients' electronic medical records, lab results and imaging reports; provides CareLink in-box notification of your patients' outpatient visits and hospital admissions and discharges; and also enables you to send/receive secure messages with Johns Hopkins providers and order consults with Johns Hopkins specialists. Enroll now and begin accessing your patients' information on July 1, 2013. For more information on Johns Hopkins CareLink and enrollment instructions, please visit www.hopkinsmedicine.org/carelink. Enrollment is quick and easy. Once you have enrolled, you and your office colleagues can take brief online training and receive technical support by calling 855-284-5465.

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Secure site for viewing your patients' information

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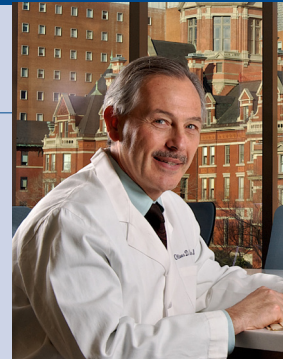
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