



RESEARCH CURRENTS

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



Photo by Mitch Mirkin

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Navy Veteran Marty Sigel peruses the vision supplements at a Baltimore health food store.

Some top-selling eye vitamins don't match scientific evidence, says study

Vitamins and supplements are a billion-dollar industry in the U.S., with millions of Americans popping pills or capsules or swallowing powdered drinks to address everything from indigestion to heart and brain health. Now, researchers have found that some of the best-selling eye vitamins don't contain the same ingredient dosages shown effective in clinical trials. Some also contain additional ingredients not validated in clinical trials.

Furthermore, the study, led by researchers with the Providence VA Medical Center, Penn State University, Brown University, Yale-New Haven Hospital, and Waterbury Hospital, found that many of the claims published in promotional material lack scientific evidence.

The basis for the new research is the landmark Age-Related Eye Disease Study (AREDS). AREDS found in 2001 that a specific formula of supplements containing high doses of zinc and other antioxidants could slow the deterioration of the eye's macula. Age-related macular degeneration (AMD) is the leading cause of blindness among older adults. The macula is the central part of the retina. It allows the eye to make out fine details.

A follow-up study concluded in 2011 that the

formula remained effective even if one ingredient, beta-carotene, was replaced with related nutrients. The publication of the second study, AREDS2, solidified the benefits of the formula in treating AMD. Sale of supplements marked as containing either the AREDS or AREDS2 formula skyrocketed.

For the new study, the researchers identified the five top-selling brands of eye vitamins and analyzed 11 products made by the five companies. All the products contained ingredients from either the AREDS or AREDS2 formula. However, only four of the products contained doses that were equivalent to those used in the studies. Another four products contained lower doses. Additionally, four contained additional vitamins, minerals, or herbal extracts that were not part of the original studies.

“With so many vitamins out there claiming to support eye health, it’s very easy for patients to be misled into buying supplements that may not bring about the desired results,” said first author Dr. Jennifer J. Yong. “Our findings underscore the importance of ophthalmologists educating patients that they should only take the proven combination of nutrients and doses for AMD according to guidelines established by AREDS and AREDS2. It’s also crucial that physicians remind patients that, at this time, nutritional supplements have yet to be proven clinically effective in preventing the onset of eye diseases such as cataracts and AMD.”

(Ophthalmology, March 2015)

Sexual dysfunction a common problem in Veterans with PTSD

When compared with the general population, Veterans with posttraumatic stress disorder are at increased risk of sexual dysfunction, confirms a new review study. The researchers found that male Veterans with PTSD were significantly more likely than their civilian counterparts to report erectile dysfunction or other sexual problems. And though



A review study of past research found that sexual problems are common for both male and female Veterans with PTSD.

data were scarce on women Veterans with PTSD, the research does suggest they experience similar issues. Problems such as vaginal pain and disinterest in sex were common among women Veterans in the studies that were reviewed.

Given the negative impact of PTSD on physical and emotional health, it isn’t surprising that Veterans with PTSD experience increased rates of sexual dysfunction. What is surprising, write the researchers, is the rate at which that dysfunction appears.

“PTSD impairs sexual functioning across multiple domains: desire, arousal, orgasm, activity, and satisfaction,” wrote the researchers, based at the Michael E. DeBakey VA Medical Center and Baylor College of Medicine in Houston, and Argosy University in Chicago.

The most commonly reported problems were erectile dysfunction, premature ejaculation, and overall sexual disinterest.

The researchers point out that while psychiatric medicines can play a role in sexual dysfunction, Veterans who were not prescribed medication still experience problems, according to the literature.

Nearly 24 percent of female Veterans seeking VA health care report a history of military sexual trauma, or MST. In the review study, this group of women displayed negative sexual consequences above and beyond the effects of civilian sexual assault. Though the researchers say the reason for the differing rates

is not yet fully understood, one explanation could be that unlike in civilian situations, survivors of MST often are required to continue working with their attacker. Researchers say this could compound the stress and make them more vulnerable to developing sexual dysfunction.

Moreover, Veterans with PTSD, whether as a result of combat, MST, or both, may also be more likely to misuse alcohol and other illicit substances. This further increases the risk of sexual dysfunction, say the researchers.

The researchers suggest clinicians first educate themselves so that they feel more confident to treat patients' sexual concerns and, perhaps most importantly, to bring them up at all. While many providers may feel more comfortable waiting for patients to express their concern about sexual dysfunction, according to the research, Veterans consistently report the topic would be easier to broach if their providers initiated the discussion.

(Journal of Sexual Medicine, April 2015)

Troubling trio—depression, PTSD, mild traumatic brain injury—linked to extra-high high disability risk

Many among the newest war Veterans, like those before them, are struggling with a web of invisible wounds—beyond the physical scars of combat. Now, a VA research team in Boston has identified a particular combination of mental and behavioral conditions that appears to confer an extra-high risk of disability.

The study involved 255 Iraq and Afghanistan Veterans. They all completed a World Health Organization disability scale that rates difficulty in getting around, communicating and getting along with others, self-care, and other daily tasks.

The overwhelming majority of the Veterans who reported having the greatest difficulties were those with a combination of depression, posttraumatic



A U.S. Army soldier provides security during combat operations in Balure, Iraq, in 2007. VA researchers have identified a “deployment trauma factor”—depression, PTSD, and TBI—that is common among Iraq and Afghanistan Veterans and appears highly predictive of long-term disability.

stress disorder, and military-related traumatic brain injury.

The researchers call this combination the “deployment trauma factor,” and it appears to be an especially dangerous triad, from a disability standpoint. It resulted in higher disability scores than any other three-diagnosis combination.

“It turns out that among all the combinations of diagnoses we find, there is one combination in particular that suggests a group of Veterans who are at high risk for long-term disability,” says Dr. William Milberg, a psychologist and one of the study authors.

Milberg and his coauthors are with VA’s Translational Research Center for TBI and Stress Disorders (TRACTS), based at the VA Boston Healthcare System.

(Journal of Traumatic Stress, February 2015)

Study on chiropractic for back pain yields mixed results

A VA study on a common chiropractic therapy used to treat chronic back pain has found that a placebo treatment may be just as effective.

The issue is more complex, though, says lead

researcher Dr. Paul Dougherty, a staff chiropractor at the Canandaigua VA Medical Center in upstate New York. He notes that chronic back pain is more than just a feeling; it is also a source of disability. And for those in the study who received chiropractic care, disability rates did improve, compared with those who received only placebo.

“That’s really the take-home point when it comes to chronic back pain,” says Dougherty. “The pain can lead to disability and impaired mobility and that can have its own health consequences, particularly in older adults.”

For the study, his group identified 136 Veterans 65 years old or older with lower back pain who had never received chiropractic care—something that proved trickier than anticipated. “We didn’t think it was going to be as hard as it was,” says Dougherty. “It was quite difficult. We had one patient who last saw a chiropractor 50 years before and we had to exclude him.”

The volunteers were split into two groups. Sixty-nine received spinal manipulative therapy, or SMT. “SMT is where you take a joint to its end range,” says Dougherty. “When you crack your knuckles and squeeze them together, you hear the pop. That pop is the joint changing pressure. SMT is basically doing just that—taking a joint that isn’t moving enough and trying to maneuver it to where it moves normally again and changes pressure.”

The remaining 67 participants were enrolled in what is known as a sham intervention, a placebo. For that group, participants lay face down and had



In a VA chiropractic study that involved 136 older Veterans with chronic low back pain, the treatment improved disability but did no better than placebo at relieving pain.

water-based ultrasound gel spread across their lower back. The chiropractor would then rub a detuned ultrasound machine across the affected area for 11 minutes. While the ultrasound machine itself was on and making noise to stimulate the participants’ senses, the wand did not transmit any sound waves. The intervention was, in effect, just a high-tech but gentle back rub.

Patients in both groups received an educational pamphlet from the Arthritis Foundation on different types of back pain.

For four weeks the participants received treatment, twice per week. At the end of the fifth week, Dougherty and his colleagues had the participants rate their pain on a standardized scale. Interestingly enough, both groups showed similar pain improvement.

Dougherty is careful to note that the study doesn’t prove or disprove anything regarding SMT. He points out that while pain is perception-based, stemming as much from the mind as the body, disability is much more physical.

(Geriatric Orthopaedic Surgery & Rehabilitation, December 2014)

Small RNA molecules in blood may help in diagnosing common war injuries

A study at the Bronx VA Medical Center and other sites has homed in on a type of RNA the researchers say could serve as a biomarker to help diagnose the



two signature injuries of the recent wars in Iraq and Afghanistan: mild traumatic brain injury and posttraumatic stress disorder.

The focus is on a group of small nucleolar RNAs—molecules within the cell nucleus that don't directly code for proteins but affect chemical changes to other types of RNA.

“We think we may have an objective biomarker pattern to help identify Veterans with mTBI and PTSD,” says brain expert Dr. Giulio Pasinetti, with the Bronx VA and Mount Sinai School of Medicine.

Pasinetti collaborated with VA's War-Related Illness and Injury Study Center in E. Orange, N.J., where 58 Iraq and Afghanistan Veterans were recruited for the study. Some of the Veterans had the combination of TBI and PTSD. Others had only one of the conditions, or neither.

The researchers tested blood samples from all four subgroups. They found differences depending on the presence or absence of TBI and PTSD.

The focus was on four specific RNA molecules, known by the designations ACA48, U35, U55, and U83A. All four were found at significantly lower levels in those Veterans who had TBI plus PTSD, versus those who had only PTSD. In Veterans with PTSD alone, only one of the molecules, U55, was low.

Interestingly, levels of the four RNAs were normal in Veterans who had only TBI, and no PTSD. It was only the combination of the two conditions

◀ Dr. Giulio Pasinetti, with the Bronx VA Medical Center and Mount Sinai School of Medicine, is leading studies to identify blood biomarkers for traumatic brain injury and posttraumatic stress disorder.

that appeared to trigger the drop across all four potential biomarkers.

The team also tested the blood of rats exposed to simulated blasts, via a “shock tube” at the Walter Reed Army Institute of Research, as well as the blood of mice that had undergone stress that causes a PTSD-like condition. The rodent results didn't exactly match up with those from the Veterans. Pasinetti says more work is needed to understand the different patterns between humans and the animal models.

Whether through using animal models or conducting other lab work, researchers throughout VA are eager to develop objective, measurable biomarkers in the blood or other tissues—or even in brain waves—that could serve to detect or confirm either of the ailments, or the combination. The availability of such biomarkers could also provide more precise benchmarks and outcome measures in clinical trials of different TBI or PTSD therapies.

(American Journal of Neurodegenerative Disease, Dec. 5, 2014)

UV light shines in infection control study

In just over 10 minutes, a pulsed xenon ultraviolet light system can disinfect a hospital room every bit as good as a human can, according to a VA study.

That's not to say that the light, which kills common and dangerous bacteria like *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant enterococci, will replace manual disinfection. Rather, say researchers, the light can supplement more traditional methods.

“There are times when surfaces are not thoroughly disinfected due to human error or because the contamination is so significant,” says

Dr. Chetan Jinadatha, chief of infectious diseases at the Central Texas Veterans Health Care System in Temple, Texas.

Researchers assess aerobic bacterial colony counts by taking samples from high-touch surfaces in hospital rooms: call buttons, railings, or TV remote controls, for example. The samples are then incubated for 48 hours, during which time bacteria present in the sample are allowed to develop into colonies. After 48 hours, the colonies are counted and categorized.

“The more colonies we find on a contaminated surface, the greater the chances that a potentially pathogenic bug like MRSA is present,” says Jinadatha, also with Texas A&M Health Science Center College of Medicine.

The presence of bacteria in hospital rooms isn’t unique to VA, of course. Studies have shown that just entering a recently occupied hospital room in the U.S., even after it has been disinfected, increases one’s chances of contracting MRSA by as much as 40 percent.

“There have been studies on how pulsed UV works alongside manual cleaning,” says Jinadatha. “We wanted to see how it performed by itself.”

For the study, the researchers selected 38 recently vacated rooms at the VA facility in Temple. Five high-touch surfaces within each room were sampled both before and after the UV disinfection.

After the samples were incubated, Jinadatha counted roughly 74 colonies, on average, from each room, with the call button and bedrail having the highest counts.

The pulsed UV light system was then wheeled into the room. Built like an unwieldy shop vacuum, the device has a large saucer-like reflector on top of a column that houses the bulb, filled with xenon gas.

When the system is switched on, high-voltage electricity passes through the bulb and releases a germicidal spectrum of ultraviolet light that kills bacteria.

“The device pulses for about five minutes and [the procedure] is always performed behind closed

doors,” says Jinadatha. “There are no staff or patients present when it is on.” The device also has safety features that prevent it from turning on when it detects any motion.

The results showed that the UV method cut the number of colonies per room by about 70 percent, roughly the same effectiveness as manual disinfection.

“Of course we’re not advocating that anyone just use pulsed UV. It should be seen as something that can complement manual cleaning,” says Jinadatha. In a past study by his group, the two methods together killed up to 99 percent of aerobic bacteria in hospital rooms.

(American Journal of Infection Control, April 1, 2015)

This germ-zapping robot emits pulsed ultraviolet light that kills bacteria.

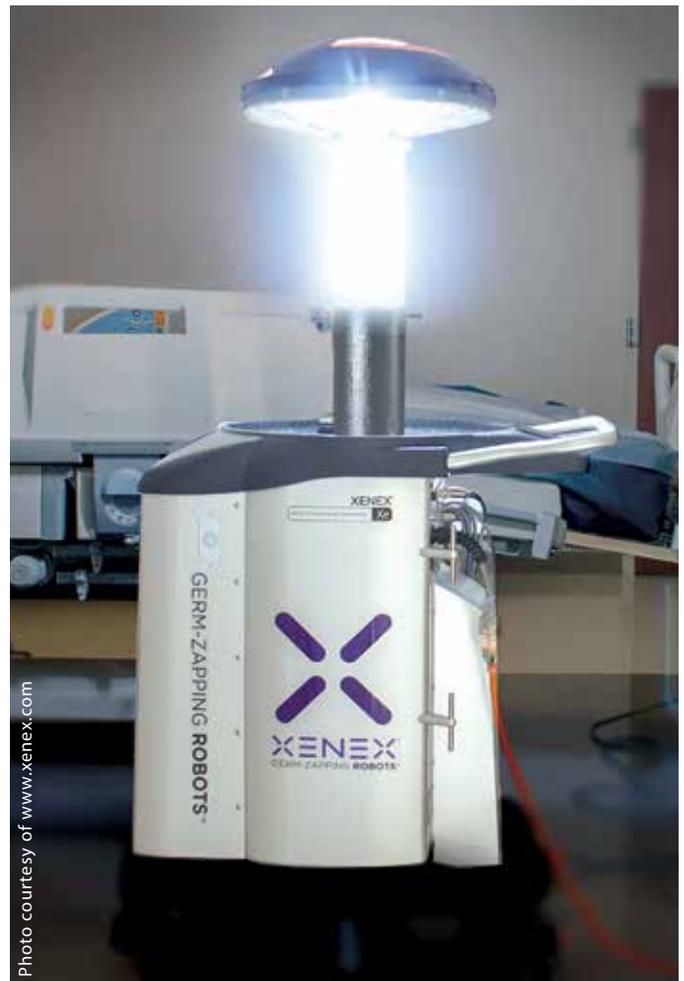


Photo courtesy of www.xenex.com

Alzheimer's home-safety project **focuses on prevention**

A research team with VA and Boston University first identified the home modifications that worked best to keep people with Alzheimer's disease safe, and to ease the burden on their caregivers. Now, they are working with VA primary care providers and others to implement the findings.



Photo by Frank Curran

In this 2009 photo, caregiver Ann Cameron helps Scott Trudeau apply tape to a step in the home she shared with her husband, Donald (in the background), who has Alzheimer's disease. To prevent accidents on the stairs, highlight step edges with contrasting tape to make steps more visible. Two-inch duct tape works well. Put one strip across the entire edge of each step, with an inch covering the stair tread and an inch folded down below the edge of the step.



“We’re not waiting until someone falls down the cellar stairs and breaks their hip, to change the way the house is formatted.”

Ann Cameron lives in a tidy two-bedroom rancher just across from the Merrimack River, outside of Boston. Her husband, Donald, a former gunner’s mate in the Navy and library custodian, has Alzheimer’s disease and is now in a nursing home. But she says he was able to stay at home with her for several years after his diagnosis—and remain safe—thanks to innovative research by a team with VA and Boston University.

“The assistance of [the researchers] and the materials they provided enabled Donald to remain at home for several years longer than he could have otherwise,” says Cameron, 68.

She and other family caregivers took part in studies based at the Bedford (Mass.) VA Medical Center and Boston University aimed at boosting home safety for those with Alzheimer’s. Now, building on this work, the investigators are teaming with VA primary care providers in two regions—New England and the Mid-Atlantic—to disseminate a research-based home safety toolkit they have developed.

It’s all about prevention, says Dr. Scott Trudeau, with VA’s New England Geriatric Research, Education, and Clinical Center (GRECC).

“We’re not waiting until someone falls down the cellar stairs and breaks their hip, to change the way the house is formatted. We’re saying, if we make these simple changes now, we stand a good chance of preventing these types of accidents.”

New effort based on past research

The research dates back to 2000. The first goal was learning what types of changes are practical and effective for families to implement. The National Institute on Aging, Alzheimer’s Association, and other organizations had put out home-safety tips

for years. But not all the tips were equally doable for caregivers, says Trudeau’s colleague Dr. Kathy Horvath, with the GRECC and Boston University’s Alzheimer’s Disease Center.

“Many of the recommendations that were available were not research-based. They were often overwhelming to people, and they didn’t know where to begin. Some recommendations were just lacking in the detail that people need.”

As an example, she cites the suggestion to highlight the edges of steps with white or colored duct tape, to provide contrast. People with Alzheimer’s have trouble with perception and are more likely to trip and fall. “As one family member asked us,” says Horvath, “does the tape have to go on all the stairs? Does it have to go across the entire stair? Just in the middle? These are the kinds of details people have questions about.”

Horvath and Trudeau, an occupational therapist, studied which interventions worked best. One factor they explored was cost: Caregivers were unlikely to make changes that were too pricey. The average cost of home-safety products installed in families’ homes was \$79 in the original study. This included items such as grab bars for the shower, nightlights, stove-knob covers, and child-safety locks for cabinets.

Families also were unlikely to make changes that took too much time, required technical help, caused an inconvenience, or altered the look of the home.

Says Horvath, “Something might sound like a great idea from the professional’s viewpoint, but if people aren’t going to do it, what have you accomplished?”

Their research resulted in a 25-page, illustrated, simple-language guide. The booklet was tested for “health literacy” to make sure people could easily understand the instructions.

Then Trudeau and Horvath put together a Home Safety Toolkit that consisted of the booklet plus a canvas bag with sample low-cost safety items, costing about \$200 in 2015. Through a clinical trial funded by VA and Boston University, they tested the kit with 108 pairs of patients and caregivers.

No approach is foolproof

The results appeared in 2013 in the *International Journal of Alzheimer's Disease*. The study found that in families that used the toolkit, versus those receiving usual care, there was less caregiver strain, more caregiver self-efficacy, better home safety, and fewer accidents and risky behaviors among those with Alzheimer's.

Now, the focus is on spreading the word, and getting the tools into the hands of the caregivers who need them. The team has funding to work with VA

primary care clinics and other partners, such as VA's Prosthetics and Sensory Aids Service, to study the best way to do just that. The funding is through VA's Quality Enhancement Research Initiative, which specializes in translating research findings into everyday care.

The researchers stress that no approach is foolproof.

"There's no such thing as a completely safe home," says Trudeau, who has worked with people with dementia for some 20 years. "What we can do is make the home environment safer, for both the caregiver and the person with Alzheimer's.

Nothing, he says, can replace the need for close supervision of someone with memory and judgment problems, "but the modifications we recommend can lessen the intensity of the vigilance required on the part of caregivers." ★



Caregivers should keep a flashlight, as well as a telephone, near the bed in case of nighttime emergencies.



Photo by Frank Curran

◀ Use a daily medication dispenser, such as a big pillbox. Don't keep medicines and vitamins out on the counter. Instead, hide or lock them in a cabinet or closet.

Install a slide-bolt lock toward the top or bottom of a door that leads outside—not near the doorknob—so the lock will be less noticeable. Also, use portable motion sensors, like the white unit sitting on the shelf near the door, to let the caregiver know when the person with dementia is trying to go out into the street. ▶



Photo by Frank Curran

Continued on page 22

Study explores use of telehealth for MS patients

VA researchers are using telehealth technology to help Veterans with multiple sclerosis get the most out of their exercise regimens.

“Blah.”

That’s the word Raina Groover, 42, uses to describe how she feels on days when her multiple sclerosis symptoms flare up.

“I get tingling, numbness, arthritic symptoms, fatigue. And my brain—we call it MS fog. It’s like ‘word search,’ trying to get the right words to come out.”

As with most MS patients, exercise is good medicine for the 42-year-old former U.S. Public Health Service nurse officer, who was diagnosed with the disease in 2010.

She says sticking with an exercise regimen—and getting feedback and support—became easier when she enrolled in a Baltimore VA Medical Center and University of Maryland study aimed at helping people with MS.

The trial, titled “Physical Telerehabilitation in Veterans with Multiple Sclerosis,” was launched in 2012 and will wrap up later this year.

PHYSICAL THERAPIST TRACKS PROGRESS REMOTELY

As part of the study, Groover had a program loaded on her laptop that served almost like



Photo by Mitch Mirkin

Study participant Raina Groover goes over some exercises with physical therapist Susan Conroy during a clinic visit.

a personal trainer, guiding her through customized stretches and other exercises, with videos and tips. It also enabled her to respond to questions and surveys—for example, about her pain and fatigue—and exchange messages with a physical therapist back at the Baltimore VA.

“Susan [Conroy, the therapist] was very good about tracking my progress,” recalls Groover. “If I hadn’t logged in for a couple of days, she would send me ‘sweet little reminders’ to let me know. She’d write things like, ‘Hey, you’re doing great so far! Don’t forget to

log in and do what you can.’”

The icon that Groover clicked on her laptop activated a Home Automated Telemanagement system. The generic HAT technology was developed some years ago by physician-researcher Dr. Joseph Finkelstein when he was at the University of Maryland. Finkelstein, now at Johns Hopkins University, has used HAT in studies on a number of chronic diseases, from diabetes to emphysema.

“It’s a platform that’s evolved over the years, and we’ve been trying to make it work for MS,” says Dr. Mitchell Wallin, a

neurologist at the Washington, DC, VA Medical Center. He is collaborating on the study with lead investigator Dr. Walter Royal, with the Baltimore VA and the University of Maryland.

The technology used to run off a land line, says Wallin. Now, it's Internet-based. "It's a multi-component system. It includes the ability to do standardized surveys, ask questions, give patients educational modules, give feedback and messages to patients. It also allows for other kinds of assessments that have become more commonplace with interactive devices—things like digital peak flows [to measure lung air flow], glucometers, scales, where data can be transmitted through a USB port."

Conroy, the physical therapist, programmed Groover's individual regimen into HAT by choosing from a menu of choices—which exercises, at what frequency.

EXERCISE IS POWERFUL ELIXIR

Patient information collected by the system is fed securely to researchers back at the medical center to analyze. One goal of the study is to compare the progress of MS patients who use HAT with that of patients who also have a tailored exercise regimen but are doing it on their own at home, without the

benefit of the technology.

In addition, all patients in the study go to the clinic at three and six months for an extensive two-hour evaluation. The work-up tests their balance, gait, range of motion, manual dexterity, cognitive function, physical stamina, and other parameters.

There's little debate among MS specialists that exercise is a powerful elixir for MS.

Royal: "For patients who are having flare-ups, it's common to have, as part of their regimen, some exercise, or a course of physical therapy. This helps speed recovery."

And it's not just during flare-ups, or relapses, that exercise can help.

"People who exercise regularly have significant gains in endurance," says Wallin. "They can actually maintain or improve their power and function."

The exact pathways through which exercise helps people with MS is probably a complex matter, suggests Royal. "There's a lot of interest in brain plasticity—we believe exercise is activating new circuits to allow people to improve their everyday function. Also, it's clear that exercise can lead to the production of certain trophic factors [growth proteins in the brain] that are neuroprotective. And exercise can also probably

have a direct impact on the inflammation that's going on in MS. So all of that comes together."

'IT KEEPS ME GOING, KEEPS ME ACCOUNTABLE'

But Wallin points out that as helpful as exercise is for people with MS, they tend to face more challenges in being able to stick with a routine.

"Because of the fatigue, there's a lot of disuse and atrophy of muscles," he says. "And the patients tend to not be as mobile, as far as various activities during the day. They may have other functional problems, such as control of movement, that prevent them from doing certain types of exercise. It's often harder for them to use the standard equipment you see at most health clubs. They may not feel as safe."

That was part of the motivation for the study.

"We want to give people an option to do things at home, without all the gym equipment," says Wallin.

Groover, for one, likes the idea. Though she is no longer formally in the study, she still has the HAT modules on her laptop, and uses them to get herself moving.

"The system is very user-friendly and helpful," says the nurse. "It keeps me going and keeps me accountable. I'm grateful for it, because it's something I can do right here in my own home." ★

From fourth-century soup to 21st-century procedure, fecal transplantation proves its worth against stubborn bacteria

Fecal transplants aren't a new idea—they've been used by traditional healers for centuries. But modern medicine is now revisiting the concept as an effective way to deal with dangerous *C. difficile* infections.

Not all bacteria are bad.

Just ask the fourth-century Chinese medical doctor Ge Hong. More than 1,700 years ago, Hong put ink to paper to document a rather unique recipe for treating diarrhea—yellow soup. It was, as one might expect, not a pleasant dish but rather a broth involving dried or fermented stool from a healthy person. Taken by mouth, the bacteria in the stool would then inhabit the gut of the sick person, and bring about a cure.

Medical scholars can debate whether Ge Hong's yellow soup was the first effort at what is now called fecal microbiota transplantation. In any case, history is replete with documented examples of the practice, from Renaissance-era veterinarians to a 1958 Colorado case involving four critically ill patients.

Now an increase in a hard-to-beat intestinal bacterium prompted VA researchers to revisit the effectiveness of FMT—a modern version of Hong's yellow soup.

SYSTEMATIC REVIEW OF EVIDENCE

Investigators with VA's Evidence-based Synthesis Program



Photo by April Eller

VA's Dr. Dimitri Drekonja and colleagues have conducted a review of the evidence for fecal transplants as a therapy to combat *C. difficile* infections.

conducted a systematic review of the evidence surrounding FMT, in part to help VA determine if the treatment was effective enough to be offered at VA facilities. By and large, the data are promising. The researchers are preparing the results for publication.

The treatment revolves around intestinal flora. In a healthy person, the bowels are chock-full of healthy bacteria. When a person is on antibiotics, the balance can be upset; after all, antibiotics kill bacteria indiscriminately, whether harmful or not. The result, all too

often, is the development of gastrointestinal disease, specifically, *Clostridium difficile*-related diarrhea and colitis.

“Historically *C. difficile* was seen mostly in those with health care exposure, almost exclusively those who have received antibiotics,” says Dr. Dimitri Drekonja, a staff physician in the infectious disease section at the Minneapolis VA Health Care System. “Lately, though, there have been increasing reports of people getting it who don't have any of that exposure. We're very good at

spreading germs around. MRSA used to be a bacterium that was only hospital-acquired, and it seems that *C. difficile* is doing the same thing, emerging from the hospital setting and moving out into the community. It is, right now, the most common cause of infectious diarrhea.”

A NEW WEAPON AGAINST AN URGENT THREAT

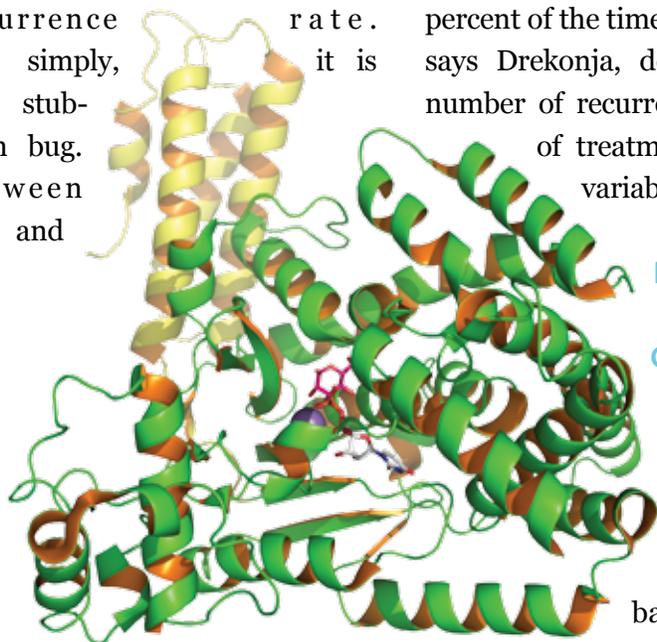
The issue is so pressing, in fact, that in 2013, the Centers for Disease Control and Prevention placed *C. difficile* into its top threat category: urgent. Infection can result in repeated hospitalizations, malnourishment, and dehydration, and it can occasionally prove fatal. According to Drekonja, who is also an assistant professor of medicine at the University of Minnesota, it’s not that *C. difficile* is hard to treat, but rather that it has a distressingly high recurrence

rate. Put simply, it is one stubborn bug. Between 15 and

30 percent of patients experience recurrent episodes of the illness. It is quickly replacing MRSA as the most common bacterial infection found in hospital settings.

“The single biggest trigger is receipt of further antibiotics,” says Drekonja. “But sometimes that’s not modifiable. If you need antibiotics for something very serious like a severe necrotizing skin condition or a bad cellulitis, then nothing else will work. That puts you in an uncomfortable position of knowing you need treatment, but you’re definitely increasing your risk of a *C. difficile* recurrence.”

Mainstream medical treatment involves therapy with vancomycin or other antibiotics active against *C. difficile* and, as expected, a break from antibiotics whenever possible. These treatments, however, tend to produce sustained success only 30 to 80 percent of the time. The variation, says Drekonja, depends on the number of recurrences, duration of treatment, and other variables.



PROCEDURE IN USE IN VA ON CASE-BY-CASE BASIS

Currently FMT is used only on a case-by-case basis in VA,

mostly through coordination with non-VA providers. “It’s in an uncertain regulatory environment,” says Drekonja. “Is this a drug? If so, it’s not FDA-approved. Different facilities are approaching it differently.”

The studies Drekonja’s group reviewed focused primarily on recurring cases of *C. difficile*, as well as non-responsive, or refractory, cases.

“The treatment isn’t usually given to acutely ill patients,” says Drekonja. “The bulk of the patients had an episode or multiple episodes and were treated through conventional means. Then once they were largely asymptomatic but at risk of a recurrence, they were given the FMT.”

The transplants were delivered in different ways: Some were given through the upper gastrointestinal tract, through the use of either a nasogastric or nasojejunal tube, more colloquially known as a feeding tube, or, in one study, by ingestion of capsules of frozen stool. Others were delivered via enema, rectal tube, or colonoscopy.

POSITIVE RESULTS OVERALL

Results overall were positive. In the frozen-capsule study, 20 patients took 15 capsules per day over two days and had a 70 percent success rate. In a study using nasogastric tubes, 81 percent of patients achieved resolution within the first three

Illustration: EAS/Wikimedia Commons

A computer-generated image of one of the toxins put out by *C. difficile*.

Continued on page 23



Photo: ©iStock/monkeybusinessimages

Study aims to curb ER use among **high-risk patients**

A study based at the Durham VA Medical Center aims to curb over-reliance on emergency room care. Nurses will work to transition repeat ER users to a more regular routine of primary care.

Every year, more than half a million medically at-risk Veterans visit VA emergency rooms. Of those who are treated and released—the great majority—1 in 5 will end up back in the ER or hospital within 30 days.

And of those who end up back in emergency care, nearly 3 in 4 will not have seen a VA doctor between trips to the ER.

A research team at the Durham VA Medical Center hopes to turn this situation around. ER care is costly, and it is far from the ideal way to provide health care. The goal, rather, is to get the Veterans

into a regular routine of primary care.

In the study, primary care nurses will reach out to the at-risk Veterans, via a series of telephone calls, to connect them with the information and resources they need to avoid repeat ER visits. The trial aims to enroll more than 500 Veterans in all.

Lead researcher Dr. Susan Nicole Hastings says the study could have major implications not only for VA, but for all health care organizations.

“The results will be directly relevant to the care of more than 500,000 high-risk patients seen in

VA emergency departments annually,” she says, “and they will also be informative to health systems outside VA that aim to reduce ED use.”

Hastings is a geriatrician at the Durham VA and Duke University. She’s also an investigator with VA’s Durham Center for Health Services Research in Primary Care, and an associate professor of medicine at Duke.

According to Hastings, telephone support has proved to be a powerful tool in improving primary care. The new study will be yet one more application.

“Telephone care programs have been shown to improve care processes and outcomes in chronic illnesses such as diabetes and heart failure,” she says. “In this study we are combining proven elements of nurse-led telephone support programs for chronic illness care, with a focus on addressing acute needs after an ER visit.”

TWO OR MORE FOLLOW-UP CALLS FROM NURSES

Veterans eligible for the study are those with two or more chronic illnesses who were recently in the ER, and who had a hospitalization or ER visit in the six months prior to that.

The first call from the study nurse, to the Veteran or in some cases to a family member or companion, will focus on reviewing ER discharge instructions and medications. The nurse will also discuss any unmet health care needs that come up during the conversation.

After that, there’ll be at least one more call, possibly two, focusing on letting the Veteran know about VA primary care, and offering referrals for

home care or home telehealth and any other VA services that may be indicated. One example would be MyHealthVet, an online program that helps Veterans stay better-informed about their own health care.

During all the calls, nurses will use the “teach-back” method, asking the Veteran on the other end of the line to explain, in his own words, the information he’s been given.

“The teach-back method has been widely recognized as an effective way to increase understanding of health information, especially for those with low health literacy,” says Hastings. Previous studies by her group have shown that more than 4 in 10 ER users at the Durham VA have low health literacy.

VA IS IDEAL PLACE TO TRY MODEL

The study will track outcomes for six months from each patient’s “index” ER visit. It will also look at patients’ satisfaction with the model, and overall costs to VA.

Hasting says VA is an ideal place to try out an approach that could impact U.S. health care at large in a big way.

“We have an advanced informatics structure and a strong primary care base,” she says. “Those are important factors in testing this type of intervention.” The planned study is described in detail in a recent issue of *Contemporary Clinical Trials*. ★



“The results will ... also be informative to health systems outside VA that aim to reduce ED use.”

The scent of war: VA studies a legacy of dust, smoke, and burn pits and what it means for Veterans

A VA research team reviewed and summarized the results of 19 unique studies of Iraq and Afghanistan Veterans to look for trends in their respiratory health.



An airman tosses uniforms into a burn pit at Balad Air Base, Iraq, in 2008. The military burns unusable uniforms to make sure they don't end up in enemy hands.

of respiratory problems during and after deployment, but are inconclusive about the impact on long-term lung health. Falvo and colleagues say more long-term studies are needed.

VETERANS ENCOURAGED TO ENROLL IN REGISTRY

More than 2.6 million service members have served in Iraq and

A persistent cough or shortness of breath can mean a lot of things—none of them very good, but for Veterans of Iraq and Afghanistan, they could be a byproduct of their service overseas and deserve additional scrutiny.

“Any changes Veterans notice post-deployment in their pulmonary functions, especially new symptoms, warrant a conversation with their provider and probably some testing,” says Dr. Michael Falvo, a research physiologist at the VA’s War-Related Illness and Injury Study Center in New Jersey.

Falvo’s team recently reviewed and summarized the results of 19 unique studies of Iraq and Afghanistan Veterans to look for trends in their respiratory health. Their work appears in the 2015 edition of *Epidemiologic Reviews*.

In short, the data appear to confirm higher rates

of respiratory problems during and after deployment, but are inconclusive about the impact on long-term lung health. For many of these Veterans and their families, post-deployment respiratory health has become a major concern.

The conversation, thus far, has focused mainly on burn pits, large open-air ditches where the U.S. military disposed of trash ranging from human waste to compact discs and plastics. At an average-sized U.S. base in Iraq, Falvo estimates burn pits would have consumed between 30 and 42 tons of solid waste per day. For larger bases, like Joint Base Balad in Iraq, which had a population of more than 25,000 in its prime, that number could jump to 100 tons of waste.

To that end, VA asked the Institute of Medicine (IOM) a non-governmental organization, to study the issue. IOM’s 2011 report found that the evidence was

“inconclusive” with regard to the long-term health effects of burn pits, and recommended further study. It also drew attention to other deployment risks, besides burn pits, that might harm respiratory health.

While IOM found no evidence tying burn pits to cancer, reproductive outcomes, or neurological, respiratory or circulatory diseases, all Veterans of Iraq and Afghanistan are encouraged to go to the website of VA’s Airborne Hazards and Open Burn Pit Registry, where they can enroll, learn about potential health effects, and read the studies themselves.

BEYOND BURN PITS

Falvo agrees that burn pits are likely only part of a much larger puzzle.

“Air quality plays a gigantic role,” he says. “The overall environment in Southwest Asia tends to be high in particulate matter, and we know a lot about exposure to particulate matter from decades’ worth of research. Unfortunately the focus sometimes gets shifted solely to burn pits, which is why we’ve adopted the term ‘airborne hazards’ as a collective term to identify all the potential sources.”

Take for example, sand and dust storms—something Veterans of Iraq and Afghanistan are all too familiar with. “One study in Kuwait found dust events occurred on average once every three days,” says Falvo, “events that far exceeded exposure guidelines for airborne particulate matter.”

As part of that same past report, air quality was tested at 15 locations in Southwest Asia, including six in Iraq and two in Afghanistan. Researchers from the Desert Research Institute in Reno, Nevada, collected more than 3,000 samples and found that particulate matter exceeded both occupational and military exposure guidelines at all 15 locations. To put that in perspective, the levels were about 10 times greater than those observed in urban areas in the U.S.

Scientists have also found heavy metals such as titanium, lead, and others, swirling around in the sand. How they got there is still somewhat of a mystery. They could be the result of natural crustal sources, industrial waste, burn pits, or even just as a result of decades of warfare.

ONE STUDY INCLUDED 46,000 TROOPS

Regardless of the source, some 70 percent of those serving in Iraq and Afghanistan during 2003 and 2004 later reported at least one acute respiratory illness during their deployment. Fifteen percent reported three or more instances, and 17 percent said they were forced to seek medical attention as a result.

Since then numerous studies have found higher risks of persistent cough or shortness of breath among Veterans of Iraq and Afghanistan. The Millennium Cohort Study, for example, analyzed data on more than 46,000 participants and found that deployed personnel—particularly those around ground combat, versus those based at sea—were more likely than non-deployers to have these problems. However, the rates of bronchitis, emphysema, and asthma were nearly identical.

And it’s not just U.S. service members. One of the studies Falvo reviewed focused on the medical records of Polish soldiers serving in Iraq and Afghanistan. For those soldiers, acute respiratory illness was one of the most common health problems during their deployment.

Beyond the smoke and the sandstorms though, Falvo says service members may actually be predisposing themselves to respiratory illness, although that is not to say it is always avoidable.

“Being physically active increases the ventilation rate,” he explains. “When we carry a load or exercise, we shift to breathing through the mouth and there’s nothing to filter those particles,” says Falvo, also an

“I would encourage Veterans to enroll in the registry, regardless of whether they are currently experiencing any health problems.”

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Group therapy shows promise for suicidal Veterans

VA researchers in Kentucky saw promising results in a study of group therapy for suicide prevention.



Photo by Mitch Mirkin

New research suggests group therapy might be effective in preventing Veteran suicide.

Veterans. The word itself invokes thoughts of honor, service and sacrifice. Unfortunately, since the wars in Iraq and Afghanistan began, another word has become linked with Veterans: suicide.

VA estimated in a 2012 report that nationwide, 22 Veterans kill themselves per day, roughly one per hour. Those numbers are sometimes mistakenly used to refer only to Iraq and Afghanistan Veterans, when in fact the majority of Veterans who die by suicide are over 50 years of age. Regardless, Veterans and current military are at an increased risk of suicide when compared to their

civilian peers, and the disparity appears to be growing.

While VA, the Department of Defense, and other groups, both private and public, scramble to determine why today's Veterans are at such high risk, experts are also trying to identify practical ways to address the problem. One possible approach, say investigators, is group therapy for those at risk.

UNDERSTANDING WHAT DRIVES SUICIDAL BEHAVIOR

Dr. Lori Johnson, a suicide prevention coordinator at the Robley Rex VA Medical Center

in Louisville, Ky., explains the underlying theory:

“According to Joiner’s Interpersonal Psychological Theory of Suicidal Behavior, suicides are determined by the urge to die and the ability to perform a lethal act,” she says. “That urge to die is comprised of two factors: thwarted belongingness and perceived burdensomeness. So if people feel fewer interpersonal connections and reasons for living, and if they feel their personal needs outweigh their contributions to family, friends, and even society, they are drawn to suicide.”

The “ability to perform a lethal act” factor ties directly into wartime service, says Johnson. Exposure to the gravely injured or dead, and even to prolonged pain and stress, can dull much of the innate fear around self-injury. What’s more, most Veterans are comfortable with firearms, a trait that is particularly noticeable in the number of successful female suicides among Veterans, compared with the civilian population.

Johnson and collaborators Dr. David Jobes, Dr. Stephen O’Connor, and Barbara Kaminer, of the Catholic University of America, Western Kentucky University, and VA, respectively, are in the third and final year of a study into the



“You can’t understand unless you feel it, having a group of people who are like me and have gone through what I have gone through.”

effectiveness of group therapy at addressing the “urge to die” component of suicidality.

RESTORING THE WILL TO LIVE

“The idea was that group therapy would provide Veterans with an opportunity to develop relationships while contributing to one another’s effort at rehabilitation,” says Johnson.

In other words, not only would Veterans build the kind of interpersonal connections that would give them a reason to live, they would begin to feel responsible for one another—rekindling the camaraderie that was ingrained into them through their military service.

Group therapy for Veterans with suicidality at Robley Rex began in 2009 and has been open to virtually all Veterans with suicidal ideation, provided they have the cognitive abilities to understand and take part in therapy and are not a risk to others in the group.

While each group has two licensed practitioners as group leaders, members have significant input into their group’s norms, rules, and discussions. The conversation, while structured, is flexible and often prompted by common therapeutic questions.

According to Johnson, a simple question like “How have you been doing this week with suicidal thoughts?” can lead to extraordinary results.

SUICIDE RATE OF .01 PERCENT AMONG THOSE PARTICIPATING

As of September 2013, 156 Veterans had taken part in the program. Sixteen of the 156 attendees attempted suicide after one or more group sessions. Of these, nine had attended only once and had not fully participated.

For example, they might have declined to speak, or worn sunglasses throughout the hour-long program.

Two of the 156 Veterans succeeded in committing suicide, one eight months after last attending the group, the other a year later.

These statistics translated into an overall suicide rate of around .01 percent among those participating in the program.

The results are in line with a recent Danish study that suggested talk therapy was effective in lowering suicide ideation and eventual suicide attempts in patients.

In that study, nearly 5,700 participants who had deliberately harmed themselves—a suicide warning sign—underwent voluntary talk therapy. They were 25 percent less likely to attempt suicide than a comparison group that did not undergo the therapy. The results of that study were published online in *The Lancet Psychiatry* in January 2015.

Johnson’s team is currently analyzing the results of their study and preparing them for publication, but already she believes group therapy has identifiable benefits, not the least of which is an increased ability to reach larger number of Veterans on a lower budget. “These results are encouraging,” says Johnson. “There is an undeniable appeal to working with large numbers of suicidal patients at once.”

As for the Veterans who take part, the benefits can’t be measured in dollars and cents, or in any other quantifiable way. The journal paper includes the following quote from a Veteran participant: “All the words in the world can’t explain it. You can’t understand unless you feel it, having a group of people who are like me and have gone through what I have gone through.” ★

Alzheimer's home-safety project

Continued from page 11



The stove can be risky for those with memory loss. Remove stove knobs and hide them in a nearby drawer, or use safety covers.



The booklet *Keeping the Person with Memory Loss Safe at Home* and an accompanying kit stocked with low-cost home safety products were tested among families by researchers with VA and Boston University.

To see more photos and explanations of the safety modifications recommended in the booklet *Keeping the Person with Memory Loss Safe at Home*, based on VA and Boston University research, visit



www.research.va.gov/news/features/alz-home-safety.cfm

The scent of war

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assistant professor at Rutgers Biomedical and Health Sciences.

Couple that with the often close quarters service members live and work in, and then include the presence of diesel exhaust from heavy equipment and vehicles, and you start to get the larger picture, says Falvo.

SMOKING ADDS TO THE PROBLEM

While hard work and austere conditions may be part of the job description for soldiers, damage caused by smoking is completely avoidable. “One of the studies looked at acute pneumonia, and one of the major factors was a change in smoking patterns. We hear stories from Veterans all the time that go from not smoking before deployment, to picking up a pack-a-day habit,” says Falvo.

The research supports Falvo. Some 40 percent of current military personnel smoke, compared to about 18 percent of the civilian population. What’s more, tobacco use tends to double when a service member is deployed.

The result of all these catalysts is a hard-to-pin-down ailment that millions of Veterans could be at risk for. The good news though, according to Falvo, is that VA is getting a handle on what the population looks like and what illnesses they might be at risk for, so that providers will know how to best diagnose and treat them.

The Airborne Hazards and Open Burn Pit Registry, says Falvo, “is an important initiative that is giving us information into the symptoms and exposures of deployed Veterans. About 30,000 have signed up so far. That gives us an idea of how they’re doing and feeling, and it also allows us to follow them over time, which is crucial to identifying patterns. I would encourage Veterans to enroll in the registry, regardless of whether they are currently experiencing any health problems. The data are important, and the more people who enroll, the better the data will be.” ★

From fourth-century soup to 21st-century procedure

Continued from page 15

months, compared with 31 percent and 23 percent in the two control groups receiving vancomycin.

Across the board, in fact, FMT proved highly effective, with no delivery method being clearly superior to the others. Nevertheless, without confirmation from a controlled trial, Drekonja doesn't believe the procedure is ready for widespread VA use. "At this point, the evidence is largely through case series," he says.

More research is needed, and perhaps a little socialization. After all, the concept itself can be a bit distressing. Drekonja says convincing patients of the

need for FMT can sometimes be a challenge.

"Those that go through it are quite satisfied. But when we have approached patients about this, a few didn't even want to finish the conversation, let alone do it. There is a certain yuck factor that will always turn off a segment of the population. Now, if they have five recurrent episodes of *C. difficile*, will that yuck factor all of a sudden drop out?"

After all, as unpleasant as a colonoscopy, nasogastric tube, or frozen stool capsule might be— they've got to be better than Dr. Hong's yellow soup. ★

WORD SEARCH

L X J J Y S S T V H J S D A T
N A N O T E C H N O L O G Y F
E O I U S H M A B S T R A C T
M I D R I P W Y I H I A C T M
L J A N T P I L O T S T U D Y
Q S T A N L B S E I S S S B C
M G A L E U A M N D U I P S A
P E B G I M E C G Y E R O M E
Z N A I C I T S I T A T S M Q
E O S X S C C C N N E E V P T
A M E I O E T T E P I P I E C
P E E R R E V I E W G L K P F
G V P S U I S U R V E Y C E Q
N A D O E R U T L U C L L E C
B R A I N B A N K W B H R X E

Abstract
Bioengineer
Brain bank
Cell culture
Clinical trial
Database
Genome
IRB
Journal
Mice
Nanotechnology
Neuroscientist
NIH
Peer review
Petri
Pilot study
Pipette
Rats
Statistician
Survey
Tissue

Find these terms related to health research. They can read forwards, backwards, up, down, or diagonally. Not all the letters in the grid are used, and some may appear in more than one word.



RESEARCH CURRENTS

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

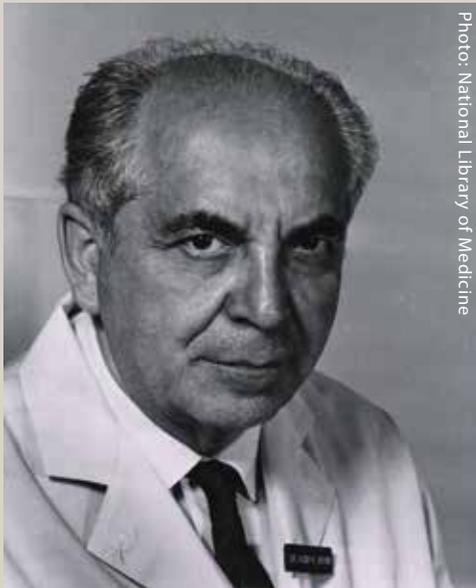


Photo: National Library of Medicine

Did you know?

Dr. Ludwig Gross, a Polish-born scientist who served in the U.S. Army in World War II and became chief of cancer research at the Bronx VA Medical Center in 1946, was considered a trailblazer. He was among the first to show that cancer, particularly leukemia, could in some cases be caused by viruses. He received a prestigious Lasker Award in 1974 for pioneering the field of tumor virology, and authored a textbook, *Oncogenic Viruses*, that became a standard in the field. Gross himself succumbed to cancer in 1999, at the age of 94.



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