



VA Research Currents

Latest 'ALLHAT' analysis shows value of diuretics for diabetic hypertensives

In people with diabetes, diuretics work as well as ACE-inhibitors and calcium channel blockers in protecting against heart attack and improving survival, and offer more protection against heart failure.

These findings, published in the June 27 *Archives of Internal Medicine*, are the latest from the “Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial” (ALLHAT), funded by the National Heart, Lung, and Blood Institute. The study included more than 7,000 veteran participants at 70 VA medical centers, among more than 42,000 participants overall. William Cushman, MD, of the Memphis VA Medical Center, was lead investigator for VA.

ALLHAT has provided the largest comparison to date of three popular classes of medications to treat high

blood pressure. ALLHAT investigators first reported in 2002 that diuretics, as an initial treatment for high blood pressure, offered more protection against adverse cardiovascular events than the other, more expensive antihypertensives. This latest analysis shows that even among diabetics and those with mildly elevated fasting glucose— a sign of pre-diabetes— diuretics are at least as effective as the other drugs, and may be more beneficial for some patients.

Compared to the ACE inhibitor and calcium channel blockers used in the study, the diuretic was:

- More protective against heart failure in patients both with and without diabetes.
- More effective in lowering systolic blood pressure—the measure of blood

pressure when the heart beats— among those with and without diabetes.

- At least as protective against fatal coronary heart disease or non-fatal heart attacks in people with diabetes, those with elevated fasting glucose, and non-diabetics.
- Equally protective against death, end-stage renal disease or cancer in people with diabetes, those with elevated fasting glucose, and non-diabetics.
- In African American study participants, more protective against stroke in people with and without diabetes (compared with the ACE-inhibitor).

More information on ALLHAT is available at <http://allhat.sph.uth.tmc.edu/default.htm>. ■

VA scientist's study of sea mammals challenges long-held beliefs on sleep

Scientists at the VA Greater Los Angeles Healthcare System and the University of California, Los Angeles, reported in the June 30 edition of *Nature* on a developmental pattern in bottlenose dolphins and killer whales that appears to be unique among mammals, with calves of both species active 24/7 during their first month, and their mothers getting very minimal sleep, but more than their offspring.

All land mammals studied to date show maximum rest or sleep at birth, with amounts gradually decreasing to adult levels. These and other findings—such as research showing that sleep deprivation for two to three weeks can be lethal in rats and flies—had led scientists to believe that sleep is critical for the development of brain and body in all animals, and serves a vital function in adults.

“Humans, when they go without sleep for even a short period of time, are unable to function effectively. And here we have animals that can go without sleep for long periods of time, without any of the deleterious effects of sleep deprivation,” said sleep expert Jerome Siegel, PhD, chief of neurobiology research at VA’s Sepulveda site, professor-in-residence at the Semel Institute for Neuroscience and Human Behavior at UCLA, and senior author on the *Nature* paper. He said knowledge gained from studying dolphins and whales may lead to new ways to treat sleep disorders or otherwise manipulate sleep in humans.

Movement and wakefulness offer several apparent advantages for the newborn sea mammals, notes Siegel,

Recent publications and presentations

The following is a sampling of recent publications by VA investigators, based on notifications received from the field. Every attempt is made to present a cross section of investigators, topics and medical centers. Only VA-affiliated authors are listed here, due to space constraints.

“Colchicine Treatment of Alcoholic Cirrhosis: A Randomized, Placebo-Controlled Clinical Trial of Patient Survival.” Timothy R. Morgan, et al, for CSP #352. **Long Beach** (and 13 other VA sites). *Gastroenterology*, April 2005.

“Does Resident Hours Reduction Have an Impact on Surgical Outcomes?” Haytham M.A. Kaafarani, MD; Kamal M.F. Itani, MD, FACS; Laura A. Petersen, MD, MPH; John Thornby, PhD; David H. Berger, MD, FACS. **Houston**. *Journal of Surgical Research*, June 2005.

“Enhancing Clinician-Communication Skills in a Large Healthcare Organization: A Longitudinal Case Study.” Richard M. Frankel, PhD. **Indianapolis**. *Patient Education and Counseling*, July 2005.

“Experimentally Induced Pain Perception is Acutely Reduced by Aerobic Exercise in People with Chronic

Low Back Pain.” Martin D. Hoffman, MD; Philip S. Clifford, PhD. **Sacramento and Milwaukee**. *Journal of Rehabilitation Research and Development*, March/April 2005.

“Ferric Cycle Activity and Alzheimer’s Disease.” Barney E. Dwyer, PhD. **White River Junction**. Society for Neuroscience annual meeting. May 12, 2005.

“Functional Incidental Training: Applicability and Feasibility in the Veterans Affairs Nursing Home Patient Population.” Joseph G. Ouslander, MD; Patricia Griffiths, PhD; Eleanor McConnell, PhD. **Atlanta, Birmingham, Durham and Sepulveda**. *Journal of the American Medical Directors Association*, March-April 2005.

“Identification of Novel Genetic Loci for Bone Size and Mechanosensitivity in an ENU Mutant Exhibiting Decreased Bone Size.” Apurva K. Srivastava; Sanjay Kapur; Suburaman Mohan; Hongrun Yu; Sonia Kapur; Jon Wergdal; David J. Baylink. **Loma Linda**. *Journal of Bone and Mineral Research*, May 2005.

“Improving Elders’ Recovery After Major Abdominal Surgery.” Valerie A. Lawrence, MD; John E. Cornell, MD; Helen P. Hazuda, PhD. **San Antonio**. Society of General Internal Medicine national meeting. May 10-14, 2005.

“Improving the Use of Hospice Services in Nursing Homes: A Randomized Controlled Trial.” David Casarett, MD, MA; David A. Asch, MD, MBA. **Philadelphia**. *Journal of the American Medical Association*, July 13, 2005.

“Macrophage Migration Inhibitory Factor is Released as a Complex with Alpha1-Inhibitor-3 in the Intraluminal Fluid During Bladder Inflammation in the Rat.” Pedro L. Vera, PhD; Katherine Meyer-Siegler, PhD. **Bay Pines**. *The Journal of Urology*, July 2005.

“Measurement of the Experience at the End of Life: A Systematic Review of the Literature.” Richard A. Mularski, MD; Karl A. Lorenz, MD; Paul G. Shekelle, MD, PhD. **West Los Angeles**. American Thoracic Society international meeting. May 20-25, 2005.

“The Neuroanatomy of Remote Memory.” Peter J. Bayley, PhD; Jeffrey J. Gold, PhD; Ramona O. Hopkins, PhD; Larry R. Squire, PhD. **San Diego**. *Neuron*, June 2, 2005.

“A Novel Mechanism for Angiotensin II Formation in Streptozotocin-Diabetic Rat Glomeruli.” Rekha Singh, PhD; Ashok K Singh, PhD; David J. Leehey, MD. **Hines**. *American Journal of Physiology Renal Physiology*, June 2005.

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Notify us of your upcoming publications and presentations

In accordance with VHA Handbook 1200.19 (available on the VA research website at www.va.gov/resdev/resources/policies/by_topic.cfm), VA investigators or their local research offices should send notifications of all publications or presentations, upon acceptance, to VA Research Communications at researchinfo@vard.org. (This email address is subject to change later this year; an announcement of the new address will be forthcoming in *Research Currents*.) Please include the article or abstract title, along with an electronic copy of the abstract, manuscript or poster; investigators’ full names and degrees; and the journal or meeting title and date. A brief lay summary of the findings should be included as well.

The above-stated requirement is in addition to any procedures required by individual Services within ORD, such as Health Services Research and Development or Rehabilitation Research and Development.

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Relaxation methods yield some gains in heart study

Patients with chronic heart failure who practiced simple meditative techniques twice daily for 15 weeks improved their spiritual and emotional scores on a quality-of-life questionnaire, but showed no gains in exercise capacity or physical quality of life, according to a VA study in the May/June *Journal of Cardiopulmonary Rehabilitation*.

Researchers at VA's Center for Health Quality, Outcomes and Economic Research in Bedford, Mass., enrolled 95 heart-failure patients in a three-arm study: The intervention group participated in a weekly class to learn breathing, meditation and guided-imagery techniques designed to elicit the "relaxation response," and were instructed to practice at home; an alternative-intervention group attended a 15-week cardiac-education program featuring experts' lectures on health topics relating to heart failure; and a control group received usual care.

The term "relaxation response" was defined and popularized in the 1970s by Harvard physician and author

Herbert Benson, MD. The response is physiologically the opposite of a stress-induced fight-or-flight state, and is marked by decreased breathing rate, heart rate, blood pressure and metabolism. Decades of research have shown its value in a range of medical conditions, but few studies have focused on heart failure.

In the new study, after 15 weeks there was no significant difference among the three groups of patients in exercise capacity or physical quality-of-life scores. But patients in the "relaxation response" group had better scores than their peers in the "peace-spiritual" and emotional scales of the quality-of-life instrument.

The authors concluded that a relaxation-response program may be helpful in improving some aspects of quality of life for heart-failure patients.

For more information on research at the Center for Health Quality, Outcomes and Economic Research, visit their website at: <http://www.va.gov/chqoer>. ■

Chronic alcohol intake and brain damage

Heavy consumption of alcohol, even for relatively short periods of time, can cause long-lasting brain damage, according to research in mice at the Geriatric Research, Education and Clinical Center at the St. Louis VA Medical Center.

A team led by Susan A. Farr, PhD, studied the behavior of mice that had consumed a diet high in alcohol for two months—the equivalent of a person drinking six to eight beers, or a bottle of wine, every day for six years.

Even after three months without alcohol, the mice still showed signs of memory problems and learning deficits. Previous research on mice had shown permanent learning deficits and neural damage only after six or more months of chronic alcohol consumption.

The findings appeared in the June issue of *Alcoholism: Clinical and Experimental Research*.

VA investigators a strong presence at AcademyHealth meeting

More than 60 investigators funded by VA's Health Services Research and Development Service (HSR&D) gave oral or poster presentations, or chaired sessions, at the recent Boston-based national meeting of AcademyHealth, the largest health-services-research membership organization in the country. In addition, four HSR&D investigators received awards at the meeting:

- **Katrina Armstrong, MD**, an investigator with HSR&D's Center for Health Equity Research and Promotion (CHERP), received AcademyHealth's Alice S. Hersh New Investigator Award for showing exceptional promise. Armstrong studies health equity and medical decision-making.

- **Rachel Werner, MD, PhD**, another CHERP investigator, received the Dissertation Award for outstanding scientific contribution based on a doctoral thesis in health

services research. Her dissertation examines whether publicly reporting information about health care providers' quality improves patient care, or whether quality report cards may cause some providers to avoid patients they perceive to be at high risk for poor outcomes.

- **Mark Meterko, PhD**, of HSR&D's Center for Organization, Leadership, and Management Research, received the Best Abstract award for a study that measured workplace civility among a large group of healthcare staff and explored its relationship to patient satisfaction.

- **Morris Weinberger, PhD**, an HSR&D Career Scientist awardee, received the John M. Eisenberg Excellence in Mentorship Award from the Agency for Healthcare Research and Quality. ■

SLEEP (cont. from pg. 1)

such as reducing danger from predators and maintaining body temperature until enough blubber develops to provide adequate insulation. The fact that this phenomenon has never been observed among terrestrial mammals, said Siegel, may simply have to do with the difference between sea and land environments.

“We can see why this behavior has evolved, and why it’s advantageous for these sea mammals, yet it still seems to violate all the assumptions we have about sleep,” said Siegel.

His team observed two adult female killer whales and their calves at SeaWorld San Diego, and four dolphins and their calves at the Gelendick Dolphinarium and the Utrish Marine Mammal Research Station in Russia. After the initial month of sleeplessness for newborns and minimal sleep for mothers, the mammals gradually increased their sleep over a few months until they reached normal adult levels. As the newborns grew, neither the newborns nor their mothers

appeared to be resting more in an attempt to compensate for the earlier sleep deprivation.

In addition to studying live animals, Siegel’s lab is now analyzing brain specimens from naturally deceased sea mammals—donated by SeaWorld and other marine parks—to figure out what brain chemistry or structures might be responsible for the animals’ seemingly unique sleep patterns.

The research was funded by the National Institutes of Health, National Science Foundation, VA, Utrish Dolphinarium and the Department of Defense. More information on Siegel’s work can be found at www.npi.ucla.edu/sleepresearch.

Funding info on website

For a list of the latest solicitations from VA’s Office of Research and Development, as well as various applications and forms, schedules, handbooks, general guidelines, and information on professional development, visit www.va.gov/resdev/funding.

PUBS (cont. from pg. 2)

“Pre-transplant Lung Function, Respiratory Failure, and Mortality After Stem Cell Transplantation.” Tanyalak Parimon, MD; David K. Madtes, MD; David H. Au, MD; Joan G. Clark, MD; Jason W. Chien, MD. **Seattle**. *American Journal of Respiratory Critical Care Medicine*, May 13, 2005.

“Resident Th1-like Effector Memory Cells in Pulmonary Recall Responses to Mycobacterium Tuberculosis.” Richard F. Silver. **Cleveland**. *American Journal of Respiratory Cell and Molecular Biology*, July 2005.

“Vaccines: Not Enough or Not Enough Time?” Walter Orenstein, MD; Allen Craig, MD; Jeanne Santoli, MD; Alan Shaw, PhD; William Gruber, MD; Robert G. Webster, PhD; Richard Webby, PhD; Mark Miller, PhD; Malak Kotb, PhD. **Memphis**. Flu Vaccine Conference, June 17, 2005.

“Variation in Outcomes in Veterans Affairs ICUs with a Computerized Severity Measure.” Marta L. Render, MD; H. Myra Kim, Sc.D; Deborah E. Welsh, MS; Karen Bickel; Stephen Timmons; Timothy P. Hofer, MD, MSc. **Cincinnati and Ann Arbor**. *Critical Care Medicine*, May 2005. ■

Inside the July '05 issue...

- Latest findings from 'ALLHAT' trial
- Studying the sleep patterns of sea mammals
- 'Relaxation Response' and heart failure

