

Study on Vietnam-era women veterans will be largest ever

Christmas, 1968. Army nurse Joan Furey, a curly-haired 22-year-old brunette, was visiting her folks on Long Island. She broke the news to them: She had requested to go to Vietnam.

“They were very emotional, crying. They were very, very proud, but also very frightened,” she recalls. Her dad, a decorated World War II combat veteran, hugged her and told her to take care of herself.

A little over a year later, Furey would come back home a changed person. What she had seen and experienced as a nurse, she says, “was beyond anything civilian life could prepare you for.”

Understanding the experience of women like Furey and the long-term health effects of their service in Vietnam is the goal of a new VA study. As many as 10,000 women, most now in their 60s, are expected to take part. The sample will include women who served in Vietnam and, for comparison, those who served stateside or elsewhere in Asia, such as in Japan, Korea, Guam or the Philippines.

“We’re going to be looking at current and lifetime prevalence of a range of physical and mental health outcomes,” says study co-chair Kathy Magruder, PhD, MPH, an epidemiologist at the Charleston

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Lifesaver—Time/Life portrait of “Nurse Hamilton,” one of about 8,000 women who served with the U.S. military in Vietnam during the war there.

Prostate cancer vaccine in phase 2 clinical trial



More than 80 men with advanced prostate cancer are expected to take part in a trial at the Iowa City VA and University of Iowa to test whether an experimental vaccine can beat back the disease.

The treatment, says lead researcher David Lubaroff, PhD, is not a vaccine in the way most people think of the word. “When people hear ‘vaccine,’ they usually think prevention of a disease. But a

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With his wife, Nancy, looking on, study volunteer John Kane undergoes an exam with VA nurse researcher Dr. Karen Griffith.

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(S.C.) VA Medical Center. She notes that the study is the largest and most comprehensive effort to date to look at this population.

Among the key questions the researchers hope to answer: How many of the women developed posttraumatic stress disorder or depression after their service, and how many cope with these conditions till today? Are these conditions more prevalent among those who served in Vietnam, and to what extent have they led to physical health problems?

Magruder says it's difficult to predict whether the prevalence of PTSD will be similar to what was found when smaller groups of Vietnam-deployed women were studied in the 1980s. Then, it was about 8.5 percent.

“There are cases of remission, as well as new onset and delayed onset. There could be new traumas totally unrelated to military service,” notes Magruder. “Also, we’re using different instruments now—there’s a whole new diagnostic system. So we don’t know what we’re going to find.”

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Data seeker—Dr. Kathy Magruder is co-chairing a VA study on the long-term health outcomes of Vietnam-era women veterans.

Chairing the study with Magruder are Amy Kilbourne, PhD, MPH, a mental-health researcher for VA in Ann Arbor; and Han Kang, DrPh, who directs VA’s Environmental Epidemiology Service and the War-Related Illness and Injury Study Center in Washington, DC.

About 8,000 of the women VA expects to enroll in the new study were part of earlier research by Kang on birth outcomes. That study, published in 2000, found higher rates of birth defects in the children of women who had served in Vietnam compared with those who had served elsewhere. The causes for the increased risk remain unknown, but researchers believe they may include exposure to herbicides such as Agent Orange.

The new study will include mail surveys, phone interviews and reviews of medical records. Teasing out the complex links between Vietnam deployment and various health factors—especially over the course

of 40 years—will be a challenge for the researchers.

Says Magruder, “There are two things we can be really certain about—whether they served in Vietnam or elsewhere, and second, their current mental and physical health.” She points out that most of the prospective respondents are nurses and have experience reporting health conditions.

In terms of mental conditions, the researchers will ask mainly about PTSD, depression, anxiety and substance abuse. The physical conditions they’ll focus on include cardiovascular disease, diabetes, multiple sclerosis, Parkinson’s disease, brain cancer, breast cancer, and gynecological cancers. Some of the conditions have been linked in past research to exposure to trauma or environmental toxins; others don’t have a particular military tie-in but are common among aging women.

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The study at a glance

- About 8,000 women served in Vietnam during the war, some 85 percent as nurses. In total, some 250,000 women served in the U.S. military during the Vietnam era.
- The new VA study will include mail surveys, phone interviews and medical-chart reviews for 10,000 women who served in or near Vietnam or in the U.S. during the Vietnam War.
- Researchers will assess the lifetime and current prevalence of PTSD and other mental health conditions and characterize the women’s physical health and disability.
- The study is funded by VA’s Cooperative Studies Program. VA will hold a briefing on the study in October in Silver Spring, Md., for representatives from major veterans’ organizations.

A time and place to heal

Today, 40 years later, Joan Furey can still see the blood-soaked uniforms.

“It was not unusual for [nurses, doctors and corpsmen] to leave at the end of the day and their uniforms would just be covered in blood, because of patients hemorrhaging, casualties coming in right from the battlefield,” she recalls. “People have no idea, because you rarely if ever see that in a hospital in the United States.”

Furey, now 63, worked a year as an intensive-care nurse at the 71st Evacuation Hospital in Pleiku, in the Central Highlands of Vietnam. She had worked beforehand in the ICU at an Army hospital in California that received casualties from overseas. But even that, she says, couldn’t prepare her for what she would face in the war zone.

“I can remember my first day in the ICU there. It’s one of those memories that’s emblazoned in my mind.” Her first patient was a young GI who had sustained a spinal cord injury, skull fracture and chest wounds in a mortar attack. “They told me what I had to do. I was terrified. But one of the other nurses and one of the corpsmen worked with me and taught me how to do it.”

From that day, her skill and confidence grew. There was no alternative. A team of three nurses and two corpsmen took care of 30 patients. They worked 12 hours a day, six days a week. During a “push”—a mass casualty situation—the days could stretch to 18 hours.

“There was no down time,” says Furey. “Everybody worked very hard and was very committed. I think we gave excellent care and were able to save a lot of lives.”

Attacks on hospital add to stress

Along with caring for the wounded, there were other challenges: insects, monsoons, roaming tigers—and red alerts, signifying incoming rockets or mortars. The nurses would don helmets and flak vests and crawl around from bed to bed to check on their patients. The beds had extended frames on which were placed spare mattresses, to shield patients from falling debris.

“There was a lot of stress,” recalls Furey. “I don’t think I was aware of how much until I got home. When you’re in the situation, you have to push down a lot of the overwhelming emotions associated with it. The kind of casualties we took care



‘Fighting Fourth’ member—Joan Furey, who received a Bronze Star for meritorious service after her tour as a nurse in Vietnam, receives a certificate from then-Maj. Gen. Donn Pepke naming her an honorary member of the Fourth Infantry Division.

of—multiple amputations, severe disfigurements, severe burns—if you got caught up in the emotions, you wouldn’t be able to do your job. So you learn to detach.”

Homecoming: Few people to talk with

Coming home in 1970, Furey had few people to talk with about what she had gone through. The friends she had known in high school were partying at discos. “I would think, how could they be doing this? Don’t they have a clue about what’s going on? I thought I would never fit in this world again.” Given the country’s political climate, she didn’t readily volunteer to people she met that she had served in Vietnam—let alone express pride in what she and her fellow nurses had accomplished. “They would call you a warmonger, a baby-killer. They would say, how could you possibly be *proud*?!”

It was five years or so before she “could really feel part of things again.” During that time she had sleep trouble, depression, intrusive thoughts. “I definitely had what would come to be known as textbook PTSD. But I didn’t know it—whether that’s good or bad, I don’t know. You just kind of learned to live with it—you figured this was the price you paid. I knew I was emotionally wounded, but I didn’t know quite what to do about it or what it was all about. I was still operating under that old belief that you were supposed to come home and

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Focus on mild TBI—

Dr. Brooks King-Casas (right), with Baylor College of Medicine and the newly funded “Neurons to Networks Center for Rehabilitation Research” at the Houston VA Medical Center, discusses an MRI brain scan with John Buikema, a research intern and Iraq veteran. The new VA center of excellence, led by Dr. Harvey Levin, will focus on improving diagnosis of veterans with mild to moderate traumatic brain injury (TBI). The center will also develop and evaluate treatments involving virtual reality and neurobiofeedback.

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Along with probing the prevalence of various conditions, the researchers will ask about demographics and life and military factors such as years of nursing experience, pre-existing health conditions, childhood traumas, wartime exposures or injuries, homecoming, social support, and health behaviors, such as cigarette smoking or alcohol use.

Magruder points out that even though four decades have passed since the war, she and her team expect that study volunteers will harbor vivid memories of their wartime experiences and how they coped afterward. Many may still struggle with mental or physical illness linked to their service. “For many of these women, the effects of the war are still present in their daily lives,” says Magruder.

Most of the women expected to take part in the study have not been regular users of VA health care. Nonetheless, VA—which has ramped up programs for women in recent years—will use the results to improve care and services for this Vietnam-era population.

“These women, for the most part, are in their early 60s,” notes Magruder. “They may have a lot more years. It’s important for us to know what they’re dealing with.”

The findings may also shed light on what the newest generation of women veterans—those returning from Iraq and Afghanistan—may face in the years ahead. —

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be OK and just go about your business. No one had ever said that wasn’t what happened.”

It wasn’t until the early 1980s, when she was working for VA as a nurse and got involved with a local Vet Center, that Furey finally started sharing the pent-up emotions. She also saw a private therapist.

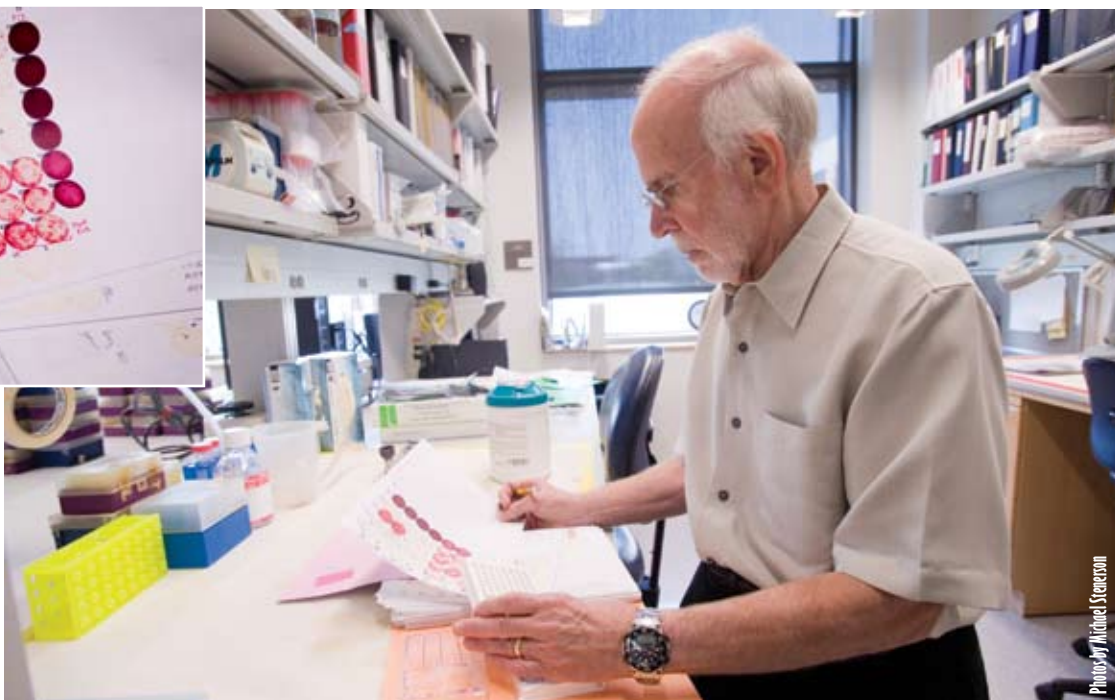
Furey would go on to work 30 years for VA—mostly in nursing management—and help create programs for women with PTSD. In 1994, she was named to lead the agency’s new Center for Women Veterans. She served seven years in that role, often testifying before Congress on women veterans’ issues and driving numerous initiatives in health care and benefits.

The VA work was critical to her healing, as was the Vietnam Women’s Memorial. Furey helped raise money for the memorial, dedicated in 1993, and has visited there often. “It’s phenomenal, the experience people have with the memorial, coming together and reuniting over this event that had such an impact on you. It gives you a place to do what you couldn’t do over there, which was to grieve.”

Twice, she met veterans she had helped nurse back to health from severe wounds. Other chance meetings also had an impact: At the dedication, recalls Furey, a man in fatigues came over to her and two other nurses and gave them a bouquet of roses. “He said ‘A nurse saved my life in Vietnam, and I don’t know her name. I’m going to give these to you, because I know you did the same for someone out there, and I want to thank you for all of us.’” —



Combating cancer—In his lab, Dr. David Lubaroff goes over test results that show how patients are responding to a vaccine against prostate cancer. The red spots indicate the presence of immune T cells that attack cancer cells.



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vaccine’s role is to produce an immune response against the antigens—the proteins associated with that vaccine.”

In Lubaroff’s vaccine, the antigen is prostate-specific antigen, or PSA. The protein, made in the prostate, helps keep semen watery. In cancer and some benign conditions, more PSA escapes into the bloodstream. For that reason, PSA tests are commonly used to screen for prostate cancer, with higher levels signaling the need for additional tests.

The men in the Iowa trial have cancer that has come back and spread even after surgery or radiation. Some have also undergone hormone therapy. None of them have a prostate gland any longer, due to the aggressive treatment they underwent to try to wipe out and contain the disease. In fact, the absence of a prostate is crucial to how the experimental therapy works. The vaccine contains the gene for PSA, inserted into a non-reproducing adenovirus. In gene

therapy, scientists often use these viruses, which cause the common cold, as carrier molecules to ferry genes into cells.

When the immune system detects PSA, it responds by sending antibodies and T cells—a type of white blood cell—on the attack to kill PSA-secreting cells. In the case of the study participants, who no longer have a prostate, the only cells

making PSA are the cancer cells that have spread from the gland and into other parts of the body. These malignant cells continue to make PSA even though they are no longer in the prostate.

So in theory, the vaccine will kill cancer cells with no damage to healthy tissue.

Vaccines are elusive goal for cancer researchers

Many scientists have tried similar approaches. So far, though, no vaccine designed to treat cancer has been approved by the Food and Drug Administration. Cancer cells have proved ingenious at outsmarting the immune system.

Lubaroff, however, is hopeful, partly on the basis of earlier animal studies, that his lab will be among the first to develop an effective vaccine to treat cancer.

“It’s an important goal that many immunologists in cancer research are trying

Cancer vaccines

- *Cancer preventive* vaccines aim to prevent cancer from developing in healthy people. The FDA so far has approved two of these: one against the hepatitis B virus, which can cause liver cancer; and one against human papillomavirus, which causes cervical cancer.
- *Cancer treatment* vaccines target cancers that have already occurred. They stimulate the immune system to detect and attack cancer cells. To date, the FDA has not approved a vaccine of this type.

Adapted from www.cancer.gov.

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Photo by Cpl. Arthur Shurtzberg

Stress reaction—Troops serving in operations Enduring Freedom and Iraqi Freedom, such as these Marines conducting a nighttime patrol in Helmand province, Afghanistan, often face longer, multiple deployments and high exposure to stressors that can increase the risk of substance abuse disorders. These disorders commonly occur along with war-related problems such as PTSD, anxiety, depression, sleep disturbances, traumatic brain injury, and chronic pain.

VA, NIH to fund \$7 million in substance abuse studies

Effort to focus on troops, veterans of operations Enduring Freedom and Iraqi Freedom

VA is collaborating with the National Institutes of Health to fund \$7 million in research on problems related to the use of alcohol, tobacco and drugs—both prescription and illegal—among U.S. military personnel who have served in Iraq or Afghanistan.

“This is the first large-scale interagency effort on this topic,” notes Theresa Gleason, PhD, a program manager with VA’s Office of Research and Development. She says the initiative grew out of interagency meetings followed by a scientific conference held earlier this year. “We realized we could do more as a group to address these issues.”

VA will partner with the National Institute on Drug Abuse (NIDA), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Cancer Institute on the initiative. Each agency will fund studies relevant to its particular mission. The focus will be on identifying the causes of substance use and abuse and improving screening, prevention and treatment.

A VA study appearing this month in the *American Journal of Public Health* found that of nearly 290,000 Iraq and Afghanistan veterans who were first seen in VA between 2002 and 2008, about seven percent had alcohol use disorders. Three percent had drug use disorders. Tobacco use was not addressed in the study, but

statistics show that VA treats nearly 500,000 veterans each year for nicotine dependence. These issues often occur along with war-related problems such as traumatic brain injury, posttraumatic stress disorder, pain, depression, anxiety, and sleep disturbances. Overall, the impact on individuals and families can be huge.

“Working in collaboration with key federal agencies, we hope to learn more about how to address the array of social and emotional problems caused by the trauma of war that bring so much pain to soldiers and their families,” said NIDA Director Nora D. Volkow, MD, in a press statement. “Even though they are no longer in combat, many of these brave men and women are now fighting substance addiction — another dangerous enemy.”

NIAAA acting director Kenneth Warren, PhD, added: “The transition period as soldiers withdraw from battlefield stress and face the rigors of readjusting to life at home can be a critical turning point. This partnership will enhance our efforts to find solutions to the complex alcohol and substance abuse problems that plague our soldiers and their families.”

VA and NIH officials estimate that about 20 studies will be funded through the initiative. ➡

Implantable patch may mend ailing hearts

It was one of the cooler videos posted recently on National Public Radio's "Science Friday" website: A mesh patch, the size of a thumbnail, appears to dance rhythmically, as if shaking to a Latin beat.

What's driving the motion? Heart muscle cells, beating in the same direction and at the same tempo, seeded onto the polymer patch.

The research—presented at an American Heart Association meeting in July—shows what may be a key strategy in cardiac care of the future.

Study leader Dr. Steven Goldman, chief of cardiology at the Tucson VA and a professor at the University of Arizona, says the biodegradable patch would be seeded with cells and implanted onto the heart to deliver a therapeutic boost. The idea would be to help rebuild dead muscle tissue after a heart attack and revitalize the hearts of people with chronic heart failure.

The patch itself is made by a California company called Theregen. In its basic form, it contains living human cells called fibroblasts. These are the building blocks for connective tissue. In early clinical trials, the patch spurred the growth of new blood vessels in the heart. In animal studies in Goldman's lab, it improved heart function after heart attack.

Study was 'proof of concept'

In the new VA study, Goldman's group showed that the patch can be a viable platform for living heart cells—in this case, heart muscle cells taken from newborn rats. Seeded onto the patch in sufficient number, they resume beating just as they did in the animal. They even beat in unison—at the same speed and in the same direction. "Within 72 hours, you can see the entire scaffold contracting," said Jordan Lancaster, a

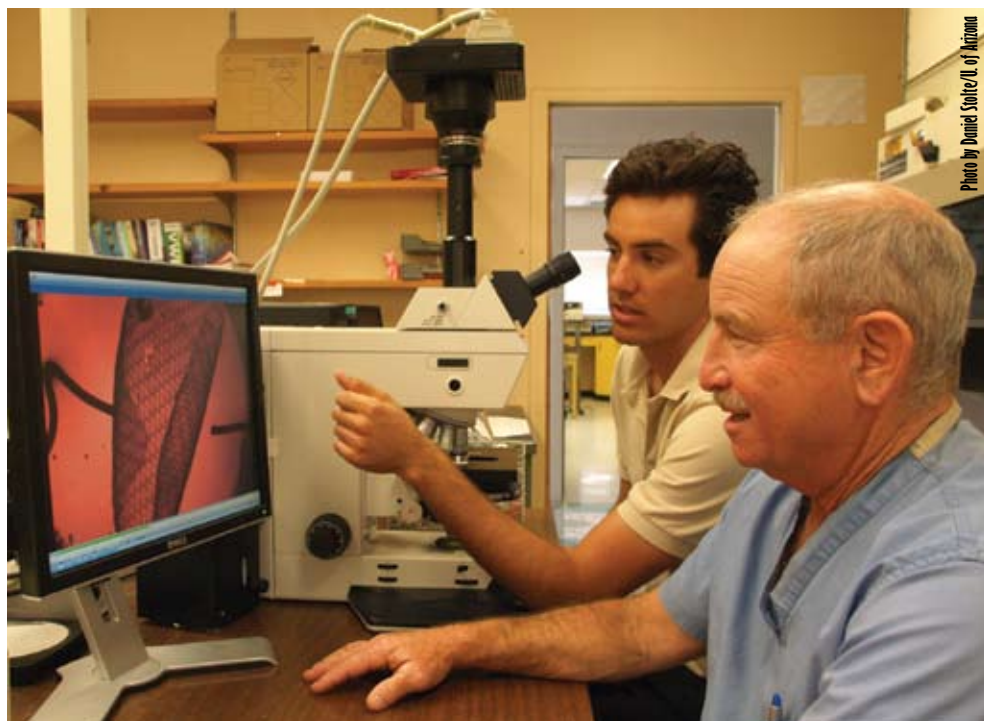


Photo by Daniel Smitell of Arizona

Cell therapists—Dr. Steven Goldman (right) and pre-doctoral fellow Jordan Lancaster view a microscope image of an implantable, synthetic mesh patch seeded with living heart cells.

pre-doctoral fellow in Goldman's lab, in an interview with NPR. Goldman, added, "The fact that they beat synchronously and the whole thing contracts, means the cardiomyocytes [heart muscle cells] are talking to each other."

Lancaster notes, "This neonatal work was a proof of concept that we could seed the cells in a way that would allow them to survive and communicate with each other."

How would the work translate into patient care? The patch would need to be seeded with cells that would divide, multiply and grow into mature heart tissue. Several types of cardiac stem cells have already been tried in humans. Lancaster mentions induced pluripotent stem cells, or IPS cells, as one option. These cells are genetically engineered in the lab from non-stem cells found in various tissues in the body. "You can harvest them, ideally, from the patient's own skin,

or even fat tissue, and culture them to have these cardiomyocyte-like features," he says.

Cells thrive on patch

The main point, say the researchers, is that the patch is a good environment for cells to thrive in—like seedlings placed in rich, fertile potting soil. "Think of it as a delivery system," explains Goldman. "Any type of cell could be put on the patch."

That could help get around obstacles that have thwarted other approaches. In past clinical trials, researchers have tried injecting cardiac stem cells directly into the heart, or squirting them into the arteries that supply blood to the heart. But not enough of the cells survive. "Delivery can be a huge problem in cell therapy," says Lancaster. "We think the patch method could promote cell survival and growth." —

Inside: Studying the health outcomes of women who served in Vietnam

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to attain, because of the strict specificity,” notes Lubaroff.

In the phase 1 trial that Lubaroff’s group conducted prior to the new phase 2 trial, 68 percent of men who received the vaccine had an immune response against PSA. That was from only one injection of the vaccine. For the phase 2 trial, the researchers have FDA permission to try multiple injections. They are now analyzing early study results to decide whether to keep the protocol at three injections or increase it. “Are we targeting the immune system in the best way to achieve the optimal clinical response and the best outcomes?” says Lubaroff.

He stresses that as part of the informed consent process, study volunteers carefully consider—along with their doctors—whether standard therapy could still help them. If so, the trial might not be the best option. “Even once they enter the trial,” says Lubaroff, “if they or their doctor feel the disease is progressing and the vaccine is of no benefit, they can always opt out.”

The VA-University of Iowa trial is funded by the Department of Defense. ➔

HIGHLIGHTS



Motion metrics—Rugby players such as Delvin McMillian, left, and Alonzo Burnett, seen here at VA’s 2009 National Veterans Wheelchair Games, and their basketball counterparts were the subject of a study by the Human Engineering Research Laboratories, a program of VA and the University of Pittsburgh. The researchers used “data loggers” mounted on wheelchair wheels to measure distance, speed, and stops and starts. The rugby players traveled, on average, about 2,365 meters (nearly 1.5 miles) in 30 minutes’ playing time at an average speed of 1.33 meters (about 4.4 feet) per second. The basketball players traveled about 2,680 meters (nearly 1.7 miles) at about 1.5 meters (about 4.8 feet) per second. The researchers say the findings, which appear this month in the journal *Prosthetics and Orthotics International*, may help coaches develop training protocols for wheelchair athletes. ➔