



RESEARCH CURRENTS

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



Photo: ©iStock/Irina Silyayeva

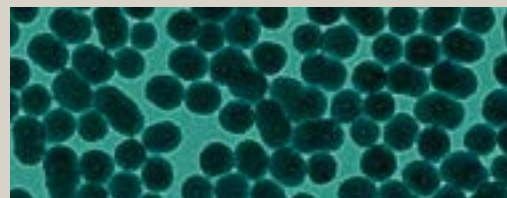
**To prescribe or not to prescribe:
When it comes to antibiotics, that is the question 8**

WHAT'S INSIDE

Virtual reality boosts job-interview skills **10**



Ancient therapy making comeback for wound healing **12**



In the works: A 'nano' approach to building bone **18**



Treating prostate cancer: Should race matter? **20**

Fast Findings

- The value of in-person social contact **2**
- Brain damage from high blood pressure **3**
- Women at no greater risk for PTSD **4**
- Longer colonoscopies and lower cancer rates **5**
- Sleep apnea linked to kidney disease **6**
- Mood disorders after deployment **7**





The print edition of
VA Research Currents
 is published quarterly by:
VA Research Communications
U.S. Department of Veterans Affairs
 31 Hopkins Plaza, Ste. 102
 Baltimore, MD 21201
 443-759-3456
 410-962-0084 (fax)
 varesearchcurrents@va.gov

Read the expanded online edition of
VA Research Currents at www.research.va.gov

 [facebook.com/VAResearch](https://www.facebook.com/VAResearch)

 twitter.com/VAResearch

Editor: Mitch Mirkin
 Layout: Michael Escalante

Any health information in this newsletter is strictly for informational purposes and is not intended as medical advice. It should not be used to diagnose or treat any condition.

Depression study points to value of in-person social contact

Isolation can be devastating, so much so that many societies use it as punishment—solitary confinement for prisoners, for example. At the heart of it is the fact that human beings are social creatures. Researchers have long known that lack of social contact and the loneliness that accompanies it are risk factors for depression, particularly in older people.

A few hundred years ago social contact would be easy to define—interacting face-to-face with someone. In today's world of virtual connectivity, friends and family can talk or see each other in real time, at any time, regardless of place. Texting, instant messaging, email, Skype, and phone all mean that a friendly face, voice, or message is literally at our fingertips. But is that enough to stave off depression, particularly for older people who may not be fit enough to get out for frequent face-to-face interactions?

New research suggests that technology can't beat an old-fashioned in-person gab session. A VA study published online Oct. 6, 2015, in the *Journal of the American Geriatrics Society* found routine in-person contact could substantially reduce the risk of depression for older adults. And generally speaking, the more such contact, the better. Written correspondence—including email—did not have the same effect. Nor did phone contact, although this

mode of contact seemed particularly helpful for those with existing depression.

The study was presented earlier this year at the annual meeting of the Society of Behavioral Medicine.

The patterns varied somewhat depending on the age group—50 to 69, or age 70 and older. But the bottom line, concluded the researchers, is that “infrequent in-person social contact with friends and family is an important predictor for the development of clinically significant depressive symptoms in older adults.”

For Dr. Alan Teo, an investigator at VA’s Center to Improve Veteran Involvement in Care and a staff psychiatrist at the VA Portland Health Care System, the study has ramifications far beyond mitigating depression in elderly patients. “We know people who are isolated have all sorts of bad mental health outcomes, not just a higher risk for depression,” he says. “And we know social contact acts as a buffer against depression, and not just for older people or people who already have depression, but for everyone.”

Teo and colleagues identified more than 11,000 participants based on data from the Health and Retirement Study between 2004 and 2010. The participants were assessed for depression symptoms and, over the course of two years, asked to identify how often they had met up, telephoned, or had some form of written correspondence with family or friends.

On average, the participants talked on the phone a few times per month, mostly with children and family members. The next most-frequent type of contact was in-person meetings, followed by email or other written contact.

One of the strongest findings: For those age 70 or older, the odds of depression were 53 percent lower after two years if they reported having had in-person contact three or more times per week with children. The odds were 48 percent lower if their regular contact was with other family, not children.

“It’s interesting to note that the positive effects we found were tied to contact with friends for those under 70,” says Teo. Participants over aged 70

benefited more from contact with family.

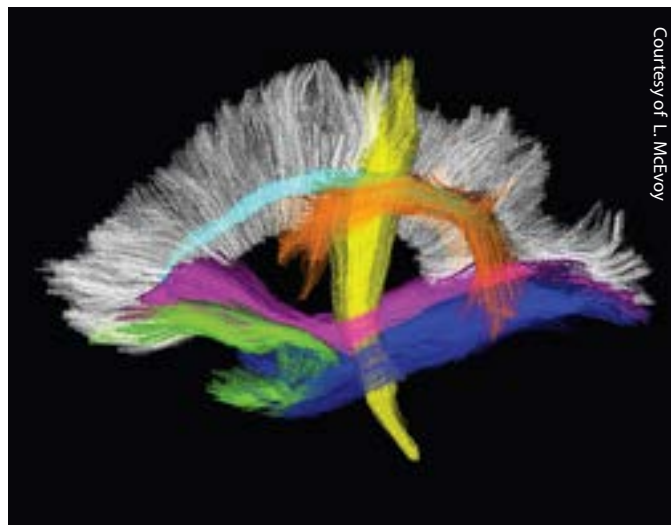
Regardless of whom they were contacting, or how, what was clear was that the participants used a variety of methods to communicate. “In a way it was good news,” says Teo. “People weren’t just shutting themselves up and using email or [other] written correspondence. They haven’t shunned meeting in person.”

Brain damage from high blood pressure starts early

If you want to keep your brain healthy as you age—and who doesn’t?—nip hypertension in the bud.

That’s the message of a new report from the Vietnam Era Twin Study of Aging, now appearing in the journal *Hypertension*, published by the American Heart Association.

VA and university researchers, based mainly in San Diego, imaged the brains of more than 300 Vietnam-era Veterans. They found similar white-matter damage in those with high blood pressure whether the condition was relatively new or long-standing. The effects were also similar regardless



Diffusion MRI images such as these can reveal subtle white-matter damage in the brain.

of whether the high blood pressure was controlled through medication.

“The results suggest that prevention—rather than management of hypertension—may be vital to preserving brain health in aging,” wrote the researchers.

In other words, once blood pressure rises above normal, subtle but harmful brain changes can occur rather quickly—perhaps within a year or two. And those changes may be hard to reverse, even if blood pressure is nudged back into the normal range with treatment.

“The findings suggest that doctors should be aggressive in preventing hypertension—for example, educating patients who are only pre-hypertensive about the importance of lifestyle changes,” says senior author Dr. William Kremen. “Patients may be more willing to make those changes if they realize that their brains may be affected by hypertension, even if medications can be used to adequately control blood pressure.”

Kremen, a psychologist, is with the Center of Excellence for Stress and Mental Health at the VA San Diego Healthcare System and the Center for Behavioral Genomics at the University of California, San Diego.

Lead author Dr. Linda McEvoy adds that most people associate high blood pressure only with strokes, but the potential effects on the brain are much wider—including the insidious microscopic damage to white matter seen in her team’s study. White matter acts like a highway in the brain, allowing for the relay of electrical signals between brain cells.

“People may be aware that high blood pressure increases the risk of stroke, which can lead to cognitive impairment and dementia, but many may not be aware that even in the absence of stroke, high blood pressure may be causing subtle cognitive decline,” says McEvoy, an associate adjunct professor in the department of radiology at UCSD. “It can be contributing to some of the changes in our ability to think that we attribute to growing older. And hypertension-related brain damage can also make

the symptoms of Alzheimer’s disease worse, or make them appear earlier in the course of the disease than they would otherwise.”



Photo by Petty Officer 1st Class Molly A. Burgess, USN

All things being equal—including combat experiences—women are at no greater risk than men for PTSD, suggests research by VA and the Department of Defense.

Women warriors at no greater risk for PTSD than men, study finds

While past research on the question has been mixed, a study by Defense and VA researchers suggests that women in the military are at no greater risk than men for developing posttraumatic stress disorder, given similar experiences—including combat.

The findings are in the September 2015 *Journal of Psychiatric Research*. The study involved active-duty troops and Veterans who are part of the Millennium Cohort Study. That effort has more than 200,000 participants in all.

The new PTSD study included more than 2,300 pairs of men and women who were matched based on an array of variables—including combat exposure—and followed about seven years, on average.

“This is the first study to prospectively investigate the development of PTSD in male and female service members who were matched on multiple important characteristics that could explain some of the differences in PTSD, including military sexual

trauma” says one of the authors, Dr. Shira Maguen. “We found no gender differences in the development of PTSD. Consequently, our focus should be on the types of traumatic experiences that people have been exposed to, rather than any inherent gender differences in the development of PTSD.”

Maguen is the mental health director of the OEF/OIF Integrated Care Clinic and a staff psychologist at the San Francisco VA Medical Center. She’s also an associate professor at UCSF Medical School. Lead author on the study was Dr. Isabel Jacobson of the Naval Health Research Center in San Diego.

All the men and women in the study were free of PTSD at the outset of the research, and they all deployed to Iraq or Afghanistan at least once. They completed a baseline survey in 2001 - 2003, and follow-up surveys in 2004 - 2006 and 2007 - 2008.

During the course of the study, 6.7 percent of women and 6.1 percent of men developed PTSD. The researchers say the difference was not statistically significant. Likewise, for those who did develop PTSD, there was no difference in severity between men and women.

Maguen points out that these rates of PTSD are lower than the commonly cited rates of 11 to 20 percent among returning Iraq and Afghanistan Veterans because the study excluded men and women who had PTSD at the outset.

Longer colonoscopies tied to lower cancer rate

If a colonoscopy seems like the type of thing you’d like to get done with quickly, think again.

Research by a Veterans Affairs team has confirmed that longer-lasting colonoscopies are associated with lower cancer rates.

The findings appear in the October 2015 issue of *Gastroenterology*. They were based on nearly 77,000 screening colonoscopies.

Experts already know about the link between



Dr. Aasma Shaukat is a gastroenterologist at the Minneapolis VA Health Care System.

colonoscopy withdrawal time and patient outcomes, but the new study provides some of the strongest evidence yet to back clinical guidelines covering this aspect of the procedure.

“Our results support the use of withdrawal time as a quality indicator, as recommended by current guidelines,” said lead author Dr. Aasma Shaukat, with the Minneapolis VA Health Care System and the University of Minnesota.

In a colonoscopy, a doctor inserts a long, thin tube with a tiny camera fitted to the end into the patient’s colon. After the tube is fully inserted, it is then slowly withdrawn. It is during this “withdrawal time” that the doctor carefully examines the lining of the colon, looking at a view of the colon on a monitor in the exam room. Any small growths, or polyps, are removed with the scope’s snipping tool and sent for biopsy. These growths may grow into cancer within a few years.

According to current guidelines, a “normal” colonoscopy—one in which there is no finding of cancer or pre-cancerous growths, and the doctor does not remove any snippets of tissue to be biopsied—should have a withdrawal time of at least six minutes.

Shaukat’s team looked at data on colonoscopies performed over six years by 51 gastroenterologists in a large community practice in Minnesota. The team calculated average withdrawal times for each

doctor. The average for the practice on the whole was 8.6 minutes—well within guidelines. But about 10 percent of the doctors had individual averages of under six minutes.

The researchers then checked the state’s cancer registry to look for cases of colorectal cancer among patients who had been screened at the same practice during the study period.

Patients who had been examined by doctors with shorter withdrawal times, on average, were more likely to have cancer. The rate was more than twice as high for patients whose doctors had average withdrawal times of under six minutes, compared with those whose physicians’ average times were over six minutes.

Sleep apnea linked to kidney disease in large study of Veterans

Obstructive sleep apnea—in which the airway becomes narrowed or blocked during sleep—was associated with a greater risk of kidney disease in a database study of more than 3 million VA patients.

The study is not the first to link the conditions, but it is by far the largest. The results appeared online June 2, 2015, in the journal *Thorax*.

“To our knowledge, this is the largest study to date to find substantial associations between a diagnosis of [obstructive sleep apnea] and kidney function decline,” wrote the authors, led by a team at the Memphis VA Medical Center and the University

of Tennessee Health Sciences Center (UTHSC).

The study also confirmed that Veterans with sleep apnea are at greater risk for other poor health outcomes: coronary heart disease, strokes, and death from any cause.

The team adjusted for a wide range of demographic and clinical variables to try and isolate apnea as a risk factor. Still, the study doesn’t prove that sleep apnea causes kidney disease and the other outcomes—only that there’s a strong relationship between them.

That said, the researchers believe there may be several ways in which sleep apnea can in fact damage and weaken the kidneys over time.

Lead author Dr. Miklos Z. Molnar, with UTHSC, says, for example, that the sleep disorder can affect the nerves that help control kidney function. It can also reduce the amount of oxygen reaching tissues in the kidneys, boost inflammation, bring on hypertension, and damage blood vessels, among other effects.

Molnar says further study may shed light on how exactly apnea affects the kidneys, but “today we

know little about the actual mechanisms.”

Those with sleep apnea often snore loudly. The snoring may stop occasionally, followed by choking or gasping for air. Throughout the night, as less oxygen reaches the body, the brain will detect when levels dip dangerously low, and the person will instinctively wake up.

Such sleep disturbances

usually result in daytime sleepiness.

Mild cases of sleep apnea can sometimes be treated effectively with lifestyle changes, such as improved sleep habits, weight loss, and smoking



Photo by ©iStock/digitalkillet

Snoring is one of the signs of sleep apnea, although not all people who snore have the condition.

cessation. In other cases, a nighttime oral appliance that adjusts the position of the jaw and tongue can help. Another common treatment is the continuous positive airway pressure (CPAP) machine, which gently blows air into the throat. In more severe cases, surgery may be needed to widen the airway.

The new study's take-home message for doctors and other health care providers, says Molnar, is that obstructive sleep apnea is clearly one of the risk factors for chronic kidney disease, along with other well-known risk factors such as diabetes, high blood pressure, smoking, and obesity.

Mood disorders after deployment: Could a parasite be partly to blame?

In a study a few years ago, rats infected with a certain parasite not only overcame their aversion to cat urine, but became attracted to it. In other words, they lost their natural fear of cats.

The parasite is *Toxoplasma gondii*. About a third of the people on earth are thought to be chronically infected with it, usually without symptoms. But in the past decade or so, scientists have begun to realize that some people—like rats—can develop serious behavioral problems when the parasite infects their brain. Schizophrenia, depression, suicidality, bipolar disorder, obsessive-compulsive disorder, neuroticism, hyperactivity—all have been linked to the bug in studies around the world.

Now, a team of VA and university researchers has raised the question of whether

T. gondii might be partly to blame for the mood disorders that some troops experience after deployment. The concern arises because *T. gondii* infection is especially common in some areas of the world where U.S. troops have deployed or trained in recent decades, including parts of Europe, Africa, Latin America, Asia, and the Middle East.

In the June 2015 issue of *Military Medicine*, the researchers reported the results of a small pilot study involving 70 women Veterans of various ages. Eight of the women tested positive for *T. gondii*, which can be detected in the blood. Six of these eight had been deployed abroad during their military career.

All the women completed questionnaires measuring PTSD and mood symptoms.

Those women who were infected scored significantly higher—worse, that is—for depression, anger, confusion, and overall mood disturbance.

The results are very preliminary and need replication with a larger sample of Veterans. Also, future studies would need to control for a wide range of health, demographic, and exposure factors.



Photo by MCS 3rd Class Kameran Guy Hodnett/USN
A U.S. Navy seaman cuts a metal beam at an engineering site in El Salvador. The country is among those with a high prevalence of *T. gondii* infection.

To prescribe or not to prescribe: **When it comes to antibiotics, that is the question**

Through in-depth interviews with 30 hospital physicians, researchers explored the factors that influence the prescribing of antibiotics. Past research suggests up to a half of antibiotic prescriptions for hospital patients are unjustified or unnecessary.

“Mr. Jones, I’m not sure if this antibiotic is really necessary, but I’m going to put you on it anyway, just in case.”

Doctors in hospitals may not put things quite this way to their patients, but they may be thinking this way.

That’s one of the insights from interviews with 30 physicians at two teaching hospitals: one a VA medical center, the other on a university campus. The findings appear in the September 2015 issue of *Infection Control and Hospital Epidemiology*.

The study probed the feelings and beliefs that underpin antibiotic prescribing—especially when there are no clear indications for the drugs. Past

research shows that more than half of hospital patients will get an antibiotic at some point during their stay, and that up to half of these prescriptions are unjustified or unnecessary.

Overuse of the potentially life-saving drugs fuels the spread of nasty superbugs such as *C. difficile*, which can cause severe diarrhea, nausea, abdominal pain, and fever. The Centers for Disease Control and Prevention says each year in the U.S. there are almost half a million cases of *C. difficile*, resulting in thousands of deaths.

VA and other hospital systems have increasingly put in place “antimicrobial stewardship” programs to help ensure wise use of the drugs. The new study,



“I do think the greater availability of diagnostic tests will help improve antibiotic prescribing.”

however, suggests there is more work to be done in terms of addressing the attitudes and beliefs that shape real-world practice.

Understanding the culture of prescribing

The study’s lead author, Dr. Daniel Livorsi, says, “We wanted to better understand the culture among physicians in the hospital, the social and psychological factors that underlie excessive prescribing of antibiotics.” Livorsi, an infectious disease specialist at the Iowa City VA Health Care System, serves as the medical director of his site’s antimicrobial stewardship program. He is also an assistant professor of medicine at the University of Iowa Carver College of Medicine.

He points out that “in theory, prescribing should always be dictated strictly by evidence and information, and be fully in line with clinical guidelines. But there are gray areas where physicians have to use their best judgement. And even in cases that are more black-and-white—where an antibiotic is clearly not indicated—there are still factors that may influence doctors’ prescribing decisions and lead them to write a prescription nonetheless, and to justify it in their mind. Through the interviews, we wanted to get insight into this thought process.”

One theme that emerged in the research was that newer doctors are strongly influenced by their supervising physicians—whose careers may span back to decades when over-prescribing of antibiotics was less of a concern.

“If they always do it [prescribe], then I feel the need to do it,” said one medical resident who was interviewed.

Another shared, “When we see broad-spectrum antibiotics being [prescribed] with relative ease, it gives us the confidence to do so as well.”

Broad-spectrum antibiotics, in particular, which are designed to kill a wide variety of bacteria, are blamed for much of the spread of drug-resistant strains.

Reluctance to challenge peers

Another theme that emerged in the interviews: Physicians seemed more concerned with missing a possible infection in their patients than with exposing them to the harmful side effects of antibiotics, or with contributing to the more abstract, global problem of antibiotic overuse.

“[The problem of antibiotic resistance] is always there at the back of your mind,” said one resident, “but...when you are faced with a particular situation, you’re stuck between trying [to think globally and] reduce broad-spectrum antibiotic use...versus trying to make sure you don’t miss a bug by going too narrow.”

Another motif that came through in the interviews was the reluctance on the part of physicians to challenge their peers, much less their supervisors, if they noticed them prescribing antibiotics without clear justification. “Avoiding confrontations and preserving strong working relationships were seen as higher priorities,” observed Livorsi and his coauthors.

The group says their findings may not be representative of all hospital physicians, but they do jibe with the results of similar research in Europe.

So what’s a hospital system to do?

Livorsi and his coauthors offer a few possible

Continued on page 17

Virtual reality boosts job-interview skills for Veterans with PTSD

Studies have shown promising results for a virtual-reality computer program that helps those with PTSD or other special challenges master their job-interview skills.

Adam Navarro-Lowery comes across as self-assured and confident, but there was a time—not long ago—when job interviews were a formidable threat for him. A former military policeman with the 101st Airborne who saw action in Kosovo, the 36-year-old has struggled with posttraumatic stress disorder and many of its related issues.

“Insomnia, anxiety, depression—I had it all,” admits Navarro-Lowery, who still attends treatment at the Jesse Brown VA Medical Center in Chicago.

But today, as a licensed leasing agent in the state of Illinois and an aspiring software marketer, he self-identifies as a “born salesman” and says he’s found his calling. Job interviews,

he says, are not nearly as stressful as they once were.

He attributes much of his success to a study he took part in at Northwestern University, involving university and VA researchers.

The study, which appeared in May 2015 in the *Journal of Vocational Rehabilitation*, showed promising results for a virtual-reality computer program that helps those with PTSD or other special challenges master their job-interview skills.

Program uses video clips of live actress

The software relies on video clips of a live actress—named “Molly Porter”—who plays a human resources representative for a retail outlet, and interacts

with users based on how they answer her questions.

The researchers have reported similar results from the training for people with severe mental illness or higher-functioning autism.

“Job interviews are a great stressor,” says Dr. Morris Bell, “and this helps people gain mastery over that stress.” He spoke about the work at a neuroscience symposium last year.

Bell is a clinical psychologist and researcher at Yale University and the VA Connecticut Healthcare System. He consulted with a company called SIMmersion to develop the software, with Small Business Innovation Research funding from the National Institutes of Health. Today he has no financial stake in the company,



Dr. Matthew Smith (standing) chats with Army Veteran Adam Navarro-Lowery as he prepares to use a virtual reality job-interview training program.

although two of his coauthors do work there.

Dr. Matthew J. Smith, a collaborator of Bell's and lead author on the group's studies of the virtual-reality training, says it helps instill much-needed confidence.

"Veterans with PTSD and people with mental illness such as bipolar disorder, major depression, and schizophrenia are prone to anxiety, which can escalate during stressful social encounters such as the job interview. The training was a big confidence builder for them," says Smith, an assistant professor of psychiatry and behavioral sciences at Northwestern University Feinberg School of Medicine.

Adds Bell: "Self-confidence is huge. What this is really a treatment for, apart from the skills training, is the anxiety of going on a job interview."

Veterans used program for 10 hours

In the PTSD study, Navarro-Lowery and 22 other Veterans used SIMmersion's virtual-reality job-interview training for up to 10 hours over two weeks. Another 10 Veterans were "wait-listed" as a control group.

The study found good adherence to the program, and high satisfaction with it. More important, those who used the program significantly boosted their job-interview skills, compared with their baseline scores.

Across all the patient groups that have used the program, Bell says, the results were consistent, suggesting that "virtual reality training may benefit a wide range of disorders." More than 9 in 10 users said the training was helpful; more than 8 in 10 said it gave them confidence.

And perhaps most important, those who used the program were far more likely to land a job.

"When we looked at employment outcomes," says Bell, "it was pretty impressive. More than double the number of people got employed after getting the job-interview training."

Training customizable for PTSD, other conditions

The program is customizable for different groups, including Veterans with PTSD. Navarro-Lowery and his fellow Veterans could choose modules that would have Molly, the interviewer, ask specific questions about their military experience. For example, "What skills did your period in the armed forces give you?" For each question, users see a menu of possible responses, and they can respond either by clicking the one they want, or reading it aloud. The program has voice recognition.

An onboard "coach"—like Molly, a live actress who was filmed—uses hand gestures such as a thumbs-up or down to cue users on whether they have chosen an appropriate response. A poor answer, such as "This interview is taking longer than I expected," will trigger a cold and curt reply from Molly, such as "We're done."

Navarro-Lowery says he liked the repetitive drilling, and the ability to advance through three levels of difficulty, with Molly going from friendly, to business-like, to serious.

Repetitive drilling is key

Besides the virtual reality interaction with Molly, the program includes other training components.

"It's a whole system of job preparation," says Bell. "There's psychoeducational information on how to prepare for a job, for example, and practice on how to fill out an online application."

As part of the study, after the Veterans had completed their virtual reality sessions, they roleplayed interviews with actual interviewers. The sessions were videotaped and scored by "blinded" human resources experts who didn't know which Veterans had received the virtual reality training.

"At the tail end of the study," recalls Navarro-Lowery, "we would do mock interviews with an actual person. At this point, you've been through

"You do 10 plays of this and you'll have learned many of the right things to say."

Continued on page 16

Research scientist Dr. Micah Flores of the North Florida/South Georgia Veterans Health System is part of a team studying maggot therapy to heal diabetic foot ulcers.



Photo by Greg Westlye

Maggots in medicine: Ancient therapy making comeback for wound healing

Maggot, or larval, therapy has been around since ancient times as a way to heal wounds. Now, the method has gone high-tech—in some ways—and it's being tested in a rigorous VA clinical trial.

These aren't your grandfather's maggots.

Maggot, or larval, therapy has been around since ancient times as a way to heal wounds. Now, the method has gone high-tech—in some ways—and it's being tested in a rigorous clinical trial at the Malcom Randall VA Medical Center in Gainesville, Fla.

The study involves Veterans with chronic diabetic ulcers on their feet. The maggots feasting on the dead or dying tissue in these Veterans' wounds—and eating germs in the process—have been sterilized in a pristine, pharmaceutical-grade lab. Instead of roaming free over the wounds, they are contained in

fine mesh bags, and removed after a few days.

Welcome to maggot therapy, 2015.

“There's an eight-step quality-control process to how these medicinal maggots are produced,” notes lead investigator Dr. Linda Cowan. “Every batch is quality-tested.”

Cowan has a Ph.D. in nursing science and is a wound-care specialist with VA and the University of Florida. She has studied maggots in the lab, combed through the available research on them, and seen firsthand what they can do in wounds.

“As a clinician, I was very impressed by the

literature on larval therapy. And sometimes we would have patients come into the clinic with what I call ‘free range’ maggots—they’re not sterile, they’re not produced specifically for medicinal purposes—the patients got them at home, unintentionally. But they really clean out the wound nicely.”

Cowan, like other researchers, tends to prefer the scientific term “larvae” over “maggots,” but they mean the same thing. The whitish worm-like creatures are young flies, before they mature into pupa and then into adults. For therapy, in most countries, the green bottle fly is the insect of choice.

Co-investigator Dr. Micah Flores, whose background is in entomology—the study of bugs—admits that “maggot” does have a negative connotation for most folks. “It can be a scary word,” he says.

Cowan points out that in the study’s recruitment flyer “we use the term ‘medicinal maggots.’ We want people to know these are not home-grown on somebody’s windowsill.”

Study comparing maggots to standard care

The VA study will involve up to 128 Veterans. It’s comparing maggot therapy with the standard of care for diabetic wounds—a treatment called sharp debridement, in which a health care provider uses a scalpel, scissors, or other tool to cut or scrape away dead or unhealthy tissue. The procedure promotes wound healing.

Nearly a quarter of VA patients have diabetes, and about a quarter of these will have foot wounds related to the disease. In many cases, the hard-to-heal ulcers worsen to the point where gangrene develops and amputation is required.

The Gainesville researchers will examine how well the wounds heal in each study group. They’ll also look at maggots’ effects on harmful bacteria. In addition to clearing out dead tissue, maggots

disinfect wounds by ingesting bacteria and secreting germ-killing molecules. They also eat through biofilm—a slimy mix of micro-organisms found on chronic wounds.

Maggots saved lives on the battlefield

Turn back the clock about 90 years, and there was a researcher who grew maggots on a hospital windowsill, as unscientific as that sounds. Dr. William

Baer had treated U.S. soldiers in France during World War I and noticed that large, gaping wounds that were swarming with maggots—sometimes thousands of the creatures—didn’t get infected, and the men survived.

Baer came back to Johns Hopkins University and experimented with the therapy, only to realize that maggots could spread disease as they devoured decaying tissue. Two of his patients died of tetanus. He made some progress with using sterilized maggots, but soon antibiotics would come on the scene and maggot therapy—with its high yuck factor—fell into disregard.

“Antibiotics were the new cure-all, and so we didn’t need the maggots around too much anymore,” says Cowan. “But they’ve never gone away completely.”

A few studies took place in the U.S. in the latter half of the last century, including some at the VA Medical Center in Long Beach, Calif. But it wasn’t enough to place maggots in the pantheon of modern medical miracles. Meanwhile, the therapy continued to attract interest in the United Kingdom, where a game-changer occurred a few years ago. A Wales-based company called BioMonde came out with the bag concept, which caught Cowan’s attention right away.

She had been interested in studying maggot therapy. But she also realized that many clinicians, as well as patients—and their caregivers at home,

“It’s hard for bacteria or other organisms to develop a resistance to something that’s going to eat them.”

who would have to change dressings—might have a hard time warming up to the idea.

Turned off by the ‘squirmy wormies’

“When we started talking about doing this study,” says Cowan, “we were interested in the yuck factor. One of my concerns was other clinicians. They have to deal with this. They may be turned off by what I call the squirmy wormies.”

Cowan recalls one nurse colleague who would recoil when patients showed up in the clinic with wounds that had attracted a few maggots.

“She just had an aversion to larvae of any kind. When a patient would come in, and they would have these free-range maggots, she would not want to deal with them. She would come and get me, and I would take care of it.

“I realized she wouldn’t be the only clinician out there who would feel like this. So I thought this product would really make a difference.”

Desperate need for wound-healing therapies

That said, Cowan believes many patients are undeterred by the insects, bags or no bags. She tells of one Veteran who has been struggling with a non-healing diabetic ulcer for three years. “He said he is willing to try anything that might work.”

That attitude is not uncommon among those with diabetic sores, says Cowan, although she senses that Veterans, as a group, may be a bit less squeamish than the general population, and thus even more receptive to the therapy.

“When we go through the informed consent

form with them, we explain the study and we tell them they could be randomized to the ‘sharp’ group, which is the standard of care, the same kind of debridement they’ve gotten in the past—or they could get the maggot therapy. We’ve done about 21 informed consents so far. Overwhelmingly, people have been disappointed if they weren’t randomized to the maggot group.”

BioMonde, the company sponsoring the trial, has said it will provide maggots for up to two weeks of

treatment for any patient who did not receive the therapy during the study but wants it, and whose physician believes it would be appropriate.

Study will also survey caregiver, clinicians

Both groups in the study will receive treatment over the course of eight days. Along with studying the Veteran patients and their wounds, the researchers will survey their caregivers and clinical providers. “One thing we want to find out,” says Cowan, “is whether this yuck factor is really an issue. And who is it the greatest issue for? Patients? Clinicians? The wife or husband who has to change the dressing?”

To examine the main study outcome, the team will photograph each wound before and after each treatment. Then, wound-care experts who are blinded to which therapy was used—maggots or sharp debridement—will visually assess how much viable versus non-viable tissue remains.

Just as important, the team will study the therapies’ effects on biofilms. A biofilm is not a movie about someone’s life—it’s a soupy mix of bacteria and



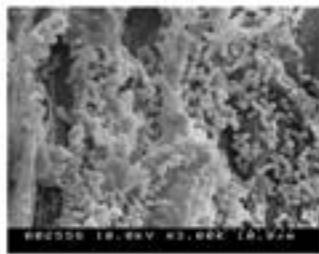
The study uses maggots that come contained in a fine mesh bag.

Photo used with permission of BioMonde

other germs that resides on or in a wound. Experts believe it may be part of why some wounds—such as diabetic ulcers—are so difficult to heal. Cowan’s group has studied biofilms in the lab, grown on pieces of pig skin, and she says the maggots are the only therapy that appears to completely eradicate them.

“A biofilm is a party of poly-microbial organisms,” explains Cowan. “It could be bacteria, fungus, virus—all of them. They spit out a protective coating that protects them from things you would put on the wound, like an antiseptic gel. Also, it protects them from things you might take inside the body systemically, like antibiotics. So it’s tough to get rid of these biofilms.

“You can debride with a scalpel, and you can cut away what looks like dead or unhealthy tissue, but you can’t see biofilm. And if you don’t completely get rid of a biofilm growth, within 24 to 72 hours it can completely regenerate, with its protective coating.”



“The photos show the difference with the larvae at 24 and 48 hours. At 24 hours there were hardly any [bacteria] to count, and at 48 hours the biofilm was completely gone. Not one organism left.”

She points out another benefit of the maggots, versus drug treatment: “It’s hard for bacteria or other organisms to develop a resistance to something that’s going to eat them.” Drug-resistant bacteria are a huge problem in U.S. health care.

Exploring the maggot gut

Flores, the entomologist, wants to peek inside the maggots, to see what they’ve ingested. After they are removed from a wound, the bagged maggots are being frozen for later analysis. (Not in the same freezer where the lab crew keeps their Haagen-Dazs, by the way.)

“My background is studying insects—flies in particular,” says Flores. “So I’m very interested in what’s inside the larval gut, what they’ve been

The photos, from a VA-UF study published in the journal *Ulcers* in 2013, show a microscopic view of a biofilm, grown in the lab on a piece of pig skin. The “before” image (left) is teeming with microbes. The “after” image was taken after maggots were applied.

feeding on. Are they picking up the same organisms we’re seeing growing on the wound? Does it match up?”

Flores and Cowan say theirs is the first study to do this type of analysis. And there should be plenty to look at: Between dead tissue, bacteria, and biofilm—an all-you-can-eat buffet for maggots—they take in enough grub to noticeably blow up in size.

“They do a great job,” says Cowan. “They plump up to the size of a small jelly bean, whereas when they go in, they’re smaller than a grain of rice. So it’s pretty impressive.”

The team is also looking at biomarkers of wound healing as another study outcome. Enzymes known as MMPs, for example, rise in response to inflammation. Levels drop as a wound heals.

Maggots make short work of biofilms

Cowan collaborated with Dr. Gregory Schultz on numerous studies involving biofilms at UF’s Institute for Wound Research.

“Both independently and collaboratively, we tested quite a number of products,” says Cowan. “We tried all kinds of expensive things. There were some that were more promising than others. We would get some good, favorable results. But there was nothing that was getting rid of everything—until we tested the maggots.”

The group published a 2013 study in the journal *Ulcers* that included before-and-after pictures, taken with an electron scanning microscope, attesting to the maggots’ handiwork.

“The results were mind-blowing,” says Cowan.

Pending the study results, Cowan hopes to see maggot therapy catch on in the U.S. as an evidence-based way to treat wounds—not just diabetic ulcers, but other types as well. One example might be deep skin wounds in combat Veterans. She’s already gotten calls from plastic surgeons interested in the therapy.

“If the maggots can clean up a wound, they can possibly make advanced therapies more effective so you don’t have to repeat them. For example, if you take a skin graft from the leg and put it on the belly, if that wound has a chronic biofilm, that graft is not going to take. But if you clean it up and then do the skin graft, it may take. What a win-win that would be.” ★

More on medicinal maggots

- The species of fly used most commonly for maggot therapy is *Lucilla sericata*, or the common green bottle fly.
- These maggots don’t bite or chew. Rather, they secrete enzymes. The secretions turn dead or sick tissue into liquid, or a liquidy pulp, which they take in as nutrition. The maggots also eat bacteria. They do not eat healthy tissue.
- Maggots disinfect wounds by secreting anti-microbial molecules that kill certain bacteria; by digesting microbes within their gut; and by dissolving biofilm—a slimy mix of bacteria and other organisms found on the surface of chronic wounds.
- Maggots may also promote the growth of new blood vessels, thus stimulating the growth of healthy tissue.
- Medicinal maggots are approved and regulated by the U.S. Food and Drug Administration as medical devices. In the European Union and some other countries, they are considered pharmaceuticals.

Virtual reality boosts job-interview skills for Veterans with PTSD

Continued from page 11

all the simulated training, and you have all these appropriate responses readily available in your mind to fall back on.”

Bell says: “The great thing about this is you do it over and over again. You do 10 plays of this and you’ll have learned many of the right things to say.”

He adds that importantly, the training seems to help people make progress in the face of long-standing deficits. Namely, it appears to lessen the effects of impaired brain function—such as that seen in schizophrenia and autism, and to a lesser extent in PTSD—on job-interview performance.

“In other words,” says Bell, “good training can overcome specific disabilities.”

The training used in the studies is commercially available and can be accessed online at www.jobinterviewtraining.net. ★



VA taking part in public-private study on Veteran reintegration

VA is among several public and private partners working with the Henry M. Jackson Foundation for the Advancement of Military Medicine on a new study aimed at learning what types of programs and services are most helpful to Veterans as they reintegrate after deployment.

Read more at www.research.va.gov/currents/0915-2.cfm

To prescribe or not to prescribe: When it comes to antibiotics, that is the question

Continued from page 9

solutions. For example:

- Set up regular forums in hospitals where doctors could meet to openly discuss their antibiotic prescribing decisions, without fear of punitive measures for poor decisions.
- Have stewardship teams provide immediate feedback to providers on their prescribing decisions. “Though this approach is resource-intensive, it can reduce anxieties and gradually change prescriber behaviors,” write the authors.
- Establish performance measures that recognize good prescribing.

On the horizon: Growing role for diagnostic tests

Perhaps an even more potent answer will come with time, suggest the researchers, as accurate diagnostic tests become more commonplace in hospitals. Such tests might show conclusively, for example, that an infection is viral and not bacterial, meaning antibiotics won’t work.

Livorsi says VA medical centers and other hospitals do currently use diagnostic tests to guide antibiotic-prescribing decisions, but the tests have limitations.

“For one, test results may not be available for several days, so doctors initially make antibiotic-

prescribing decisions based on their own clinical assessments,” he says. “In addition, there are several types of infections that cannot be diagnosed, or ruled-out, with a simple diagnostic test, so the doctor’s judgment ultimately prevails.”

Livorsi notes that rapid diagnostic tests are becoming more available for specific types of infections, but there can be “financial and logistical obstacles to their routine use. In addition, doctors have to be guided on how to correctly interpret the test results. For example, several centers have had success using rapid diagnostic tests to optimize therapy for patients with bloodstream infections—as long as a stewardship team was available to provide real-time feedback to the physicians.”

Eventually, though, says Livorsi, such tests will help doctors to appropriately forego the use of antibiotics when they otherwise might have succumbed to the pressure to write the prescription.

“I do think the greater availability of diagnostic tests will help improve antibiotic prescribing, because a large proportion of antibiotic overuse stems from diagnostic uncertainty,” says Livorsi. “With that said, culture change will also be an important part of addressing the problem.” ★

Does the term ‘hypertension’ lead some patients astray?

“Hypertension” and “high blood pressure” mean exactly the same thing. But a VA research team in Boston believes the first term may give some patients a distorted idea of the condition—and undermine efforts to treat it.

 Read more at www.research.va.gov/currents/0815-3.cfm



Photo: ©iStock/IPGutenbergUKLtd

In the works: A 'nano' approach to building bone

VA scientists in Atlanta are developing a nanoparticle based on the mineral silica that they hope will one day be an alternative to current osteoporosis drugs.



Photo by Adam Hernandez

Drs. M. Neale Weitzmann (left) and George R. Beck Jr. are developing nanoparticles that they hope will become an alternative to current osteoporosis drugs.

VA scientists in Atlanta are developing a nanoparticle based on the mineral silica that they hope will one day be an alternative to current osteoporosis drugs.

The work is only in the early stages, but co-lead researcher Dr. M. Neale Weitzmann says the particle, called NP1, “is a completely different type of drug and could potentially be one of the first-generation nano-therapeutics if ultimately successful and safe in humans.”

NP1, ball-shaped, is only 50 nanometers in diameter. About 2,000 of the particles could line up across a human hair.

Super-tiny particles like these have emerged as a huge trend in drug development. They can potentially be used in “smart” drugs that deliver therapeutic compounds directly to certain organs or types of cells, with less toxicity. A few existing

medicines already use the approach, such as the cancer drug Doxil. Several others are in clinical trials. Little is known, though, about the long-term risks and benefits of the approach, and the Food and Drug Administration is watching closely.

A team led by Weitzmann and collaborator Dr. George R. Beck Jr., both with the Atlanta VA Medical Center and Emory University, published their latest results in the May 2015 issue of *Nanomedicine: Nanotechnology, Biology and Medicine*. They were able to use NP1 to reverse bone loss in aging mice. The nano-drug not only stalled the loss of old bone but also promoted the formation of new bone. Mice that received weekly injections of NP1 over 16 weeks showed increased

bone mineral density and volume.

In previous work, the group had shown how NP1 builds new bone in young mice. They had also explored its effects on cells in culture.

Silica formed around magnetic core

The team’s chemist Dr. Shin-Woo Ha synthesizes NP1 in the lab starting with a liquid form of silica. This method allows the scientists to control the shape and size of the particles, as well as add in compounds. The final engineered spheres used in the study have a silica shell with a magnetic core that allows the researchers to view the particles with an electron microscope once they have penetrated inside cells. The nanoparticles can also be made with a fluorescent dye bonded to the silica, allowing the researchers to track the particles in cell experiments. The team can also “decorate” the shell with polyeth-

ylene glycol. This allows the particles to circulate for a longer time within the mice, thus boosting their biological impact.

The core, made of cobalt and iron, also serves other research purposes. “Because it’s magnetic,” says Weitzmann, “we can use a strong magnetic field to recover the nanoparticles after they have been introduced into cells. We have used this technique to determine what types of proteins and biochemical pathways the particles interact with inside cells.”

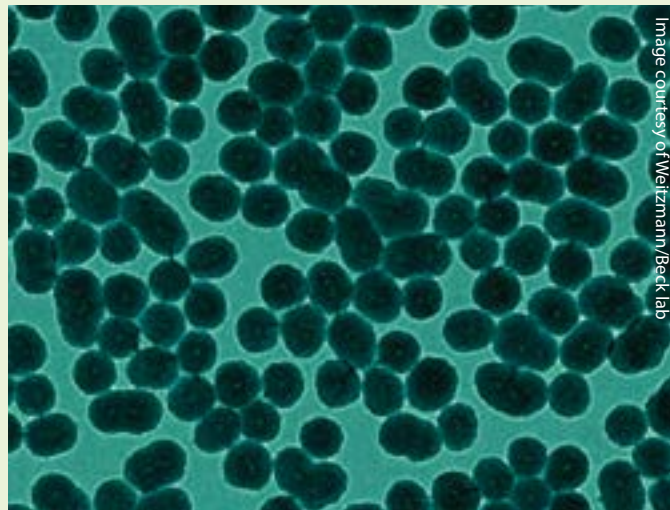
The payload, though, is the silica shell—although the scientists aren’t sure exactly how it works.

Dietary silica, which is the chemical element silicon once it’s been exposed to oxygen, is known to promote healthy bone. “Mice fed diets deficient in silicon develop skeletal defects and decreased bone mineral density,” notes Beck. “Higher intakes of dietary silicon positively correlate with bone mineral density in humans.” Scientists speculate that the mineral helps produce and maintain collagen, an important protein in bone.

But the silica in NP1 apparently works through a different mechanism, explains Beck. The particles appear to trigger changes in gene expression that boost the activity of osteoblasts—the cells that form new bone—and dampen the activity of osteoclasts—the cells that break down old, worn bone.

Those changes, says Beck, appear to be due in part to the unique physical structure of NP1.

“Our current investigations suggest that the size and shape of the silica nanoparticle are critical to its biological activity,” says Beck. “So in this sense the biological effect is related as much to the size and shape as to its material composition.”



A pseudo-colored microscope image of the bone-building nanoparticles being tested at the Atlanta VA and Emory University.

Alternatives needed for current drugs

The delicate dance between osteoblasts and osteoclasts is at the center of the complex cycle of bone repair and renewal that occurs throughout life. Known as remodeling, it works fine through about age 30—when our bone is at its thickest and strongest—but then typically declines slowly and steadily from there. As we age, there is a net loss of

bone. Add in negative influences like poor diet and a lack of exercise—along with genetic risk factors, plus any of the many inflammatory conditions that become more common with age—and the result can be osteoporosis. The bones become thin, porous, and easily fractured.

The standard treatment, drugs known as bisphosphonates, may stop bone loss in the short term, but they’ve been shown to ultimately hinder new bone formation as well—not an ideal solution.

Weitzmann and Beck hope NP1 emerges as a better option, although they are also experimenting with other potential therapeutics. Meanwhile, they still have to learn more about how NP1 works—and whether it could potentially harm, or perhaps help, other tissues in the process of building bone.

“These preliminary studies are encouraging, but it is too early to make the claim that these nanoparticles are fully biocompatible,” says Weitzmann. “As with any new drug, extensive toxicology studies are needed, and there are likely to be some side effects on bystander cells or organ system, given that the particles are bioactive. The trick, as with most pharmaceuticals used in clinical practice, is to identify a dose that provides an optimal risk-benefit ratio.” ★

Treating prostate cancer: **Should race matter?**

Do African American men, by dint of their DNA, have more aggressive prostate tumors? And should their doctors, accordingly, take a more aggressive approach in tackling their disease?



Photo by Mitch Mirkin

Clarence Massey visits with radiation therapist Nader Girgis, who was part of his treatment team at the Brooklyn campus of the VA NY Harbor Healthcare System.

It was in early 2010 that Clarence Massey first sensed something wasn't right. He didn't know it yet, but there was a tumor growing in his prostate gland. It was far enough along to start interfering with normal urination.

Massey lives in the historic Harlem neighborhood of New York City, just north of Central Park. He went to see his VA doctor in Manhattan and was sent to a urologist.

"They took bloodwork and urine samples," says Massey, now age 68. "I came back and they told me they think something may be wrong. So I had a biopsy. All this time, I was a bundle of nerves. I went back in and they told me it was positive."

He then went for a consult with cancer specialists at the Brooklyn VA. Both sites are part of the VA New York Harbor Healthcare System.

There are several treatment options for prostate

cancer; Massey ended up doing nine weeks of external beam radiation. The treatment itself wasn't bad, he recalls: "Going through it was beautiful. I was singing."

The side effects, afterward, were a different story. "They hit me like a ton of bricks," says Massey. He couldn't control his urination. Sleeping was a challenge. He grew weaker.

The side effects waned after a couple of months. "I started coming around. I started feeling better and better."

Fast-forward to 2015, and Massey now comes to the Brooklyn VA only once a year, to be checked by his cancer specialist—and to visit with the therapists and support staff who helped

him through his crisis.

"I'm so grateful to the doctors here, and to the guys who work the radiation machine," shares Massey. "Every time I come here I stop back there to thank them again. It was a team effort. Everyone here was so kind."

Dr. David Schreiber, who treated Massey, also does research, and one of the questions his group has looked at is the role of race in prostate cancer. Their studies are part of a growing body of research attempting to answer questions that are critical for men like Massey:

Do African American men, by dint of their DNA, have more aggressive tumors? And should their doctors, accordingly, take a more aggressive approach in tackling their disease?

Higher incidence, mortality for African Americans

What researchers know for sure is that African Americans are at higher risk for prostate cancer in the first place. They tend to be younger, on average, than white men when they are diagnosed—by about three years. Their tumors appear to be larger and faster-growing. Their blood levels of prostate-specific antigen—a common, if somewhat unreliable, marker for prostate cancer—tend to be higher. And they are more likely to die from the cancer—up to three times as likely.

What is unknown is whether all this is a function of race per se. Perhaps race is really a marker for lower income. Could it be that black men simply don't get the same access and quality when it comes to health care? That could explain why their tumors are more advanced when they first get in to see a doctor.

Most experts say the access factor probably accounts for part of the picture, but not all of it.

“The socioeconomic factors are definitely a component,” says Schreiber. “There are patients who are getting diagnosed later, or not being treated. Some can't afford the co-pays.”

Research suggests that VA and other “equal-access” health care systems do help level the playing field. They help erase the racial survival gap for men with prostate cancer.

A group at the VA Connecticut Healthcare System reported in 2013 that “mortality among black and white patients with prostate cancer is similar in equal-access healthcare systems.” The conclusion was based on five previous studies done in the Department of Defense and VA health systems, and in England, where health care is basically free to all citizens. The team also collected original data on 1,270 Veterans followed for up to 16 years at nine VA sites.

More recently, a team with VA and UCLA studied more than 1,200 California Veterans with prostate cancer and found “no significant differences in tumor burden, treatment choice or survival outcomes between African Americans and Caucasians cared for

in the equal-access VA health care setting.”

On the other hand, several studies do point to biological differences between black and white men with prostate cancer. For instance, in 2011, a team with VA and Duke University found higher levels in black men of “aggressive disease biomarkers.” The study used biopsied tissue from 131 men treated at the Durham VA Medical Center. Though the researchers admitted larger studies are needed, they say the findings provided “additional evidence that prostate cancer in black men may be biologically different than prostate cancer in white men.”

One of the most comprehensive reviews to date of racial differences in prostate cancer, published in 2012, concluded that the “disparities seem to be complex in nature, involving biological, socioeconomic and socio-cultural determinants.”

Role of race in other diseases

In certain other diseases, the role of race—particularly its biological effects—seems clearer. For example, heart doctors know that African Americans and whites respond differently to warfarin, a commonly used blood thinner.

In a recent article about the drug, Dr. Elvin T. Price, a pharmacist with VA and the University of Arkansas for Medical Sciences, talked about “ancestry-informed genotype-guided strategies” as a way to boost warfarin's efficacy and limit its toxicity. In other words, at least for certain conditions, patients' racial or ethnic ancestry—along with their genetic profile—should be factored in to treatment plans.

For prostate cancer, though, the evidence on race, especially how it affects disease progression, remains murky.

Schreiber, along with his colleague Dr. David Schwartz, chief of radiation oncology at the Brooklyn VA, and their team are among those working to solve the riddle.

A study they published in August 2015 in the journal *Clinical Genitourinary Cancer* looked at data on nearly 1,800 men from the national Surveillance,



“The question is whether African Americans should have the same criteria for active surveillance as everyone else.”

Epidemiology and End Results (SEER) database. They expected to find significant differences between blacks and whites in factors like the Gleason score, which basically tells how aggressive a prostate tumor is. The higher the score—the closer to 10—the more abnormal the cancer cells look under a microscope, and the more likely they are to spread.

But the study found that the black and white patients were more alike than expected, from a pathology standpoint. There was little to suggest that prostate cancer takes a more aggressive course in black men.

“We couldn’t detect much difference,” says Schreiber. He notes that the finding contrasted with those from previous studies looking at the same question, but those studies were much smaller.

“We could now look at larger samples,” says Schreiber, “but the findings from the smaller studies were based on samples of only around 60 or 100 men, so we think we have strong evidence. You would think that if there really is a significant difference, it would show up in 1,800 patients.”

One limitation of Schreiber’s study, though, is that the SEER data reflected only a snapshot in time. The men were all biopsied and underwent removal of the prostate relatively soon after diagnosis. Had they been left untreated, could it be the black men would have fared worse?

“It could be that that the disease was not yet aggressive at this early stage, when it was detected and treated. It could potentially convert later on and become more aggressive,” notes Schreiber.

Another possibility he suggests is that African Americans could have more “micrometastatic” disease. “This means the cancer has made its way

out of the prostate and into the bloodstream and deposited itself somewhere,” explains Schreiber, “but it’s so microscopic that it’s undetectable. It could pop up years later.”

Are blacks, whites equally suited for active surveillance?

The real question for Schreiber’s group is whether blacks are equally good candidates for a treatment strategy known as active surveillance. Actually, it’s not so much a treatment at all. Formerly known as “watchful waiting,” it involves closely monitoring and testing the patient over time, to see if the disease is progressing or not. In most cases, prostate cancer grows slowly and causes no problems. More men will die with the disease than from the disease. Many men can go without treatment and never suffer any symptoms. They are fortunate, since treatment could involve grim side effects such as impotence and incontinence. For those affected, quality of life can plummet.

Active surveillance has caught on as experts have come to see the risks of over-diagnosing and over-treating prostate cancer—namely, those slow-growing tumors that are unlikely to cause any harm during the patient’s lifetime. According to a recent study led by Dr. Matthew Cooperberg, with VA and UCSF, between 1990 and 2009, fewer than 10 percent of men with low-risk prostate cancer were treated with active surveillance. For the period between 2010 and 2013, the figure jumped to 40 percent.

The challenge is figuring out which tumors don’t fit this milder picture, and whether blacks are more likely to be in that category. For those with aggressive tumors, timely treatment can prevent an early death.

Says Schreiber: “The question is whether African Americans should have the same criteria for active surveillance as everyone else. Maybe their disease is by nature more aggressive, and they can’t be safely surveilled—or maybe only a subset of these men can be safely surveilled, and the rest need treatment.”

Even as they sift through all the conflicting findings, researchers like Schreiber seem to agree that biomarkers are the wave of the future—for prostate cancer as well as many other diseases. Doctors will prescribe treatment based on the specific proteins or other molecules found in a patient’s blood—as determined by his or her genes. This is already happening, to an extent, with breast and lung cancer.

Schreiber cites a study just out in the *Journal of Clinical Oncology* in which researchers tested 20 previously established biomarkers of prostate cancer to see which, if any, showed up more frequently in African American men, versus those of European ancestry. The team, led by Dr. Kosj Yamoah at the H. Lee Moffitt Cancer Center in Tampa, came up with a final set of six markers that were in fact more common in the black patient sample. The researchers say their results “show that there are differences in the biology ... of prostate cancer in African American men compared with European American men that affect” both diagnosis and treatment. “The ability to identify a subset of African American men who harbor aggressive disease will enable clinicians to more accurately risk stratify these patients for appropriate treatment recommendations.”

In the era of personalized medicine, will race become irrelevant?

The biomarker panel may still need to be tested in larger groups of men, but Schreiber says “something like this will be the future. How fast we’ll get there, I don’t know. But that’s the goal for every type of cancer. We’ll be able to individualize care and say, OK, you have these biomarkers, you get this treatment.”

Yet even with this type of gene-based “precision”

or personalized medicine, race may not drop out of the equation totally. As in the Yamoah study, certain biomarkers may serve to sort out low-risk from high-risk patients only within a particular racial or ethnic group, rather than for patients at large.

Flip it around, though, and you realize that race itself is merely a function of genetics. As Schreiber puts it: “Race is what we see, but underlying that is the genetics. That’s what we don’t see and don’t yet fully understand. And that’s what really dictates what’s going on.”

That point may be especially relevant for mixed-race patients. However these patients may identify racially, the bottom line for their doctors will be what proteins are expressed in their bodies, and in their tumors. If the patient’s ancestry—as straightforward or as blended as it may be—can somehow help point to the right diagnosis and treatment, all the better.

Schreiber says that for now, his clinic “doesn’t differentiate by race. We use the current standards, which are PSA, Gleason score, and physical exam to stratify patients. We don’t necessarily say that because you’re African American, you’re automatically intermediate or high risk. That is not proven yet. It’s developing research.”

He adds: “From a treatment standpoint, if we offer a patient more aggressive treatment, such as hormones along with radiation, that would eliminate testosterone in the body for a certain period of time, and that entails certain side effects: loss of sex drive, inability to maintain an erection, hot flashes, swelling of the breasts, all of which men obviously don’t want. There are also more serious side effects, such as heart disease. So to throw that at them just because they’re African American—we don’t have the data to support that.”

For his part, Clarence Massey is glad to be over his ordeal, and thankful he and his team chose the right treatment. “I give credit to them, but mostly I give credit to God,” he says. “I am blessed.” ★



RESEARCH CURRENTS

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

Did you know?

In 1990, endocrinologist Dr. John Eng at the Bronx VA Medical Center discovered a peptide in the venom of a Southwest desert lizard that would become the basis for the diabetes drug exenatide, sold as Byetta. Eng, seeking new hormones, was intrigued by research showing that venom from some snakes and lizards, including the Gila monster, enlarged the pancreas, where insulin is made. Eng learned that the Gila monster is able to maintain steady blood sugar levels even after long periods of not eating. He showed that the peptide he discovered triggers the synthesis and release of insulin from beta cells in the pancreas, thus laying the groundwork for exenatide's development.



Photo: ©iStock/GlobalP



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

VA Research Communications | 31 Hopkins Plaza, Ste. 102 | Baltimore, MD 21201
varesearchcurrents@va.gov | 443-759-3456



Read the expanded online edition of
VA Research Currents at www.research.va.gov



facebook.com/VAResearch



twitter.com/VAResearch