



RESEARCH CURRENTS

Research News from the U.S. Department of Veterans Affairs



Mind-body medicine

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Vietnam Veteran Stan Fisher takes part in a qigong class led by Dr. Mike Basdavanos at the Washington, DC, VA Medical Center. The class is offered through the site's War-Related Illness and Injury Study Center—one of three such centers in VA nationwide.

Photo by Robert Turtill



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U.S. Department of Veterans Affairs
Veterans Health Administration
Office of Research and Development





Health science specialists Sean Walker (left) and Jim Averill handle central nervous system tissue at the VA Biorepository Brain Bank, based at the Tucson VA Medical Center.

Photo by Nicole Thurston

Biorepository aims to **help solve mysteries of ALS, Gulf War illnesses**

The VA medical center in Tucson is an adobe-style complex set amid palm trees, cacti, and the blazing Southwest sun. But inside is a brain bank where extreme cold—minus 80 degrees Celsius—keeps specimens well-preserved and ready to be shipped out to research labs throughout VA and worldwide.

The 120 brains currently in the facility were all donated by Veterans who had suffered with ALS, or Lou Gehrig’s disease, before their death. They were among more than 2,000 Veterans with ALS who took part in a registry that VA funded from 2003 to 2009.

“This tissue is rare. We provide samples to some of the top ALS investigators in the nation,” says Katrina Trevor, PhD, a research pathologist who serves as technical director for the brain bank. Her Tucson VA colleague Stephen Renner, MD, is the lead site investigator for the project.

The facility, formally known as the VA Biorepository Brain Bank, is now expanding to also focus on Gulf War Veterans’ Illnesses (GWVI).

A ‘LIVING’ STUDY

Concerning the Gulf War phase of the project, the researchers have a clear message for interested, eligible Veterans: Sign up now, even if you expect to live another half-century or more.



The Boston group that staffs the VA Biorepository Brain Bank and related Gulf War Veterans' Illnesses Biorepository includes (from left): neuropathologist Dr. Thor Stein; project coordinator Latease Guilderson; data manager Sally Perkins; project support assistant Melissa Weiner; principal investigator Dr. Neil Kowall; project coordinator Shelley Amberg; and director of scientific operations Dr. Christopher "Kit" Brady.

Photo by Frank Curran

"This really is a 'living' study, says Christopher Brady, PhD, director of scientific operations for the project. "If you're a Gulf War-era Veteran and you want to help out your fellow Veterans, this is one way to do it."

Brady is a neuropsychologist at the VA Boston Healthcare System and assistant professor of neurology at Boston University. He works closely with the Tucson team, as do his Boston colleagues working on the biorepository: Ann McKee, MD, and Thor Stein, MD, PhD, are neuropathologists, and Neil Kowall, MD, is lead investigator.

Brady explains that the Gulf War biorepository, in addition to collecting tissue from Veterans when they eventually die, will track the health of enrolled Veterans while they are alive, ideally over many decades. That information itself is valuable for research purposes.

"We're extremely interested in finding out all we can about these Veterans while they're living," says Brady. "The tissue that we obtain upon the person's death becomes so much more valuable for research purposes when we know

what the person was doing all the years prior to death."

Trevor adds: "The value of any tissue—whether it's the brain, or other organs, and whether the focus is neurological disease, cancer, or any other condition—is having all the clinical and demographic annotation that goes with it. That's what the real value of our bank is, and VA has been very supportive of that."

STUDY DATA KEPT STRICTLY CONFIDENTIAL

In addition to completing brief surveys every six months to a year, Veterans who sign up for the Gulf War project agree to have researchers access their VA electronic medical record.

"We get a lot of information from the medical record," says Brady. He stresses that all study data are kept strictly confidential.

"We have access to the records," says Brady, "but once we enter the data into our system, they are completely de-identified. Once it goes into our database, it's all by number.

The name is no longer attached to the health information. Any data that get released with a tissue request from a research lab are also de-identified. We are committed to protecting the confidentiality of Veteran's personal health information."

Brady emphasizes that the Gulf War project is not only for those who were deployed to the Gulf in the early 1990s and developed symptoms afterward. It's for *any* Gulf War-era Veterans, regardless of whether they were deployed, and regardless of their health status since.

"Enrolling healthy Gulf War Veterans is critical," he says. "One way to understand why some people get sick is to understand why others don't—especially if they were also deployed and exposed to the same things. Healthy Gulf War Veterans who enroll are going to help us figure out what's wrong with their brothers and sisters who are ill."

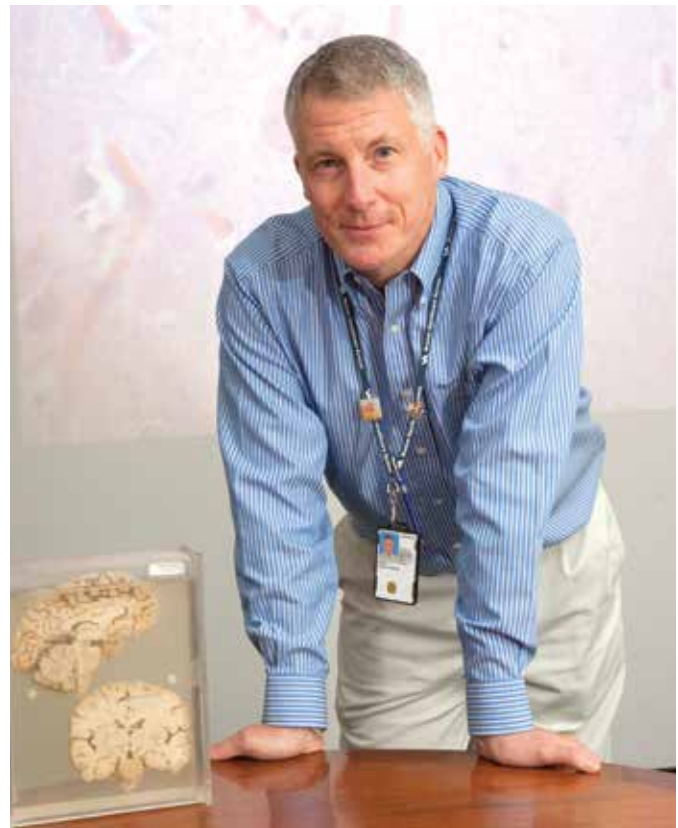
The brain bank, which also collects spinal cord tissue, remains open to those with ALS. Unfortunately, their life expectancy is short; most patients with the disease die within five years. The researchers give brief surveys to enrollees with ALS every six months to a year to collect crucial demographic and clinical information while they are still alive.

'NEVER TOO SOON TO SIGN UP'

Some of the information collected from both groups of Veterans is the same. Researchers want to know about health symptoms, medications, military exposures, lifestyle habits, family members' health, and other factors that could help them unravel the mysteries of ALS and GWVI. Is there a genetic connection? Specific toxins that caused the illness? These are among dozens of questions researchers continue to study.

Brady says: "The bottom line is, it's never too soon to sign up. We enroll folks while they're living and follow them through the lifespan. That's what makes this research a notch above a traditional brain bank." ★

More information on the VA Biorepository Brain Bank is available on the Web. For information on ALS research being conducted within the framework of the brain bank, visit www.research.va.gov/programs/tissue_banking/als. To learn more about the Gulf War study, go to www.research.va.gov/programs/tissue_banking/gwvib.



Dr. Christopher "Kit" Brady is director of scientific operations for the VA Biorepository Brain Bank.

Photo by Frank Curran

VIDEO TRIBUTE TO VETERAN RESEARCH VOLUNTEERS

Every year, thousands of Veterans volunteer to take part in VA research studies. In connection with Veterans Day 2013, VA Health Services Research and Development—part of VA's Office of Research and Development—produced a video paying tribute to these Veterans. The video, under four minutes, features VA health-services investigators expressing their gratitude. They also talk about the role Veterans play in their research, and how the work promises to benefit Veterans at large. To view the video, visit www.hsrd.research.va.gov/news/video/thankyou_vets.cfm.

VA's special war-injury centers use mind-body approach

On a stretch of lawn framed by tall pines and crimson-colored hedges, a group of Veterans practices qigong, an age-old form of exercise from China. Their movements are slow and deliberate, in sync with their breath. The soothing sounds of traditional Chinese string and bamboo instruments float up from a portable CD player that sits on the grass.

The setting is peaceful. It's a sharp contrast to the stress of war that some of the Veteran still carry in their minds—and in their bodies—even decades after deployment.

"I like the exercise. It helps me stretch, open up, work on my range of motion," says Stan Fisher, 68, who served with the Marines in Vietnam.

Qigong is one of many healing activities offered at the War-Related Illness and Injury Study Center (WRIISC) based at the Washington, DC, VA Medical Center. The WRIISC in the nation's capital is one of three such VA centers nationwide. The others are in East Orange, N.J., and Palo Alto, Calif.

IN THE VANGUARD OF INTEGRATIVE MEDICINE IN VA

The centers offer comprehensive clinical evaluations for post-deployment Veterans with complex health conditions with no known cause. They also do assessments for Veterans from any era, referred by their VA providers, who believe they may have been exposed to toxic chemicals or other environmental hazards during their deployment.

In recent years, complementary and alternative medicine, or integrative medicine, has become a staple at the WRIISCs. The trend reflects—and perhaps has helped drive—a wider such trend at VA medical centers nationwide. A 2011 survey found that 9 in 10 VAMCs offer in-house, or provide referrals for, at least some complementary and alternative treatments. The most popular are meditation or other forms of stress management and relaxation therapy.



Veteran Shirley Gorum-Cambridge says she learned how to meditate through classes at the War-Related Illness and Injury Study Center at the Washington, DC, VA Medical Center.

Photo by Robert Turtill

"The Veterans are coming because they're very interested," says Dr. Amanda Hull, a psychologist who runs the Integrative Healthcare and Wellness Program at the Washington, DC, WRIISC. "They are very excited to see what we offer. They and their providers are looking for something that may help."

She says the WRIISCs apply a rigorous research approach to everything they do—including mind-body practices such as qigong, acupuncture, and various forms of yoga and meditation, all of which offer mental as well as physical health benefits. The treatments are backed by scientific evidence, and the WRIISCs are conducting further study as they go along.

TELEHEALTH YOGA BEING STUDIED

A group at the Palo Alto WRIISC, for example, has been studying the pros and cons of delivering yoga via telehealth to Veterans who live far from locations with live VA classes. So far, the interactive video hookup has reached Veterans at VA community-based outpatient clinics in the California cities of Stockton, Fremont, San Jose, Monterey, and Modesto. More than 100 Veterans have been referred for the program. Yoga instructor and researcher Louise Mahoney says, "We have had no adverse events, and Veterans report enjoying the classes and receiving benefits such as increased strength,

energy, and flexibility, and reduced pain and stress.” She says the technology could potentially “open the practice of yoga up to a whole new group of Veterans.”

Yoga is also on the research agenda at the Washington, DC, WRIISC. Among other studies, investigators there have been examining whether iRest Yoga Nidra can help Veterans with traumatic brain injury cope with chronic pain. This type of yoga involves mindfulness meditation. It’s been studied extensively at Walter Reed Army Medical Center and other sites, and is now used widely in VA, but researchers are still exploring its benefits for specific populations and health conditions.

Hull, a trained iRest facilitator, also has a strong interest in what she calls “nutritional psychology”—the science of how nutrients affect mood and behavior. She leads an eight-week class on integrative health education that includes some of these topics.

“I’ll talk about what sugar does in the brain. I’ll draw a cell and say, ‘Here’s how fat is used in the body. This is why we need this type of fat but not that type.’ It’s very basic, but very powerful. It’s not the type of education most people are getting.”

The emphasis, she notes, is on giving Veterans “tools for their toolbox. They play an active role in their own care.”

GROUP ACUPUNCTURE AMONG MOST POPULAR CLASSES

One of the most popular drop-in classes sponsored by the Integrative Healthcare and Wellness Program at the Washington, DC, WRIISC is group ear acupuncture, held every Tuesday and Thursday. Up to 20 or so Veterans, of all ages and backgrounds, sit in chairs around a long table in a basement conference room. The walls, painted lavender, are adorned with framed photos of flowers. Despite the busy hallway outside the door and occasional intrusions from the PA system, acupuncturists Dr. Jeanette Akhter and Alaine Duncan work to create a calming atmosphere.

As a session begins, Duncan reminds the group to turn off their cell phones, remove their hats and eyeglasses, even loosen their belts and untie their shoes. She asks them to shift their attention to their weight in the chair, to focus on the moment, their body in space. Mellow New Age music fills the room, sounding like a gentle rain shower.

“Notice the circle of Veterans around you,” Duncan says



Acupuncturist Dr. Jeanette Akhter administers ear acupuncture to Veterans attending a drop-in session at the War-Related Illness and Injury Study Center at the Washington, DC, VA Medical Center.

Photo by Robert Turtill

softly to the group. “As the room starts to feel quieter, you might start to feel quieter on the inside too. It’s all part of getting your qi—your energy—ready to receive treatment.”

The treatment consists of five tiny needles placed at specific points on the outer ear. In traditional Chinese medicine, the ear is thought to contain a “map” of the entire body. So tapping into the ear’s energy points can trigger a cascade of calming effects.

“You can access a lot of body organs and body systems through the ear,” explains Hull.

She tells of one Veteran who told her his pain goes away for at least three days when he gets treated. If he skips a session, the pain comes back.

Veteran Shirley Gorum-Cambridge, who lives in the Washington, DC, suburbs, used to receive the ear acupuncture and says she found it “very relaxing.”

She also learned how to meditate through WRIISC classes, and maintains a daily practice on her own. “The techniques were very nice. I learned how to settle down, to clear my mind.”

The soft-spoken 61-year-old served at the Pentagon during the Vietnam era and today suffers from spinal stenosis. A bone in her neck is pressing against a nerve. A few years ago, a doctor recommended surgery. Her WRIISC team recommended physical therapy instead. She went that route and is happy she did. At physical therapy, she walked a lot—another habit she keeps up with on her own, doing up to four miles a day.

All in all, she says, “My tolerance for pain has gotten a lot better. I hurt, but I’ve learned how to deal with it.” ★

GULF WAR CORPSMAN STRUGGLING WITH LINGERING HEALTH ISSUES

Melanie Yvette Jackson recalls the bluish-black smoke she saw rising from the oil well fires in Kuwait. She was stationed as a Navy corpsman in the neighboring country of Bahrain. It was toward the end of the Gulf War, in 1991.

“We were near the oil fires,” says Jackson. “The sky was totally dark. You’d blow your nose and black stuff would come out. I’d wash my hair and the sink would be black. I was inhaling whatever was burning.”

Jackson, 52, of Maryland, is among more the roughly 175,000 Gulf War Veterans who reported health problems after their deployment. She, like the others, can still only guess at the exact cause. She received multiple vaccinations, was exposed to extreme temperature changes, endured the mental stress of war. But what triggered the sudden decline in her health following the war remains a riddle.

“I was 18 when I joined the Navy. I was healthy—no issues,” she says. Now, her chief complaint is irritable bowel syndrome. She manages it mainly through diet, but she’s had bad flare-ups of related conditions, such as Crohn’s disease and ulcerative colitis, during which she was put in the hospital and lost nearly 30 pounds. She’s struggled with other serious health issues as well, including neuropathy and thyroid cancer. She also attended a women’s group at a Vet Center for several years to help cope with PTSD.

Today, Jackson and about 60 other Gulf War Veterans have enrolled in studies led by Dr. Mian Li, a neurologist, at the Washington, DC, WRIISC.

Following up on epidemiology findings

Li is following up with Gulf War Veterans who are part of a Gulf War Registry started in 1995. Jackson is among them. “I’ve identified the people who said they were sick—who have pain, fatigue, sleep trouble, difficulty exercising,” says Li. “I am dealing with people who tell me, ‘I used to be a strong, athletic soldier. Now I’m disabled.’ They want to know why.”

Veterans in the registry have been surveyed twice so far—in 1995 and 2005—by Drs. Han Kang and Clare Mahan and other epidemiologists with VA’s Office of Public Health. The goal is to find clues to better understand the cause and nature of their illnesses.



Dr. Mian Li administers a neurology test to Gulf War Veteran Melanie Yvette Jackson.

Photo by Mitch Mirkin

Whereas the epidemiology findings are based on Veterans’ self-reports, Li brings them into the clinic to administer a battery of nerve tests. So far, his work has confirmed higher rates of certain nerve problems in some ill Gulf War Veterans, compared with healthy Gulf War Veterans who have volunteered for the study as “controls.” The findings center on the small nerve fibers that are part of the autonomic nervous system. They control the sensation of pain and enable signals to flow between the brain and organs such as the bladder, stomach, intestines, sweat glands, and peripheral blood vessels. Li says these small-diameter nerves may become therapeutic targets in future research.

By keying in on the autonomic nervous system, Li hopes to pinpoint what has gone awry in those affected by chronic multisymptom illnesses—and what puts them at higher risk of “organic” diseases such as heart disease and arthritis. VA’s long-term epidemiology data show higher rates of some chronic diseases among deployed Gulf War Veterans, compared with their non-deployed peers.

“My research is exploring whether there’s an organic basis for the symptoms that can be treated,” says Li. “Looking at the autonomic nervous system, we can detect small, subtle changes that don’t show up in routine tests. If we find pathways in the disease process that are modifiable, we can find new treatments.”

Jackson realizes the research may not solve all her health problems anytime soon, but that doesn’t stop her from volunteering. “I don’t mind participating in research,” she says. “I’m sure it’ll help me and some other people down the road.”

VA biomedical labs get facelift

Renovations boost safety, efficiency, capacity

Visitors touring the Nashville VA Medical Center nowadays are likely to be shown the recently spruced up biomedical labs. Mike Walsh, administrative officer for research at the site, says the new lab space is a source of pride for his staff.

“There’s an increased sense of pride among our research personnel,” says Walsh. “The space has served as a destination during a national architect and engineering conference held in Nashville, and it’s been a factor in faculty recruitment. In general it’s become a site for other visitors to our health care system to check out.”

The renovations—still ongoing at Nashville—are part of a nationwide effort, initiated by Congress in 2006, to review the state of VA biomedical labs and make the necessary improvements. Priority was given to safety hazards and non-working or severely deteriorated systems, but a range of renovations have been made so far at many of the 74 VA sites assessed nationwide, and more are underway or in the planning stage.

Some sites also have had new construction approved partly as a result of the assessments, which were carried out by three architectural and engineering firms through a contract with VA.

Karen Scott, who oversees the project for VA’s Office of Research and Development, notes that like hospital operating rooms, “biomedical research space is very costly to build and maintain according to modern standards.” Scott took over the project from Dr. Deanna Robbins, who retired from VA in early 2013.

NEW TRENDS IN BIOMEDICAL RESEARCH

Scott says that in addition to VA’s own standards, and those of the National Institutes of Health—which funds a good chunk of the lab research conducted by VA investigators—there are nearly a dozen other organizations whose safety or technical standards were consulted and followed. They include, for example, the American National Standards Institute, for safety showers and eyewashes; the Illuminating Engineering Society of North America, for lighting levels; and the National Fire Protection Association, for guidance on hospital electrical systems.

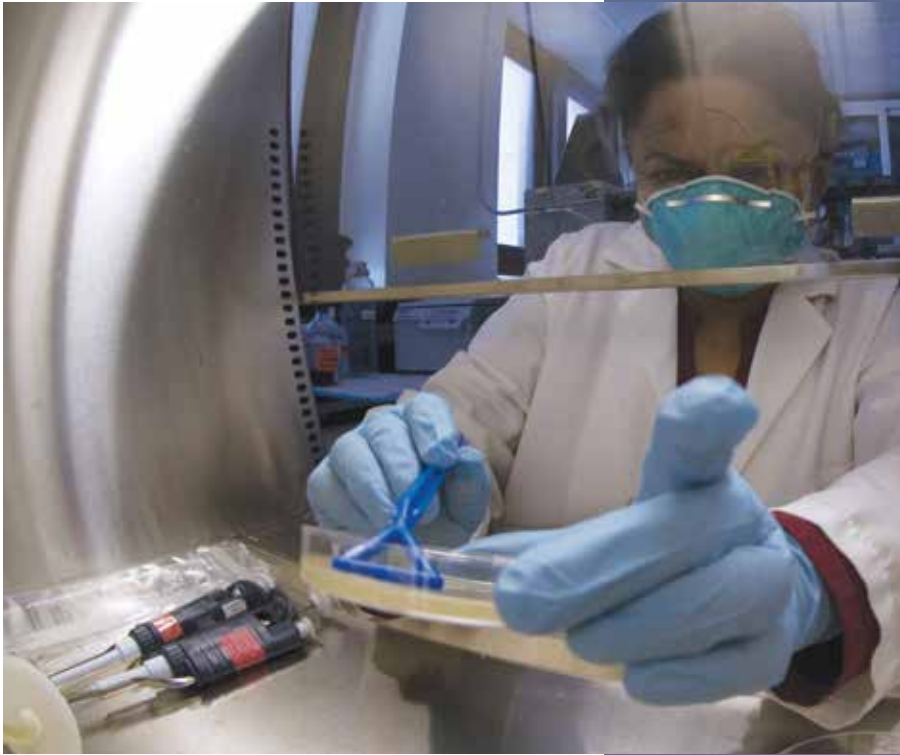
Walsh, at the Nashville VA Medical Center, says part of the need for the overhaul stemmed from new trends in how biomedical research is conducted. “There are more collaborations

between groups of researchers,” he explains, “and increased dependence on IT resources and digital imaging.”

The old space at the Nashville VA, he says, was a “series of labs and offices, each with its own door, and each assigned to different PIs [principal investigators] or groups of PIs.” Because unused rooms had to be locked for security rooms, he says, and certain equipment was housed in those labs, researchers often had to work around others’ schedules to get their work done.

Walsh says the new open, modular floor plan makes it easier for researchers to access shared equipment such as centrifuges, freezers, and biological safety hoods, also known as fume hoods. He says the new arrangement “provides maximum flexibility to the various lab groups and enhances collaboration.”

Dr. Donald Rubin, an infectious disease specialist who serves as the associate chief of staff for research at Nashville, expands on Walsh’s point about sharing resources. He cites, as an example, the CO₂ tanks that service the incubators in which cell cultures are stored for experiments. The special gel that preserves the cells needs just the right acid-base balance in the air, and the extra CO₂ does the trick.



Dr. Suman Laal, a microbiologist, works at the Manhattan campus of the VA NY Harbor Healthcare System. The facility is one of many VA sites nationwide where biomedical labs have been upgraded.

Photo by Lamel Hinton

In the past, each researcher had his or her own incubators. That meant lots of extra gas tanks to keep around, with the attendant costs and safety concerns. Now, the incubators are shared, thanks to the open floor plan, and far fewer gas tanks are required.

Same with the biological containment hoods. There were 51 in all in the building, pre-renovations. When the work is complete, there'll be about half that amount. A similar story applies to the high-powered electron microscopes that many research groups rely on.

“Ultimately,” says Rubin, “this saves the taxpayer from buying items that can be shared, such that more money can go into the actual novel parts of an investigator’s research project.” ★

RESEARCH INFRASTRUCTURE PROGRAM BY THE NUMBERS

In response to a congressional mandate, VA’s Office of Research and Development (ORD) established the VA Research Infrastructure Evaluation and Improvement Project, known as the Research Infrastructure Program for short. Here are key details:

- Assessment mandated by Congress in 2006 and concluded in 2010
- Included all sites with at least \$500,000 in VA research funding per year and an onsite biomedical research program
- 171 buildings at 74 VA campuses assessed, covering 1.7 million square feet of lab space
- Nearly \$774 million in deficiencies identified
- More than \$100 million spent by ORD to date to buy new equipment and fix certain safety hazards (costs for repairs, renovations, and brand new construction is covered by other VA funds)

WHAT TYPES OF PROBLEMS WERE FOUND?

Below are examples of common deficiencies found in each of the five categories assessed in the Research Infrastructure Program:

- **Architectural**—presence of asbestos, wrong types of surfaces, corrosion from chemicals, ceiling leaks, lack of code-compliant safety showers and emergency eyewashes
- **Plumbing**—aging systems, lack of proper backflow prevention, lack of separate waste systems for labs
- **HVAC**—lack of appropriate air changes and exhaust systems, air intakes located near automobile parking areas, lack of appropriate equipment for dehumidification and refrigeration
- **Electrical**—insufficient space on electrical panels for additional circuits, lack of backup systems, lack of GFCI outlets near sinks
- **Fire safety**—aging systems, lack of complete sprinkler systems and adequate smoke detection.

VA and DoD lead the way in integrating chaplains into mental health care

The Rev. Austin Ochu knows a little something about trauma. Before coming to VA, the Roman Catholic chaplain worked with Liberian refugees in the Ivory Coast in West Africa, so on a recent day at the Baltimore VA Medical Center, when an Afghanistan Veteran mentioned suicide, Ochu knew exactly what to do. “I listened to his story. We talked about guilt, fear, forgiveness, and lack of hope, and when we were done, he promised to come see me again.”

Ochu is part of a growing movement in VA and the Department of Defense (DoD) to integrate spirituality with mental health care, as discussed in an April 2013 report in the *Journal of Health Care Chaplaincy* coauthored by Dr. Keith Meador, director of VA Mental Health and Chaplaincy, with colleague Dr. Jason Nieuwsma and others.

‘THEY GO TO THEIR CHURCH FIRST’

While chaplains have long served the needs of service members and Veterans, they are increasingly being seen as important to providing integrated mental health care services. Part of this is due to the unique role chaplains play in a service member’s life. “People don’t go straight to their psychiatrist,” says Ochu, who meets several times per week with his peers on the mental health side to workshop ways they can better assist Veterans. “They go to their church first.”

That, according to Meador, is one reason why chaplains must be integrated into overall mental health care. “The reality is chaplains are inevitably looked to as first line providers with regard to mental health issues,” says Meador, who is based at the Durham VA Medical Center “Chaplains are trusted. Even if they [Veterans] are not particularly religious, they see the chaplain as someone they can talk to ... yet historically the two [mental health and chaplaincy] have not worked together.”

Meador points to research identifying a link between spirituality and mental health. For example, studies have shown that many of the struggles Veterans experience with



William (Wayne) West is a chaplain in the Central Arkansas Veterans Healthcare System.

Photo by Jeff Bowen

posttraumatic stress disorder are worsened by difficulty with forgiveness and spiritual beliefs. Based on data from that and many other studies, VA and DoD launched the VA/DoD Integrated Mental Health Strategy (IMHS) in 2010. A key component focused on the need for collaboration between chaplains and mental health providers. As part of the IMHS, Meador and his colleagues conducted site visits to 33 VA or DoD facilities over a two-year period, collected more than 2,000 surveys from chaplains, hosted expert forums, and developed a task group of leaders and experts in the fields of chaplaincy and mental health.

DEVELOPING A MODEL OF INTEGRATION

The researchers found that although chaplains were extensively involved in mental health care, they were limited in their effectiveness as a result of training, location, and a lack of understanding and cooperation between chaplains and mental health professionals.

As a result of the IMHS study, Meador and his colleagues developed a model to integrate chaplains into overall VA mental health care. The first step is training. Despite the fact that chaplains are often on the front lines of mental health care and are well-educated, Meador and Nieuwsma research identified gaps in how chaplains viewed their training. They reported not feeling optimally prepared to deal with anxiety,

depression, and other common mental health issues, despite the fact that those are the issues they are overwhelmingly faced with. “We want to better equip them to meet the needs that they clearly are encountering without taking away from that traditional chaplain role,” says Meador.

Similarly mental health professionals often reported not knowing how to use the chaplains they worked alongside. “Although we encountered a number of mental health professionals who knew little about chaplaincy, by the end of a day-long site visit we frequently saw that the two disciplines were having ideas about how they could work together,” says Dr. Jason Nieuwsma, associate director of VA Mental Health and Chaplaincy. Researchers have begun joint training, webinars, and systems redesign efforts to increase interaction and build skills.

TENDING TO THE ‘BODY AND SPIRIT’

In addition to training, researchers proposed having teams of chaplains and mental health experts develop integrated tools and plans for bridging the gap between clergy and mental health professionals. The idea of working together highlighted another major barrier: location. Chaplains and mental health workers should be located together, Meador says, and that is not normally the case.

The end goal is to develop integrated teams to care for all of a patient’s needs. “A person is both body and spirit,” says Ochu. “Just as you treat someone’s physical needs, you must also worry about their spirit. That is what patient-centered care is about and that is what we do here at VA.”

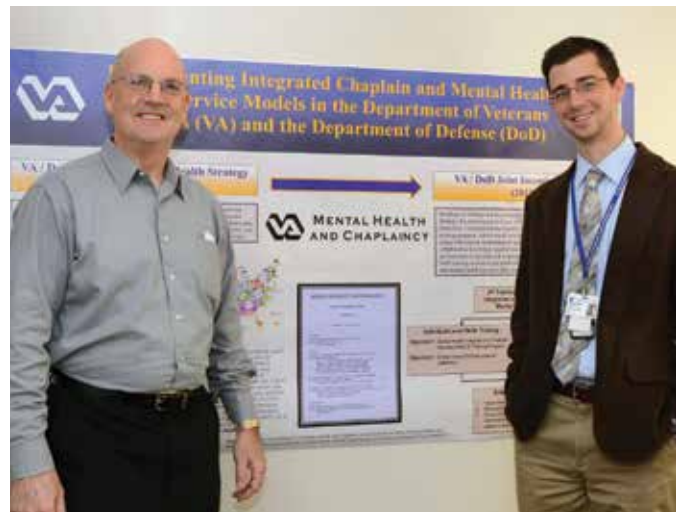
Although the study was unprecedented, there were limitations. Researchers didn’t have the time or capacity to solicit information from Veterans and service members or to garner more input from mental health professionals. Meador and Nieuwsma’s integration model also remains untested and will likely need to be refined before it can fully function. Also, they anticipate some natural resistance from the mental health community to the integration plan.

Challenges notwithstanding, Meador remains optimistic. “VA and DoD are leading in this. Incorporating chaplains and clergymen into health care will be a major asset, not just for the VA, but across the health care spectrum. These are good changes.” ★



Rev. Austin Ochu is a chaplain at the Baltimore VA Medical Center.

Photo by John Crawford



Chaplain Bill Cantrell (left) and Dr. Jason Nieuwsma are with VA Mental Health and Chaplaincy.

Photo by Linnie Skidmore



Dr. Maurice Dysken, a geriatric psychiatrist at the Minneapolis VA Health Care system, led a VA study testing vitamin E and other treatments for Alzheimer's disease.

Photo by April Eilers

Vitamin E slows Alzheimer's in VA trial

Vitamin E, known for its antioxidant power, helped slow the progression of Alzheimer's disease in Veterans with mild to moderate symptoms in a trial reported Jan. 1 in the *Journal of the American Medical Association*.

More than 600 Veterans from 14 VA medical centers around the country took part in the VA-sponsored trial. Researchers followed them for up to four years, with an average follow-up of about two years and three months.

Although the disease progressed in all treatment groups, vitamin E slowed the disease by about six months, compared with placebo. In other terms, it slowed the worsening of Alzheimer's disease by almost 20 percent per year, compared against placebo. The main outcome measure was a test of how well the patients could perform activities of daily living.

Lead researcher Maurice Dysken, MD, a geriatric psychiatrist, says a delay of this size in the disease's progression can have a significant impact on quality of life for patients and their family members.

"It could be very meaningful for someone with early Alzheimer's who is still functioning at a high level, and for his or her caregivers, to have a delay of six months in the progression of the disease over about a two-year period," says Dysken. "When the disease has progressed to a severe stage, the benefits of a delay of this size are less apparent."

Dysken is former director of the Geriatric Research, Education, and Clinical Center at the Minneapolis VA Health Care System. He is also a professor of psychiatry at the University of Minnesota.

VITAMIN E BEATS OTHER TREATMENTS

In the study, his team compared vitamin E against three other treatments: the drug memantine (sold as Namenda), vitamin E plus memantine, or placebo. Vitamin E beat all the other approaches, including the combination treatment. Outcome measures included not only patient's daily function and cognitive health, but also caregiver burden.

More than 600 Veterans from around the country took part in the study.

In the raw data, caregivers of those on vitamin E reported about two hours less per day of caregiving activity compared against the other three groups. After statistical adjustments, though, the difference remained significant only when the vitamin E group was compared with the memantine group.

According to existing clinical guidelines in VA and other health care systems, memantine is generally used only for more advanced cases of Alzheimer's. It typically provides some temporary slowing of the disease. Evidence for its effectiveness in less severe cases has been lacking. The new VA study supports those guidelines.

All the patients in the study were also on a cholinesterase inhibitor drug. These medications, known by brand names such as Aricept and Razadyne, block an enzyme that breaks down acetylcholine, a brain chemical involved in learning and memory. The drugs are a firstline treatment for Alzheimer's, especially in the mild to moderate stage.

These drugs often have adverse side effects, though, particularly nausea and diarrhea. Based on the new trial results, Dysken says vitamin E is an attractive alternative, in terms of effectiveness. "We would say vitamin E is comparable to any of the existing medications." He notes that it's also less expensive.

RESEARCHERS WATCHED CLOSELY FOR VITAMIN E SIDE EFFECTS

Vitamin E supplementation is not without its own risks. Some research has suggested it may slightly increase the risk of death. No such effect was seen in the VA study.

"We looked at that very carefully as we designed the study protocol," says Dysken, "and the patients were monitored very closely throughout the trial." He notes that no patients in the trial, including those with existing heart disease, appeared to do any worse on vitamin E, compared with their peers in the other treatment groups.

Vitamin E is found in a wide variety of foods, including eggs, whole grains, and beef. But Dysken says getting the nutrient from food is unlikely to achieve the same benefits seen in the study.



Patients in the study who received vitamin E were given 2,000 IUs per day.

Photo: iStock

"We gave patients 2,000 IUs [international units] per day," says Dysken. "That's about 20-fold greater than the dosage commonly found in a multivitamin containing vitamin E. The dose used in the study is pharmacological, as opposed to nutritional. It's really a huge difference."

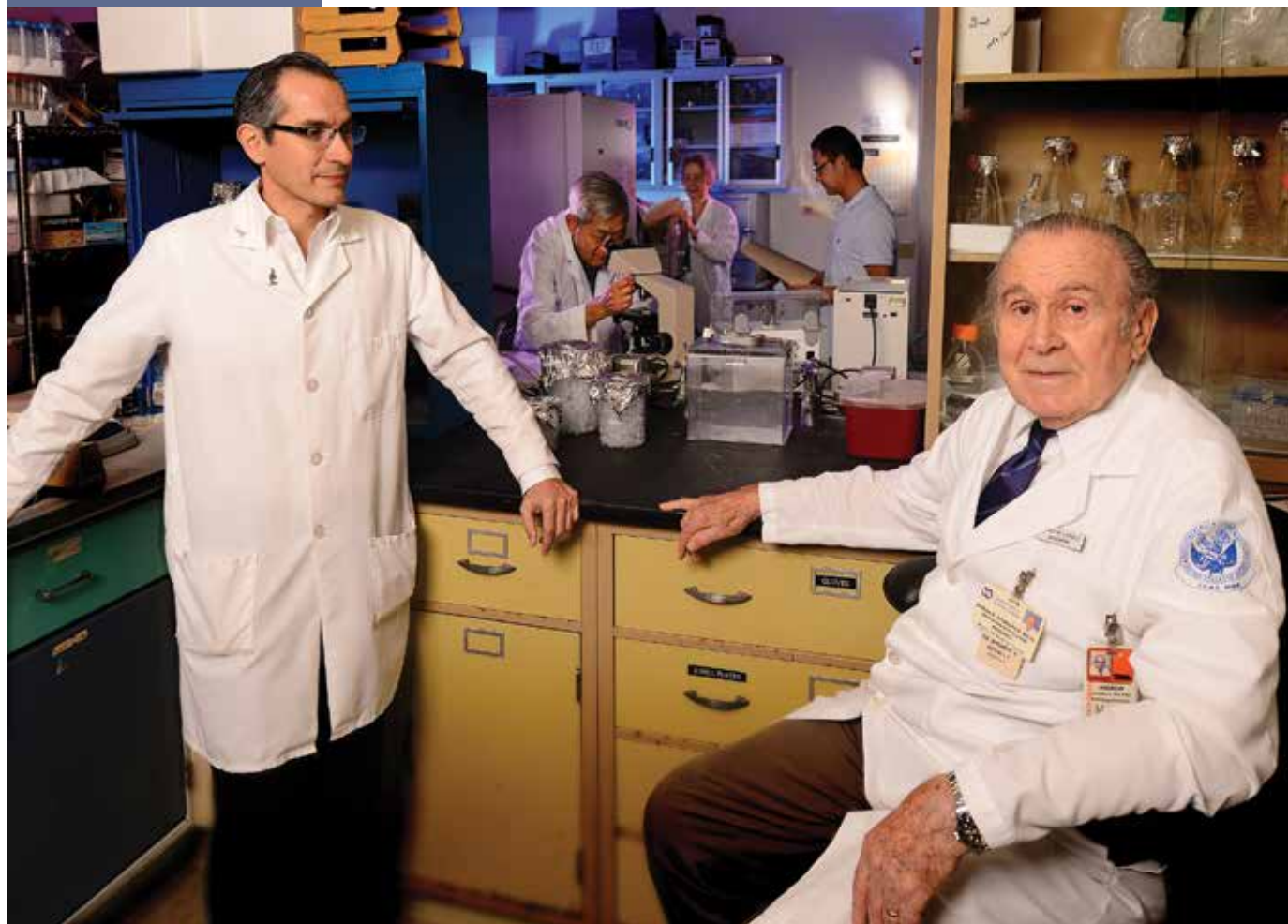
Vitamin E comes in several forms, including alpha-tocopherol, which has been found to be the most biologically active in humans. The VA study used a synthetic formulation of alpha-tocopherol. Dysken says this was the same agent used in a late 1990s trial that found vitamin E effective in later stages of Alzheimer's. The new VA trial is among the first large studies to show benefits in earlier stages of the disease.

Dysken says there's no evidence to suggest other types of vitamin E supplements—such as natural, food-based formulations, versus synthetic chemical-derived ones—would have any different impact on Alzheimer's.

According to Dysken and other experts, vitamin E's effects against the brain-ravaging disease are likely due to its antioxidant properties. Researchers in VA and elsewhere are studying a variety of other antioxidants for their effects against Alzheimer's. They include, for example, compounds found in red tea, red grapes, and the spice turmeric.

Dysken says it's still "an open question" as to whether vitamin E is unique in its anti-Alzheimer's properties, or simply one of many antioxidants that could achieve the same effect.

The trial was sponsored by VA's Cooperative Studies Program. ★



Dr. Andrew Schally (right) of the Miami VA Medical Center, a past Nobel Prize winner, is part of an international team that has developed a new type of artificial pancreas. To his left is lab manager Ricardo Rincon.

Photo by Larry Gilstad

Miami VA part of international breakthrough in cell therapy

An international research team including scientists at the Miami VA Medical Center has devised a way to transplant healthy cells into the body without the usual risk of rejection. The study, published November 19 in the *Proceedings of the National Academy of Sciences*, involved a middle-aged man with diabetes, but it may be relevant to a range of diseases.

Study co-author Dr. Andrew Schally, a half-century veteran of VA

research who won a Nobel Prize in the 1970s, called the results “historic.”

The researchers, based in Germany, Israel, England, and the U.S., developed what they term a “bioartificial pancreas.” The pancreas is where the body makes insulin, the hormone that helps move sugar from the bloodstream into the body’s cells, where it supplies energy. In type 1 diabetes, an autoimmune disease, the body kills off the pancreas’ insulin-producing beta cells.

The Israeli scientists developed a biocompatible chamber that encloses clusters of beta cells, called islets, in their own oxygen-rich environment. The cells are packed in a gel that shields them from attack by the host immune system, and the whole assembly is housed in a biocompatible plastic shell. The chamber, about 2.5 inches in diameter and a half inch thick, is surgically implanted and linked to ports that the patient himself can use to inject in fresh

The researchers, based in Germany, Israel, England, and the U.S., developed what they term a “bioartificial pancreas.”

oxygen, at least until new blood vessels develop around the graft.

BOOSTING THE VIABILITY OF TRANSPLANTED CELLS

The Miami VA team, including Schally and Dr. Norman Block, played a key role in the development and animal testing of the system. They showed that compounds that mimic growth hormone-releasing hormone (GHRH) could boost the viability of transplanted beta cells and their ability to make insulin. This means a graft would need fewer functioning beta cells to be effective.

The compounds are not yet approved for human use, but their effectiveness in animal experiments helped spur the Miami group’s Israeli and German colleagues to pursue the idea of an implantable pancreas.

The 63-year-old patient who took part in the new study was followed for 10 months, after which time the artificial pancreas was removed. The graft had remained healthy, with the transplanted beta cells pumping out insulin. His blood sugar levels showed only small improvements, though. The researchers said having more islets available to transplant—or treating the cells with one of the compounds from

Schally’s lab—could have yielded even better results.

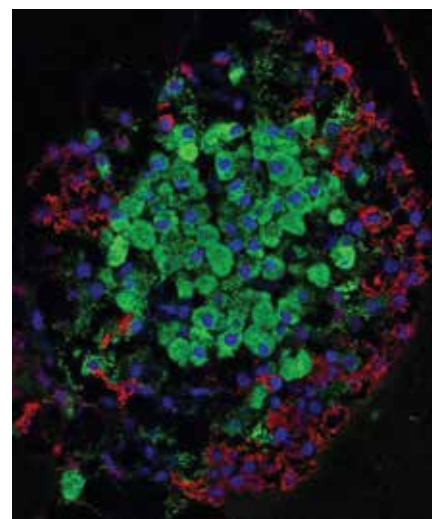
Importantly, the patient tolerated the transplant well without taking drugs to suppress the immune system. The drugs often entail major adverse side effects and have limited the use of medical transplants until now.

TECHNOLOGY COULD HAVE WIDE APPLICATION

Lead author Dr. Barbara Ludwig and her group, based in Dresden, Germany, say the new system could be a realistic treatment option for type 1 diabetes patients within a few years.

Block points out that the therapy could potentially also help those with type 2 diabetes—namely those with more severe forms of the disease, who rely on daily insulin shots. About one in five VA patients has type 2 diabetes.

Human beta cells for transplantation are hard to come by, but research has shown that cells from pigs are a good alternative. Block says the new study shows that transplanted cells can be protected from attack by the immune system, and the approach, in theory, should work as well with pig cells as with human cells. That may expand how many patients could



In this section of a rat pancreas, the insulin-producing beta cells are stained green. VA scientists and colleagues have now successfully transplanted human beta cells into a patient with diabetes.

Photo by Masur, via Wikimedia Commons

potentially benefit from the procedure.

He adds that the new transplant method could also potentially apply to a variety of other serious health conditions.

“Other diseases that could be helped by individual cells or groups of cells, as opposed to organ transplants, could well benefit from this technology,” says Block, a former VA cancer surgeon and current clinical director of the Endocrine Polypeptide and Cancer Institute at the Miami VA, where Schally has led research on diabetes, cancer, and other diseases since relocating from New Orleans in the wake of Hurricane Katrina in 2005. ★

Israeli prize to BrainGate team

The Brown University-VA research team that created the investigational BrainGate brain-computer interface won a major international award, the \$1 million Moshe Mirilashvili Memorial Fund B.R.A.I.N. Prize, at a brain science technology conference in Israel this past October.

Israeli President Shimon Peres presented the prize, including a bronze brain statue, to Drs. John Donoghue and Arto Nurmikko.

“We are deeply honored to receive this award,” said Donoghue, co-director of the BrainGate team, a researcher at the Providence VA Medical Center, and director of the Brown Institute for Brain Science. “It will support our continued research to help people with paralysis, some of whom cannot speak, to restore their connection to the world around them.”

The prize is awarded “for a recent breakthrough in the field of brain technology for the betterment of humanity,” according to a statement by Israel Brain Technologies, a non-profit organization inspired by Peres that grants the award. The contest’s panel of judges—experts in neuroscience and technology, including two Nobel laureates—considered presentations from 10 finalists before selecting BrainGate.

The BrainGate system, now being studied in clinical trials with partners including Massachusetts General Hospital, Stanford University, and Case Western Reserve University, uses a baby aspirin-size device with a grid of 96 tiny electrodes that is implanted in the motor cortex—the part of the



(From left) **Drs. Arto Nurmikko and John Donoghue** accept a bronze brain statue, part of the \$1 million Moshe Mirilashvili Memorial Fund B.R.A.I.N. Prize, from Israeli President Shimon Peres.

brain that controls voluntary hand and arm movements. The electrodes record the activity of neurons. An external computer translates the impulses into commands for robotic arms or other assistive devices.

The co-leader of the BrainGate team, Dr. Leigh Hochberg was not on hand for the presentation in Israel, as he was lecturing at the annual meeting of the American Neurological Association.

“All of us on the BrainGate research team are deeply honored to receive this award,” said Hochberg, an associate professor at Brown, neurologist at Massachusetts General Hospital, and researcher at the Providence VA’s Center of Excellence for Neurorestoration and Neurotechnology. “Our team of clinicians, scientists, engineers, and the extraordinary participants in our ongoing pilot clinical trial continue to work every day toward developing a technology that will restore communication, mobility, and independence for people with neurologic disease or injury.” ★

“[The award] will support our continued research to help people with paralysis, some of whom cannot speak, to restore their connection to the world around them.”



Testosterone replacement therapy is advertised as a way to boost libido, improve energy, and sharpen performance for men with low testosterone levels.

Photo: iStock

Testosterone therapy associated with higher risk of death, heart attack, or stroke

Men with heart problems may be at an increased risk of heart attack, stroke, or even death if they are treated with testosterone therapy, a VA study has found. Researchers say the results should provide additional information for patients and their physicians about potential risks, given the booming testosterone trade.

Testosterone therapy is widely advertised as a way to increase libido, improve energy, and sharpen performance for men suffering low testosterone. Sales have tripled over the last decade. In 2011 alone, the U.S. market for testosterone involved 5.3 million prescriptions to the tune of \$1.6 billion.

But according to a team led by Dr. Rebecca Vigen, a researcher with VA and the University of Texas and lead author of the VA-sponsored study, Veterans undergoing testosterone therapy had a 29 percent greater risk of death, heart attack, or stroke than those not on the hormone over an average follow-up period of 27.5 months.

The study looked at 8,709 male Veterans with a history of heart problems. The participants all underwent a coronary angiography, a procedure for identifying blockages in the arteries, at a VA facility between 2005 and 2011.

Of the participants, 1,223 patients were started on testosterone therapy in the form of patches, gels, or injections. The researchers monitored the men for more than 27 months. At three years, 26 percent of Veterans who had received testosterone had either died or suffered a heart attack or stroke, compared with 20 percent of those not receiving therapy.

“These findings raise concerns about the potential safety of testosterone therapy,” the study authors wrote. They called for future studies to further identify any potential risks, particularly for those already suffering from heart conditions.

Because the men had existing cardiovascular conditions prior to beginning therapy, it is possible that the risks of testosterone therapy highlighted in the study apply more to those already at elevated risk for heart attack. Nevertheless, with the overall popularity of testosterone therapy on the rise, the researchers suggest that Veterans discuss their options with their doctor and weigh the benefits and risks before pursuing the treatment. ★

(Journal of the American Medical Association, Nov. 6, 2013)

Army Sgt. Danielle Modglin, left, and Spc. Ricky Morris take part in a Veterans Day ceremony in Washington, D.C., in 2008. The Soldiers, who were wounded in Iraq, were recovering at Walter Reed Army Medical Center.

Photo by Michael J. Carden



For women Veterans, better friendships equal better health

Maintaining the social support of military peers after active duty is associated with better physical health among women Veterans, regardless of whether or not they have posttraumatic stress disorder, say researchers at the VA Puget Sound Health Care Center.

The study involved more than 3,600 women Veterans from across the country. The women, who included Vietnam-era as well as Iraq and Afghanistan

Veterans, underwent PTSD screening. Seventy percent reported trauma exposure and among those 19 percent screened positive for PTSD.

Among other questions, the researchers asked the Veterans about military social support. Specifically, they asked them how much they agreed with the statement: “You have been able to maintain the social support of your military friends.”

That information, in addition to the women’s PTSD status, was analyzed against self-reported physical health and the number of times the women had accessed VA care. Screening positive for PTSD was linked to poorer health and more use of health care resources. Greater military social support was associated with better health and less frequent health care utilization. The positive impact of social support was significant regardless of the women’s PTSD status.

“This research demonstrates that military social support for women Veterans is a significant predictor of their physical well-being regardless of whether they screened positive or negative for PTSD,” said lead author Dr. Keren Lehavot. “It suggests social support is an important protective factor that warrants further investigation.”

The study was limited in that Veterans may have misreported hospital visits, trauma, or other information. Furthermore, social support is complex and what holds true for women Veterans might not for male Veterans. For example, one 2013 study found that military peers protected men from mental health issues and civilian support played a larger role among female Marine recruits.

Despite the limitations, the study offers a glimpse into potential red flags as well as possible treatment options to improve overall health among women Veterans. ★

(Journal of Traumatic Stress, December 2013)



Patients receive hyperbaric oxygen therapy in the U.S. Air Force School of Aerospace Medicine's hyperbaric medicine division, also known as the Davis Hyperbaric Laboratory.

Photo courtesy of US Air Force

Trial reveals hyperbaric oxygen has little effect on TBI symptoms

The third of four planned trials on treating symptomatic mild traumatic brain injury with hyperbaric oxygen therapy has been completed and supports prior research, with researchers saying there are no statistically or clinically significant benefits to the therapy.

The most recent trial, conducted jointly by the Department of Defense and VA, took place at the Naval Medicine Operational Training Center at Naval Air Station Pensacola in Florida. It involved 60 active duty Marines from Camp Lejeune in North Carolina and from Marine Base Quantico in Virginia. All the Marines in the trial had experienced at least one mild TBI (concussion) over the previous 39 months and had ongoing symptoms associated with the injury. Common symptoms included headaches, dizziness, memory difficulties, and sleep problems.

Over a 10-week period, each Marine underwent 40 one-hour compressions in the hyperbaric chamber. For trial purposes, the researchers used 2.0 times sea level pressure for all 60 subjects and adjusted the mixture of air gases to simulate room air oxygen (about 21 percent oxygen), 1.5 times room air and 2.0 times room air. Each participant

underwent standard post-concussion and PTSD testing, in addition to neuropsychological testing, neurologic exams, computerized balance testing, pain questionnaires, and computerized eye tracking evaluation before and after the trial. In the end, researchers found no significant difference in the Marines' scores following the therapy.

Initially developed to treat diving disorders, hyperbaric therapy delivers higher oxygen content, often up to pure oxygen, at elevated pressures to induce healing. It is covered by Medicare for approved conditions—those for which studies have shown clear benefits. But its effectiveness has not been demonstrated in treating brain injuries. A parallel trial, also sponsored by VA and DoD, involving 50 service members in Texas, also failed to show any benefit to the treatment.

Other studies on the effects of hyperbaric oxygen therapy on TBI are currently underway. As of now, researchers say hyperbaric oxygen therapy has not been shown to improve symptoms after mild TBI. ★

(Journal of Head Trauma Rehabilitation, online Sept. 18, 2013)



(Below) **VA researchers** are collaborating with scientists from Britain to study the anti-bacterial properties of *Hypericum olympicum*, commonly known as St. John's Wort.

Photo by H. Zell, via Wikimedia Commons



Detroit VA researchers (from left) Dr. Bryan Schindler, Susan Seo, and Dr. Glenn Kaatz helped show that St. John's Wort may play a role in combating MRSA.

Photo by Larry Marchionda

Flower emerges as possible **weapon** against MRSA

Flowers may be among the most delicate creations in nature, but they have also developed powerful mechanisms to fend off harmful microbes and other environmental threats.

So it is with the *Hypericum olympicum*, commonly known as St. John's Wort, a small Eurasian shrub adorned with distinct star-shaped yellow blossoms that is already used by many as an herbal remedy for depression. Researchers at the Detroit VA Medical Center, collaborating with scientists at the UCL School of Pharmacy in London, suspect extracts from the flower might be able to defeat methicillin-resistant strains of *Staphylococcus aureus*, or MRSA.

MRSA is resistant to many common antibiotics, and infections caused by this organism can be difficult to

treat. The infections can quickly spread throughout the body and become potentially life-threatening. MRSA is particularly dangerous in hospitals and other medical facilities, where patients may have open wounds or weakened immune systems.

Hoping to find a new antibacterial, the researchers collected parts of the flower from the Royal Botanic Garden Kew in the United Kingdom and ground them into a powder. The powder was then isolated in a Soxhlet apparatus, a device first used in labs more than 120 years ago that is still used by scientists today to filter out impurities.

The study involved bringing the resulting compound into contact with several different *Staphylococcus* strains,

including antibiotic-resistant types, across a variety of testing conditions, to see how the bacteria reacted. Researchers found that the compound did in fact display antibacterial properties. Although the presence of blood tended to disrupt its effectiveness, researchers believe the compound could prove useful as a topical application to disrupt bacteria living on the skin, or inside the nasal passages, where MRSA tends to thrive.

Further research is required to better isolate the flower's antibacterial properties, but the study may suggest a novel way to tackle drug-resistant infections. ★

(International Journal of Antimicrobial Agents, December 2013)

Stem cell advance uses adult blood

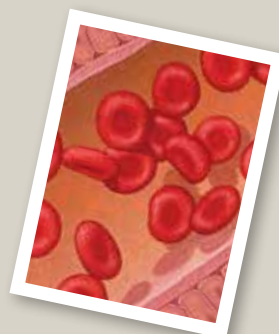
Researchers at VA and Loma Linda University in Southern California have discovered a way to reprogram adult blood cells into stem cells. The research offers hope for patients suffering from a variety of diseases.

Stem cells have long been seen as the cornerstone of regenerative medicine. Their ability to reproduce forever and be reprogrammed into an assortment of tissues separates them from other cells. Early research showed promise, but the cells are hard to come by. Fetal stem cells raise ethical concerns, and there is more demand than umbilical cord blood alone can meet.

This study is the first to report that blood cells drawn from adults can be reliably reprogrammed into multipotent stem cells that can be made into any number of other types of cells.

According to Dr. Xia-Bing Zhang, lead author of the study, human-induced mesenchymal stem cells, or iMSCs, are found in the blood and can be grown into muscle fibers, bone, cartilage, and more. The tissue can then be used to rebuild injured bones or regenerate organs.

One challenge is that it takes time to develop iMSCs. Doctors have to harvest them from bone marrow or connective tissue during surgery. Even then there are problems. "These cells have shown potential for clinical therapies, but often insufficient amount of cells or subpar regenerative potency of the harvested cells hampers their wide-spread application," said VA researcher Dr. William Lau, who worked on the study.



VA researchers in Loma Linda have found a way to reprogram adult blood cells into stem cells.

Another option is to grow the cells from scratch using skin cells taken during biopsies. But this process is difficult and can take months. In some cases, tumors can develop as a result of contamination.

Zhang's team instead found a way to develop iMSCs from adult blood by using a single protein. The cells were converted using OCT4, a protein involved in stem cell renewal.

"The new development—using patient's own blood cells—considerably simplifies the conventional approaches," said Lau.

Sixteen percent of the OCT4-converted cells turned into iMSCs in two weeks. This ability to reprogram blood cells "has important implications for regenerative medicine," wrote the authors.

The researchers hope the shortened development time will lead to faster responses to medical needs. An added benefit is that patients' own cells can be used to treat their illness. This kind of targeted medicine is particularly useful in ensuring patients' bodies don't reject donated organs.

Lau believes the research will lead to further developments in adult-derived iMSCs and eventually impact treatment for Veterans, particularly those suffering skeletal injuries. ★

(Cell Research, May 2013)



Women with a variant of a gene called CRHR-2, involved in the body's response to threats, could be at reduced risk for PTSD following a trauma, suggests a study by VA researchers in Boston.

U.S. Marine photo by Sgt. James R. Richardson

Genetics plays role in lessening PTSD in some women

Women with a specific genetic variant are less likely to suffer the effects of posttraumatic stress disorder, according to a new VA study.

Researchers already knew that the corticotropin releasing hormone (CRH) system is associated with anxiety and mood-based disorders and plays a role in the biological response to threat. Now a study of 491 trauma-exposed Veterans and their intimate partners has revealed that women with a variant of a gene, called CRHR-2, involved in regulating the CRH system may experience reduced symptoms of PTSD following trauma

exposure. The research could lead to new ways of preventing and treating trauma disorders.

Genetic variation could explain why only a subset of those exposed to trauma ever develop the disorder. Some 50 to 90 percent of the general population experience trauma in their lives, yet only 8 to 14 percent ever develop PTSD. "This suggests that individual differences in biological risk may increase or decrease the likelihood of PTSD," wrote the study authors, led by Dr. Erika Wolf and principal investigator Dr. Mark Miller, of the National Center for PTSD at VA

Boston Healthcare System and Boston University School of Medicine.

Wolf and colleagues looked at 491 Caucasian participants between 21 and 75 years old who reported traumatic exposure. Sixty-five percent of the participants were males and just over 60 percent met criteria for a diagnosis of PTSD at some point in their lifetime.

For the study, researchers recruited Veterans via fliers, phone calls, and clinical referrals and then conducted videotaped interviews to determine if individuals met criteria for PTSD and other mental health diagnoses. Participants were then asked to

provide a blood sample that was genotyped to examine genetic variation across the genome, including in the CRHR-2 gene.

The researchers found several locations within the CRHR-2 gene that were associated with reduced risk of PTSD and reduced severity of PTSD symptoms. These associations did not vary across individuals with different levels of trauma but did differ across men and women in that the effect was more pronounced among the women in the sample. “The findings provide initial evidence that the relationship of the CRHR-2 genotype to PTSD may be specific to women,” wrote the authors. The study is the first of its kind to look at how this CRH variant and trauma affect risk for PTSD. ★

(*Depression and Anxiety*, December 2013)



New center to study heart and lung disease—Dr. Sharon Rounds, chief of the medical service at the Providence (R.I.) VA Medical Center and a professor at Brown University, directs the new CardioPulmonary Vascular Biology Center of Biomedical Research Excellence. The National Institute for General Medical Sciences, part of the National Institutes of Health, established the program in October with a \$10.1 million grant. The center will support a team of five junior investigators studying the biology of heart and lung disease, with an eye toward developing new treatments.

Photo courtesy of Brown University

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RESEARCH CURRENTS

Research News from the U.S. Department of Veterans Affairs



DID YOU KNOW?

Dr. William Oldendorf, who is credited with pioneering the theory behind the CT scan and other forms of medical imaging, was a neurologist at the Los Angeles VA Medical Center in the late 1950s when he received a \$3,000 grant from the hospital to pursue his research. He used part of the money to build a prototype of a CT scanner in his home—using, among other things, tracks from a model train set. Oldendorf won the prestigious Lasker Award in 1975, and was later nominated for a Nobel Prize.



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