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INTERNATIONAL MEDICINE

PHILADELPHIA INTERNATIONAL MEDICINE® NEWS BUREAU

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For immediate release:

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Editors note: Research, new techniques and improved facilities by Philadelphia International Medicine hospitals and physicians may lead to new ways to treat some of our most challenging diseases. Below are just some examples from our hospitals.

New Hope for Patients Facing Leg Amputation

PHILADELPHIA— Eight months ago, 46-year-old Fareed Tucker was told he needed to have his right leg amputated...immediately. Instead, he sought a second opinion from Temple University Hospital vascular surgeon Eric T. Choi, MD. Temple University Hospital is a member of the Philadelphia International Medicine network.

Today, Fareed still has both of his legs and can walk without the aid of crutches. “What Dr. Choi did for me is a blessing and a miracle,” says Fareed.

Fareed had been in nearly constant pain for several years, suffering from peripheral vascular disease and a genetic clotting disorder. “My grandmother had her leg amputated years ago,” he recalls. “I was on and off blood thinners for years, and I had several bypass surgeries for my lower leg at other hospitals. This past summer, after my fifth surgery, my foot was turning black and I had no feeling in it. The doctors told me that there was nothing more they could do, and they tried to sell me on a prosthetic leg,” says Fareed. “My brother is an OR technician at Temple, and he said he heard about a new doctor there – Dr. Choi – who specializes in saving people from having their leg amputated,” Fareed adds.

“No patient should have a leg amputation before seeing us,” declares Dr. Choi, who joined Temple last summer as Chief of Vascular Surgery.

For a number of years, Dr. Choi has been studying techniques to improve blood flow to prevent the need for amputation – and he now brings that clinical, research, and teaching expertise to his patients and colleagues at Temple. “There are patients with critical limb ischemia (insufficient blood flow) who

have been told by their physician that they have to have a leg amputation,” notes Dr. Choi, “but there are alternative, multi-specialty therapies available at Temple to enhance the traditional approaches to limb salvage. We believe that no one in the greater Philadelphia area should have a leg amputation without seeing us first for these alternative therapies.”

Over 150,000 leg amputations are performed in the U.S. each year – over 1,000 of them in the Philadelphia region. “Particularly in the diabetic population, there are unacceptably high numbers of patients who have leg amputations,” says Dr. Choi. For a diabetic, it could be a just a matter of days before a serious foot infection requires an amputation. Other groups are also vulnerable, Dr. Choi notes, including smokers and patients with kidney failure.

To address these problems, Dr. Choi is spearheading the Limb Salvage Center at Temple University Hospital – the first in the region to offer a limb-saving model of focused comprehensive care.

Preventing tissue death and promoting healing requires that arterial blood flow be restored without delay. Instead of going from specialist to specialist in search of the right physician who might save their leg, which could take weeks and cause their problem to worsen beyond repair, patients who come to TUH's new Limb Salvage Center receive one-stop, multidisciplinary management that brings all medical perspectives to the patient at the same time. Patients receive a customized assessment and comprehensive treatment in a timely manner – when time is particularly precious.

Patients get treated quickly because the Center brings together all the specialties they need in one place with a multidisciplinary team of physicians and ancillary care professionals – including vascular surgery, podiatry, diabetology (a subgroup of endocrinology focusing on diabetic patients), cardiology, plastic surgery, orthopaedic surgery, interventional radiology, physical therapy, and orthotics (devices that support or correct limb function). “We could provide the opportunity to save their leg that other medical centers perhaps would not be able to,” Dr. Choi declares.

TUH's Limb Salvage Center is fortifying its comprehensive interdisciplinary treatment approach with the power of cutting-edge research. Dr. Choi is the first to bring clinical trials to Philadelphia that focus on angiogenesis in the leg – a technique which entails improving blood flow to the leg using innovative therapies designed to grow new blood vessels. “Temple is the only major academic medical center in the Philadelphia region looking at angiogenesis as a possible therapeutic alternative to leg amputation,” says Dr. Choi.

The Center's progressive research trial approach will evaluate several cutting-edge therapeutic options to patients who would face otherwise life-altering or life-threatening difficulties.

One of those trials uses therapy that stimulates bone marrow to create stem cells as a means to grow new blood vessels and improve blood flow to the leg. “There are so many diabetics out there whose wounds fester, and they don't know about other opportunities to save their leg,” says Dr. Choi. “I've seen

young patients who required leg amputations that could easily have been avoided if they had come to us earlier.”

TUH’s Limb Salvage Center also sees “traditional” patients with wounds that need urgent attention. “If they have a foot or leg wound, we will see them. We can refer them to other specialists if their wound does not pose a serious risk of amputation,” Dr. Choi notes. “For patients who are at serious risk,” he says, “we want to be the go-to experts to help prevent that final option of amputation.”

“From my first meeting with Dr. Choi, I trusted him. He’s very down-to-earth. He looked at me in my face and said, ‘We got it,’” recalls Fareed.

During the surgery, Dr. Choi harvested a vein from Fareed’s left arm and grafted it to his injured leg. “Doctors would not traditionally use the vein from the arm. Technically it’s very difficult,” says Dr. Choi, of the surgery, “but we don’t give up on a patient’s leg...we go that extra step.”

“When I woke up in the recovery room after surgery at Temple, I could already feel the difference. My toes weren’t feeling numb, my foot wasn’t cold, and there wasn’t that throbbing, internal pain,” says Fareed.

Eight months later, Fareed now walks up and down stairs unassisted. “I’ve been able to do that for the past month or so,” he declares, proudly. He got rid of his crutches six weeks after his surgery at Temple, and he uses a cane for longer walks.

Fareed recently visited Dr. Choi for a follow-up visit. “He checked the pulse in my foot, ankle, and leg. The pulse was strong, and Dr. Choi told me, ‘You’re doing great!’”

“I told Dr. Choi, ‘You’re my champion,’ and that made him smile,” says Fareed.

Reflecting on his experience for a moment, Fareed beams: “I would be on one leg right now if I hadn’t seen Dr. Choi. I’m glad I came to Temple.”

For more information, see PIM’s website at www.philadelphiamedicine.com. To make an appointment, contact PIM at physicians@philadelphiamedicine.com, or call 215-563-4733. For more information about Temple University Hospital, see their website at www.tuh.templehealth.org.

Fox Chase Researchers Develop a Screen for Identifying New Anticancer Drug Targets

Tumor suppressor genes normally control the growth of cells, but cancer can spring up when these genes are silenced by certain chemical reactions that modify chromosomes. Among the most common culprits responsible for inactivating these genes are histone deacetylases, a class of enzymes that remove acetyl groups from DNA-scaffolding proteins, and DNA methyltransferases, a family of enzymes that add methyl groups to DNA.

Drugs that counteract these enzymes, and thus reactivate tumor suppressor genes, are promising cancer therapies. For example, histone deacetylase inhibitors have been approved for the treatment of a

type of T cell lymphoma, and are being tested in clinical trials for the treatment of a wide range of cancers. Similarly, DNA methyltransferase inhibitors have been approved to treat a certain kind of leukemia, and are undergoing clinical studies for the treatment of other cancers. But these medications can have serious side effects. Now, Fox Chase Cancer Center postdoctoral associate Andrey Poleshko, PhD, along with Research Professor Richard A. Katz, PhD, and their colleagues have developed a screen to identify proteins that work in conjunction with these enzymes to repress gene expression.

Finding additional proteins that inactivate tumor suppressor genes, and understanding how they work, could lead to the broadening of this class of therapies beyond the two enzyme families, Dr. Poleshko said. “If we can find a way to block the action of such proteins, it may be possible to reactivate aberrantly silenced tumor suppressor genes and restore controlled growth in certain cancer cells,” he noted. Such an approach would avoid interfering directly with the vital chromosome-modifying enzymes.

The researchers genetically programmed human cells to glow fluorescent green upon reactivation of the silent genes they harbor. By shutting down the activity of genes one by one and observing whether cells turned green, they were able to identify factors that help to suppress gene expression.

The method was efficient enough to permit screening of the entire genome, including 21,122 genes, and revealed 128 factors that are involved in regulating gene expression.

Research Assistant Professor Margret B. Einarson and Professor Anna Marie Skalka from Fox Chase are co-authors on the study.

Minimizing Side Effects from Chemoradiation Could Help Brain Cancer Patients Live Longer, Jefferson Study Suggests

Minimizing neurological side effects in patients with high-grade glioma from chemoradiation may result in improved patient survival, a new study from radiation oncologists at the Kimmel Cancer Center at Jefferson suggests. These findings were reported in the April issue of the British Journal of Cancer.

The researchers found that the occurrence of early side effects, such as fatigue and loss of short-term memory, that manifest during or soon after treatment is significantly associated with both late side effects (after 90 days) and overall survival in patients who suffer from malignant brain tumors, such as glioblastoma.

High-grade glioma patients who did not experience neurological side effects during chemoradiation for the brain cancer were found to have lived four months longer compared to those who did experience such effects.

The findings suggest the importance of normal tissue damage in determining long-term survival and how minimizing side effects could end in more positive outcomes. The team reports their findings

from a retrospective analysis of high-grade glioma patients from the Radiation Therapy Oncology Group (RTOG) database.

“As survival in glioblastoma multiforme increases, the prevention of treatment related side-effects becomes more important,” said Yaacov Richard Lawrence, MRCP, an assistant professor in the Department of Radiation Oncology at Thomas Jefferson University and director of the Center for Translational Research in Radiation Oncology at Sheba Medical Center in Israel.

“It is generally considered that the only way to improve survival in malignant brain tumors is to more effectively attack the tumor,” Dr. Lawrence said. “Fascinatingly, our research suggests that damage to surrounding normal tissue may also play a role in determining a patient's long term outcome.”

There are approximately 17,000 primary brain tumors diagnosed in the United States each year, 60 percent of which are gliomas. The most common and malignant glioma is glioblastoma, the type of brain cancer that claimed the life of Senator Ted Kennedy.

Standard treatment for the cancer typically includes surgery, radiation and chemotherapy after the tumor is identified. It is often impossible to determine whether these treatments, the combination of these treatments or the tumor itself cause neurological symptoms, which include fatigue, headache, nausea, motor/sensory disturbance, short-term memory loss and/or seizures.

For the study, researchers analyzed data amongst 2,761 patients from 14 RTOG radiation therapy glioma studies that accrued patients from 1983 to 2003. Patients considered were more likely to have side effects if they were older, frailer, had more symptoms, and were receiving radiation twice daily.

“Our results support the personalized approach to brain tumor management currently being developed within the Jefferson Multidisciplinary Brain Clinic, and emphasize the importance of minimizing side effects,” Dr. Lawrence said.

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