

Hand transplants to be evaluated Surgery team with VA, Emory will track outcomes

Only nine patients have ever received a hand transplant in the U.S. It's a staggeringly complex operation that can take up to 16 hours—twice the time of the average heart transplant. Surgeons must painstakingly knit together nerves, tendons and blood vessels—along with skin, muscle, bone and cartilage—into a seamless biological unit that looks just like the patient's natural hand and works almost as well.

The surgery is available at the Atlanta VA Medical Center and its affiliate, Emory University, as well as at a few elite centers nationwide. The VA-Emory surgeon who performs the procedure, Linda Cendales, MD, is now looking to track outcomes among patients through a new study funded by VA, the Department of Defense and other sources.

Who is eligible to take part in the study? "Any upper-limb amputee, below

the elbow, who is between 18 and 55," says Cendales. "It doesn't matter how long ago the amputation was—30 or 40 years, or just a couple of months."

Cendales has a rare combination of skills: She is trained in hand and microsurgery, as well as in transplant surgery, which includes the immunosuppression techniques that help avoid rejection of a new limb. She took part in the first two hand transplants that were done in the U.S. A few months after his 1999 transplant, the nation's first hand-transplant patient, Matthew Scott, from New Jersey, used his new left hand to throw out the ceremonial first pitch at the Philadelphia Phillies' opening-day game.

"A limb transplant is an option to recuperate a human hand," says Cendales. "In my experience with hand trans-

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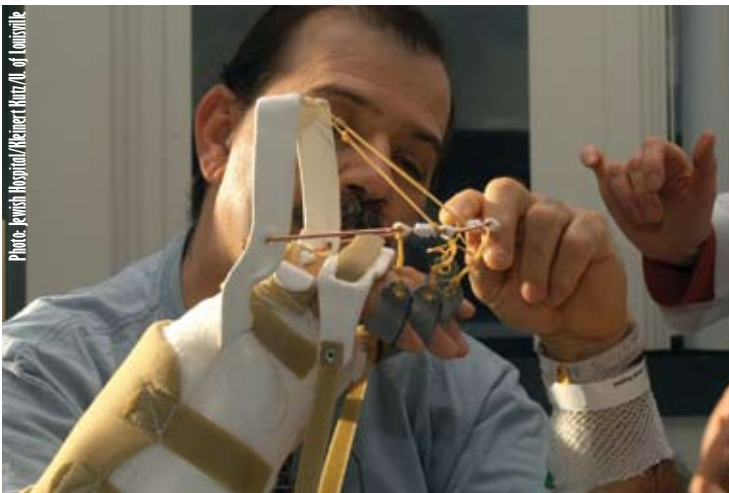
Navy Veteran Robert Corrie sought help to cope with the loss of his daughter, Nicole.

Trial tests therapies for chronic, disabling grief

Grief is part of life. Losing a loved one—whether a spouse, combat buddy, or any close friend or relative—naturally entails weeks or months of shock, sorrow, anguish and a range of other wrenching emotions.

Most people gradually recover and move on. For some, though, grief lingers and intensifies, even over several years. It gets in the way of normal life. Clinicians call this "complicated grief." The disorder affects about one in ten people after bereavement. It's not yet a formally recognized condition in its own right—it shares symptoms of depression, anxiety and PTSD—but some experts, like Sidney Zisook, MD, a psychiatrist with VA and the University of California, San Diego,

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Michigan resident David Savage, who in 2006 became the third person in the U.S. to receive a hand transplant, works his new hand during a physical therapy session following the procedure.

HAND *(from page 1)*

plantation, the patients report that the new hand has been better for them than the prostheses they were wearing.”

She explains some of the advantages: “It’s a human hand, not a device. For many people body image is important. The hand recovers sensation and the patients are able to perform activities such as turning doorknobs, holding the newspaper, tying their shoes. It’s not a life-saving organ—it’s a quality-of-life transplant.”

Cendales adds that some upper-limb amputees prefer not dealing with the potential inconveniences of prostheses: “They need to take it off and put it on. If it’s myoelectric, they need to pay attention to the weather changes.” Also, she notes, a person might need to change from one hand prosthesis to another—each designed for a different scope of activity—to do various tasks.

At the same time, she points out that a hand transplant is not the best option for every upper-limb amputee. As with a liver or kidney transplant, patients have to be on anti-rejection drugs for as long as they have the transplant. Side effects from medi-

cations can include diarrhea, headache and high blood pressure. Cendales notes that her team minimizes the long-term use of some of the drugs involved, such as steroids, which can cause diabetes and other problems.

The team approach also includes evaluations to explore the potential psychosocial impact of the procedure on patients. Cendales says that to date, all those who have received a hand transplant have come to “consider the new hand as their own, with no problems.”

Cendales says she and other surgeons value the role of other disciplines in rehabilitating those who have lost limbs. She acknowledges advances in upper-limb prostheses—such as the DEKA arm, now being tested by VA (see the May 2009 *VA Research Currents* at www.research.va.gov/currents)—and says such technology will offer more options for amputees.

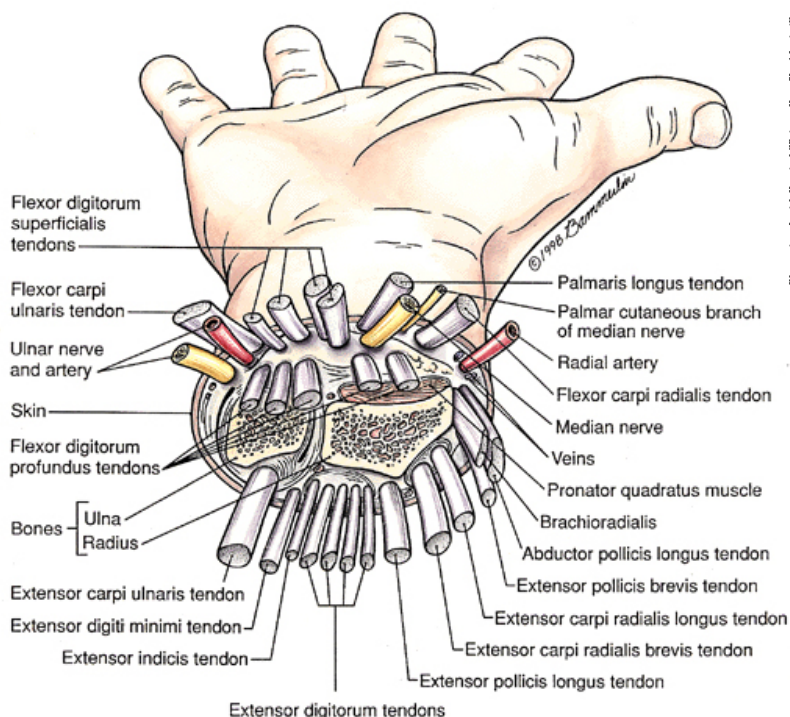


Illustration: Jewish Hospital/Werner Hutz, M.D., Louisville

A hand transplant can take up to 16 hours because of the complexity of the tissues that must be repaired and reattached. In comparison, a typical heart surgery takes six to eight hours.

“Perhaps a good approach is the model we follow,” says Cendales. “We have a multidisciplinary team that is patient-centered. Our program aims to provide another option for a selected group of patients, and to provide the best options overall for our amputees. If it’s a prosthesis, the best prosthesis, and if it’s a hand, the best-matched human hand.”

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Hand transplant facts

- A hand transplant is an extremely complex procedure, but it is not as difficult as a hand replantation—reattaching a patient’s own injured hand—because the latter usually involves severely damaged tissues.
- When doing a hand transplant, surgeons first fix the bone, and then repair tendons, arteries, nerves and veins.
- Post-surgery complications can include poor blood flow, infections and rejection.

GRIEF (from page 1)

say it should be. Zisook and colleagues published an article in last month's *Journal of Clinical Psychiatry* recommending that complicated grief be included in the next edition of the *DSM*, the official diagnostic guide for mental health professionals. What's more, they are now conducting a four-site clinical trial to determine the best way to treat the condition.

"It's becoming an increasingly well-defined disorder," says Zisook. "But it is vastly under-recognized, and, we think, un- or under-treated."

That's dangerous, says the psychiatrist. He says the condition brings people's lives to a standstill and robs them of a sense of purpose. Some seek to deal with the ongoing intense grief by taking on unhealthy behaviors such as smoking and overeating. They may become at higher risk for high blood pressure and heart disease, as well as complicating psychiatric conditions like major depression or panic disorder. They are also at risk for suicidal thinking and behavior. Zisook and colleagues write, "Suicidal urges are usually related to hopes of finding or joining the deceased loved one or feeling that life without the deceased person is unbearable."

"It's very clear," says Zisook. "Complicated grief must be taken seriously and treated appropriately."

The new trial will include 440 adults, including Veterans and others between 18 and 85. Two therapies will be put to the test, alone and in combination: an antidepressant, and a form of psychotherapy designed especially to treat complicated grief.

"We're testing the effectiveness of antidepressant medications for complicated grief, both when used alone and also when administered with complicated grief



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—Dr. Sidney Zisook, VA and UCSD

therapy, as well as the effectiveness of complicated grief therapy with and without medications," explains Zisook. "We feel these goals are very important and that our results will shape the treatment of this condition for years to come."

Complicated grief therapy was developed by Zisook's collaborator Katherine Shear, MD, now with Columbia University and formerly with the University of Pittsburgh. One component involves the patient revisiting the story of the death and reflecting on it. Proponents of the therapy say it helps quench the raw, burning emotion that persists in those with complicated grief and helps them come to terms with the finality and consequences of the death. The therapy usually entails

**Therapy helps Veteran
after loss of daughter**

About five years ago, Robert Corrie had to cope with losing his sister, father and brother, all within a six-month period. In 2009, an even heavier blow struck: His daughter died suddenly at age 40 from an accidental overdose of prescription drugs. She and her four children had been living with Corrie and his wife. For Corrie, the grief was almost too much to bear.

A partially disabled 20-year Navy Veteran, Corrie is a regular patient at the VA San Diego Healthcare System. He had attended support groups there to deal with his earlier grief episode. Some months after his daughter's untimely death, he again turned to VA and was referred for complicated grief therapy.

As part of the therapy, he would retell the story of the death. The psychologist recorded the stories and asked Corrie to listen to them again at home. Corrie says he was able to emotionally distance himself from the painful event as he told about it in the therapist's office. Listening to the recording at home was more difficult.

"It took me back to the actual time. I found it very upsetting," recalls Corrie. At the same time, he found "it triggered other memories I had tried to push away."

Working with his therapist over four months, Corrie discovered it was guilt that was driving much of his grief—guilt over not being a good enough parent and not resolving the sore spots in his relationship with his daughter while she was still alive. The therapist explored the feelings with Corrie. She asked him to talk about pleasant experiences he had shared with his daughter, and difficult ones as well. In one of the last recordings he made in therapy, he visualized himself standing with his daughter on the day of her death, saying all the things he wished he had told her. That session—and his subsequent listening to the recording—were especially cathartic, says Corrie.

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Photo by Elizabeth Binette

Tough routine to break—Army Veteran John Borlik, now a visual information specialist with VA, has smoked for 25 years. He says he's tried to quit numerous times, going cold turkey or using the nicotine patch. His most successful attempt kept him away from cigarettes for a year.

Can the Internet help smokers kick the habit?

A study based at the Durham (N.C.) VA Medical Center is testing whether an Internet-based program can help Veterans quit smoking.

More than 400 Iraq and Afghanistan Veterans are taking part in the research. Half are being given premium membership to a website called QuitNet (*quitnet.com*). The website is based on guidelines of the U.S. Public Health Service. It features chat rooms, advice from experts, medication tips, buddy match-ups and other tools to support smokers in their quest to stop smoking. Launched on a wide scale 10 years ago with help from Boston University's School of Public Health, the site is used by some 60,000 smokers and ex-smokers worldwide. Those referred to the website are also being offered nicotine replacement therapy from VA. This entails a telephone assessment and shipments of supplies—usually skin patches or chewing gum—through the mail. These Veterans can opt for medication, too, if they want to commit to clinic visits along with their website usage.

The other 200 or so study participants are receiving standard care. This means a referral to a specialty clinic at the Durham VA

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Durham VA and the nicotine patch

VA has been a leader in developing new approaches to help people kick the smoking habit. The Durham VA Medical Center, in particular, has a rich legacy in this regard: The widely used nicotine patch was developed there, at least in part. The patch delivers low doses of nicotine into the bloodstream to satisfy cravings, thus helping smokers wean themselves from cigarettes. The device is credited with doubling smokers' odds of quitting.

The therapy's co-inventor, neuroscientist Jed Rose, PhD, conducted much of his key clinical research in Durham after transferring there from the West Los Angeles VA in 1989. Today, Rose continues to direct the Duke Center for Nicotine and Smoking Cessation Research.

Rose was featured recently in an article in the *ipHandbook*, a publication about best practices in the commercialization of intellectual property. "It is very exciting and gratifying to know that our work has made a difference in people's lives," said Rose. "This shows the potential impact that clinical research can have on society."

VA, NIH fund new studies on substance abuse

VA has partnered with the National Institutes of Health (NIH) to award \$6 million in grants for research on substance abuse in relation to military deployments and combat-related trauma.

NIH agencies taking part in the initiative are the National Institute on Drug Abuse, the National Institute on Alcohol Abuse and Alcoholism, and the National Cancer Institute.

Several studies will look at treatment seeking patterns—why and when Veterans ask for help, and why many don't. Scientists will also explore treatment strategies, including cognitive behavioral therapy and Web-based approaches, as well as the most effective therapies for soldiers who have substance abuse issues along with other disorders, such as depression.

Researchers will also determine if early intervention can improve outcomes. Other projects will focus on how Veterans readjust to their work and families after returning from war.

Institutions receiving the grants include Brandeis University; Dartmouth College; the Medical University of South Carolina; the National Development and Research Institutes in New York City; the University of California, San Francisco; the University of Minnesota, Twin Cities; the University of Missouri in Columbia; and the VA medical centers in West Haven, Conn.; Philadelphia; Little Rock, Ark.; and Seattle.

The West Haven VA group will explore differences in addiction behaviors between men and women Veterans. In Little Rock, VA investigators will conduct in-depth interviews with Veterans coping with substance abuse to better understand post-deployment addiction



Photo by Lance Cpl. Robert Morgan/USMC

The stress of war can put troops at higher risk for substance abuse.

and treatment-seeking. In Seattle, a VA group will look at tobacco use among Veterans who are taking part in the Millennium Cohort Study—a major epidemiologic research effort involving VA and the Department of Defense. At the Philadelphia VA Medical Center, investigators will work with Veterans who have an addiction and PTSD to study whether the two issues are best treated at the same time or one after the other. ➔

SMOKERS *(from previous page)*

geared to help returning Veterans quit smoking. The clinic uses a mix of methods, such as group behavioral counseling, telephone support, nicotine replacement therapy and medication management. For those Veterans prescribed a drug, bupropion (sold as Zyban) is the most common choice.

Up to half of patients who regularly attend such programs will quit, research shows. About a quarter will stay away from cigarettes long-term. The main problem with clinic-based programs, though, is poor

attendance, says lead investigator Patrick Calhoun, PhD, a psychologist at the Durham VA and Duke University. According to Calhoun, barriers to Veterans' participation include long distances to clinics—especially for those in rural areas—and limited availability of specially trained counselors. These factors make it harder for patients to fit in clinic visits around their work schedules.

At the Durham VA, only one in six Veterans referred to the smoking-cessation clinic takes advantage of the program, says

Calhoun. And only about a third of those who attend the program go on to complete it. The rates of attendance at private-sector smoking cessation clinics are no better, studies show.

Calhoun believes Web-based methods can be a potent alternative. “We think the approach has great promise for increasing access to smoking cessation care, especially among Veterans in rural areas. The Internet in combination with telehealth for nicotine replacement therapy may help to increase motivation and avoid barriers to access.” ➔

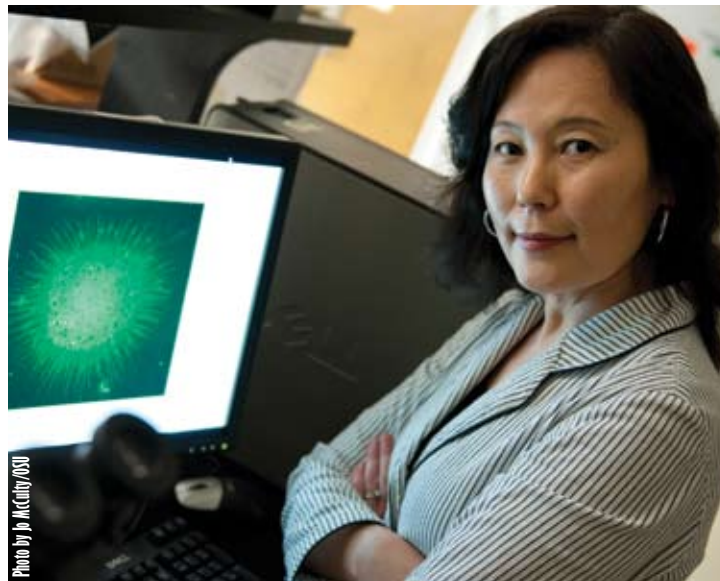
Social factors may explain race gap in use of heart procedures—Past research has shown that blacks are less likely than whites to receive invasive cardiac procedures. The reasons for the disparity remain unclear. Researchers with the VA Boston Healthcare System and the Bedford (Mass.) VA Medical Center surveyed 48 black and 189 white Veterans with heart disease who had been advised by their VA physician to undergo cardiac catheterization and angiography as a diagnostic measure. Despite the physician recommendation, fewer blacks than whites (77 versus 90 percent) underwent the procedure. The researchers found three social factors that appeared to explain the trend: Blacks were less likely to know someone who had undergone the procedure, less likely to be encouraged by family to do so, and less likely to have strong social support. Senior author Nancy Kressin, PhD, says, “While solving this problem or the source of the disparity may not be within the purview of the health care system, if providers understand some of what is driving the disparity, perhaps they can use those factors to help address it.” She said one way to address the issue might be through “peer educators or supporters.” (*Journal of General Internal Medicine*, August 2010)



Immune-system genes linked to Parkinson’s—Researchers with several institutions, including the VA Puget Sound Health Care System, found that a group of genes that help control the body’s immune response may figure in the development of Parkinson’s disease. The team examined the genetic make-up and health histories of nearly 4,000 people—half with the disease, half without—and found that those with the disease were more likely to have certain variations in a group of immune genes known as the human leukocyte antigen system. Cyrus Zabetian, MD, of VA and the University of Washington, told *Reuters* that the new findings from the group’s genome-wide association study are the strongest evidence yet of a role for the immune system in the development of Parkinson’s. “We don’t know specifically which gene because there is a cluster of genes in that region,” he said, “but it is the first really strong link that the immune system plays a role.” (*Nature Genetics*, online Aug. 15, 2010)




Glutamine pathway in bowel disease—Researchers with Ohio State University and the Cincinnati VA Medical Center have identified a small RNA segment that blocks a gene that makes glutamine, an amino acid essential for the health and integrity of the colon. While glutamine is already in use as a supplement to treat many digestive ailments—namely those that involve diarrhea, bloating and abdominal pain, as results of intestinal permeability—



Dr. QiQi Zhou's team discovered a key pathway of glutamine, an amino acid.

the new research may suggest ways to internally boost the production of glutamine in the body. In addition to their ongoing biomedical research, lead author QiQi Zhou, MD, PhD, and colleagues plan to conduct a clinical trial to rigorously test the effectiveness of glutamine supplementation for patients with irritable bowel syndrome. (*Gut*, June 2010)



Military sexual trauma—A VA study looked at the records of 125,729 Veterans who received VA primary care or mental health services between 2001 and 2007 and found that 15 percent of women and .7 percent of men reported military sexual trauma. Both women and men who screened positive for military sexual trauma were more likely to be diagnosed with a mental health condition. The authors say military sexual trauma tends to be under-reported, so the rates they found in the study may not reflect the full extent of the problem. At the same time, they emphasize that the study included only Veterans who have enrolled in VA health care, and the findings may not apply to the military in general. VA screens all new patients for military sexual trauma—among other issues—and provides free care for all related conditions. (*American Journal of Public Health*, August 2010) 

Mark the date...

National VA Research Week
May 2 – 6, 2011



Brain-bank tissue study may offer clues on ALS—A team led by Ann McKee, MD, seen here with medical students at one of the brain banks she oversees at the Bedford (Mass.) VA Medical Center, found pathological evidence of a link between repeated head injuries—such as those experienced by athletes in contact sports such as boxing, football and hockey—and a motor neuron disease that resembles amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. The results appear in the September issue of the *Journal of Neuropathology and Experimental Neurology*. To read more, go to "Features" at www.research.va.gov.

Studies find intriguing link between PTSD, dementia

Study results reported this month in the *Journal of the American Geriatrics Society* suggest that Veterans with posttraumatic stress disorder (PTSD) have a higher risk for dementia than their peers without PTSD. The authors emphasize that while PTSD was associated with higher risk, the great majority of Veterans with PTSD in the study did not develop dementia.

"We found Veterans with PTSD had twice the chance for later being diagnosed with dementia than Veterans without PTSD," says Mark Kunik, MD, MPH, a psychiatrist at the Michael E. DeBakey VA Medical Center in Houston and senior author of the article. "Although we cannot at this time determine the cause for this increased risk, it is essential to determine whether the risk of dementia can be reduced by effectively treating PTSD. This could have enormous implications for Veterans now returning from Iraq and Afghanistan."

The study included 10,481 Veterans at least 65 years of age, almost all men. One group had a PTSD diagnosis and had received a Purple Heart for having been

wounded in action. A second group had a Purple Heart but no PTSD, and a third group PTSD but no Purple Heart. This way, the researchers could tease out the effects of PTSD versus combat trauma that did not lead to PTSD. A fourth set of Veterans with neither PTSD nor a Purple Heart served as a comparison group.

Of the four groups, those with PTSD and no Purple Heart had the highest prevalence of dementia—about 11 percent. Next was the PTSD group with a Purple Heart, at 7 percent. The other two groups were at 6 percent, for those with a Purple Heart and no PTSD; and about 5 percent, for those with neither. The differences remained even after the researchers adjusted for factors such as traumatic brain injury, substance abuse and heart disease.

Overall, the rates in the study may be lower than those seen in the American population at large. A major National Institutes of Health study published in 2007 estimated the prevalence of dementia among Americans age 71 and older to be 14 percent. This was a somewhat older group,

though, and dementia risk does increase with age.

Lead author Salah Qureshi, MD, a staff psychiatrist at the Houston VA, says a future research goal will be pinpointing factors that help explain why some Veterans with PTSD develop dementia while others do not. "Despite the increased risk for those with PTSD, it is noteworthy that most Veterans with PTSD did not develop dementia during the period we studied," he says. "It will be important to determine which Veterans with PTSD are at greatest risk and ... whether PTSD induced by situations other than war injury is also associated with greater risk."

The authors note there could be several explanations for their findings. It could be that both PTSD and dementia share certain underlying risk factors, or that PTSD itself is a risk factor for dementia.

A separate study by a VA group in San Francisco, published in June 2010 in the *Archives of General Psychiatry*, also found a

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Inside: Can the Internet help smokers kick the habit?

GRIEF *(from page 3)*

weekly sessions over four months. Zisook has great faith in the therapy, although he points out that the revisiting exercises can be difficult for patients.

“The treatment asks people to confront painful emotions, but it’s administered in a respectful, collaborative manner to ensure a sense of support and companionship in the pain,” Zisook says. He adds that part of each session is aimed at helping the person focus on pleasurable activities and work toward meaningful life goals. “No treatment works for everyone,” he says, “but this appears to be the most effective way to help people with complicated grief so far. Existing data indicate that gains are maintained long-term.”

The study will take about five years. Besides San Diego, patients will be enrolled at Columbia University in New York; the University of Pittsburgh; and Massachusetts General Hospital. The effort is funded by the National Institute of Mental Health and the American Foundation for Suicide Prevention. ➔

HELP *(from page 3)*

He was eventually able to process the emotions that had weighed so heavily on him. Gradually, he felt more at peace. He



New insight on racial disparities in heart procedures—Page 6

became less agitated at work, less irritable at home with his wife and the grandkids.

Corrie knows he has likely not seen the last of the grief.

“The therapy teaches you that it’s cyclic,” he says. “There could be anything, anytime that could trigger the emotions. There’s no day when you’re done.”

But now he feels he has the skills to cope. “I’ve learned that if one of those episodes happens, it’s natural. Accept it, let it flow through me, and get back to what I was doing as soon as I can. I’ve learned not to berate myself for having those emotions.” ➔

PTSD *(from page 7)*

roughly doubled risk for dementia among Veterans with PTSD. That study looked at much larger sample—more than 181,000 Veterans. The incidence rates were about the same as those seen in the Houston study. Lead author on the San Francisco study, psychiatrist Kristine Yaffe, MD, offered theories similar to Kunik’s on how PTSD and dementia may be linked. Among other possible explanations, she said, PTSD may alter the production of stress hormones in a way that eventually damages the hippocampus, a brain area crucial for memory; or certain pre-existing genetic factors may boost the risk of both conditions. ➔