



VA Research Currents

Arthritis researcher wins Middleton Award

Memphis-based researcher Andrew H. Kang, MD, whose pioneering work on collagen has significantly advanced the study of arthritis, will receive the 2003 Middleton Award, VA's highest award for biomedical investigators. He will receive the award during an upcoming national meeting of associate chiefs of staff for research, Jan. 22 – 23 in Washington.

Kang is a staff physician and former associate chief of staff for research at the Memphis VA Medical Center. He is director of the Center of Excellence for Diseases of Connective Tissue and the Goodman Professor of medicine and

biochemistry at the University of Tennessee.

Kang is perhaps the world's foremost expert on collagen, the main protein in cartilage, bone and other connective tissues. Over the past 35 years, his research has provided much of the basic knowledge of the various collagen molecules. Most notably, in the late 1970s he developed a model of collagen-induced arthritis in mice that has since figured in thousands of studies on rheumatoid arthritis. In fact, Kang's original publications on the model have been cited in more than

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National meeting cancelled

The VA Research national meeting scheduled for March 9 – 12, 2004, has been cancelled. Instead, the Office of Research and Development will conduct several smaller meetings in Washington, including a meeting of associate chiefs of staff for research, Jan. 22 – 23, and a training session for administrative officers, Feb. 26 – 27. The national meeting of the Health Services Research and Development Service will take place March 9 – 11.

New antibiotic effective for diabetic foot infections

An open-label clinical trial led by a VA researcher and conducted at 30 U.S. and 15 European sites shows that the new antibiotic linezolid is at least as effective as two older therapies for treating diabetic foot infections. The drug may be an important new agent for physicians treating infections that are increasingly caused by bacteria resistant to standard antibiotics, and that in severe cases may require amputation. The study appears in the current issue of *Clinical Infectious Diseases*.

Foot infections are among the most serious complications of diabetes, and a leading cause of diabetes-related hospitalizations. Amputation may be needed when infections fail to respond to therapy. People with diabetes account for about two-thirds of the 134,000 lower-limb amputations performed each year in the United States.

Linezolid, sold as Zyvox, was approved by the Food and Drug Administration (FDA) in 2000 to treat a variety of infections, including some caused by bacteria resistant to the drug methicillin. Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a major cause of infections—

including diabetic foot infections—both in hospitals and communities. For years the antibiotic vancomycin had been a last line of defense against infections caused by MRSA and other antibiotic-resistant “superbugs,” but in recent years vancomycin-resistant infections have been reported.

Because of the growing problem of MRSA and vancomycin-resistant enterococci (VRE), new agents have been developed. Linezolid is among the first new treatments for MRSA infections since vancomycin was introduced in the 1950s. Based on the results of the new trial, the FDA has now specifically extended the drug's use to most diabetic foot infections.

Unlike other newer antibiotics for MRSA and VRE, linezolid can be given orally as well as intravenously, making it suitable for outpatient use.

“The approval of this drug for appropriately selected diabetic foot infections is important because it may reduce the need to hospitalize patients and the risk of IV-related

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Recent publications and presentations

Due to space constraints, only VA investigators and affiliations are noted.

“The Association of Psychosocial Factors and Depression with Hypertension Among Older Adults.” Hayden B. Bosworth, PhD; Maren K. Olsen, PhD. **Durham.** *International Journal of Geriatric Psychiatry*, Dec. 2003.

“The Effects of Parathyroid Hormone and Alendronate Alone or in Combination on Bone Mineral Density and Turnover in Post-Menopausal Osteoporosis: 12-Month Results of the PTH and Alendronate Trial.” Kristine E. Ensrud, MD, MPH. **Minneapolis.** *New England Journal of Medicine*, Sept. 25, 2003.

“Gamma Tocopherol Upregulates Peroxisome Proliferator Activated Receptor Gamma Expression in SW 480 Human Colon Cancer Cell Lines.” Sharon E. Campbell, PhD; William L. Stone, PhD; Sarah G. Whaley; Min Qui; Koyamangalath Krishnan, MD. **Mountain Home** (Tenn.) *BMC Cancer*, Oct. 2003.

“Gender Differences in NSAID Use Among Older Adults with Osteoarthritis.” Kelli L. Dominick, PhD. **Durham.** *Annals of Pharmacotherapy*, Nov. 2003.

“Higher Hemoglobin Level is Associated with Better Early Functional Recovery After Hip Fracture Repair.” Valerie A. Lawrence, MD, MSc; John E. Cornell, PhD. **San Antonio.** *Transfusion*, Dec. 2003.

“Hypertensive Patients’ Willingness to Participate in Placebo-Controlled Trials: Implications for Recruitment Efficiency.” David J. Casarett, MD; David A. Asch, MD. **Philadelphia.** *American Heart Journal*, Dec. 2003.

“Impact of Angina Burden and Other Factors on Treatment Satisfaction After Acute Coronary Syndromes.” Sean C. Beinart, MD; Anne E. Sales, PhD; Mary E. Plomondon, MSPH; Nathan R. Every, MD, MPH; John S. Rumsfeld, MD, PhD. **Puget Sound and Denver.** *American Heart Journal*, Oct. 2003.

“A Novel Model of Pneumonia from Intraperitoneal Injection of Bacteria.” Glen A. Franklin, MD; William G. Cheadle, MD. **Louisville.** *American Journal of Surgery*, Nov. 2003.

“Obesity-Associated Hypoventilation in Hospitalized Patients: Prevalence, Effects and Outcome.” Clifford W. Zwillich, MD. **Denver.** *American Journal of Medicine*, Jan. 1, 2004.

“Provocative F Waves May Help in the Diagnosis of Thoracic Outlet Syndrome: A Report of Three Cases.” Ramon L. Cuevas-Trisan, MD; Maricarmen Cruz-Jimenez, MD. **San Juan.** *American Journal of Physical Medicine and Rehabilitation*, Sept. 2003.

“Randomized Controlled Trial of a Cognitive Behavioral Intervention for Anxiety and Depression in Chronic Obstructive Pulmonary Disease.” Connie Veazey, PhD; Dianna Densmore, MPH; Mark Kunik, MD, MPH. **Houston.** Association for Advancement of Behavior Therapy convention, Nov. 20 – 23, 2003.

“The Continuing Increase in the Incidence of Hepatocellular Carcinoma in the United States: An Update.” Hashem B. El-Serag, MD, MPH; Jessica A. Davila, PhD; Nancy J. Petersen, PhD. **Houston.** *Annals of Internal Medicine*, Nov. 18, 2003.

“Staging of Head and Neck Squamous Cell Cancer with Extended-Field FDG-PET.” David L. Schwartz, MD; Joseph Rajendran, MD; Bevan Yueh, MD. **Puget Sound.** *Archives of Otolaryngology Head and Neck Surgery*, Nov. 2003.

“Suggested Guidelines for Evaluation and Treatment of Glucocorticoid-Induced Osteoporosis for the Department of Veterans Affairs.” Robert A. Adler, MD; Marc C. Hochberg, MD, MPH. **Richmond (RAA), Baltimore.** *Archives of Internal Medicine*, Nov. 24, 2003.

“Test Performance of Positron Emission Tomography and Computed Tomography for Mediastinal Staging in Patients with Non-Small-Cell Lung Cancer: A Meta-Analysis.” **Palo Alto.** Michael K. Gould, MD, MS; Ware G. Kuschner, MD; Douglas K. Owens, MD, MS. *Annals of Internal Medicine*, Dec. 2, 2003.

“Utilities Derived from Visual Analog Scale Scores in Patients with HIV/AIDS.” Joseph M. Mrus, MD, MSc; Joel Tsevat, MD, MPH. **Cincinnati.** *Medical Decision Making*, Sept.-Oct. 2003.

“Weight Uniformity of Split Tablets Required by a Veterans Affairs Policy.” Brian R. Martin, PharmD. **Baltimore.** *Journal of Managed Care Pharmacy*, Sept./Oct. 2003.

“Wild-Type Nonneuronal Cells Extend Survival of SOD1 Mutant Motor Neurons in ALS Mice.” Robert J. Ferrante, MD. **Bedford.** *Science*, Oct. 2003. ■

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Improving communication between oncologists and dying patients

Helping oncologists relate better to terminally ill patients is the goal of a new study titled “Studying Communication in Oncologist-Patient Encounters” (SCOPE), led by James Tulsky, MD, of the Durham VA Medical Center and Duke University.

Researchers on the five-year study, funded with \$2.1 million from the National Cancer Institute, will record talks between doctors and cancer patients transitioning to end-of-life care. They will compare the findings to best practices and produce an interactive CD to teach oncologists to better handle this sensitive juncture in their patients’ care.

“Our goal is to better equip the dying patient’s physician to help the patient make the transition from seeing their cancer as potentially curable to recognizing that medical treatment will no longer be effective,” said Tulsky, a health-services researcher who won a Presidential Early Career Award in 2002 for his work on end-of-life care.

Tulsky directs the Program on the Medical Encounter and Palliative Care at VA and co-directs Duke’s Institute

on Care at the End of Life. He said cancer patients undergo a series of losses throughout their illness: “They may lose sense of their personality, their beauty, their sexuality—any number of things keep being taken away.” Patients entering a stage where treatment is no longer effective, he said, undergo a shift in focus: “The transition goes toward good function and quality of life while a short time is left, and toward other kinds of goals, whether they be spiritual goals or some sort of legacy for family and loved ones.” Tulsky said patient-centered consultations from the physician at this point are important for the patient’s psychological well-being.

“The physician’s challenge is to help a patient through this transition in a way that enhances, or helps preserve, their relationship with the patient, and not increase the emotional suffering the patient is going through.”

Adapted from the Fall 2003 issue of Research Update, published by the Institute for Clinical and Epidemiological Research at the Durham VA Medical Center.

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complications,” said lead author Benjamin A. Lipsky, director of the General Internal Medicine and Antibiotic Research clinics at the VA Puget Sound Health Care System and professor of medicine at the University of Washington School of Medicine.

In the study, 371 patients with diabetic foot infections were randomly assigned to receive either linezolid or one of two standard combination treatments, consisting of an aminopenicillin and a betalactamase inhibitor, a drug that blocks an enzyme that inactivates penicillin. Vancomycin could be added to the regimen for patients in the non-linezolid group if their infection was caused by MRSA.

Linezolid produced a clinical cure for 81 percent of patients, while the comparator combination was effective for 71 percent of patients. Statistically, the overall results for the two groups

were about equal. However, linezolid outperformed the aminopenicillin treatments in the largest subgroup: patients with an infected ulcer, as opposed to cellulitis, osteomyelitis, or other less common types of diabetic foot infections.

The study was supported by VA and Pharmacia, now part of Pfizer, the maker of linezolid. Lipsky has served as a consultant and speaker for Pharmacia and Pfizer.

Research courses in Seattle

The Sixth Annual Seattle Epidemiologic and Biostatistical Research Methods Summer Session, offered by VA and the University of Washington, will take place June 21 – 25. For details go to www.eric.seattle.med.va.gov/education or contact Carrie McCloud at (206) 764-2773 or carrie.mccloud@med.va.gov.

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23,000 scientific papers. The work has led to the understanding of rheumatoid arthritis as a tissue-specific autoimmune disease.

Kang’s current research, funded by the National Institute on Arthritis and Musculoskeletal and Skin Disorders, involves cloning and engineering collagen genes to develop a successful immunotherapy to treat rheumatoid arthritis. His findings may also have implications for other inflammatory, autoimmune diseases.

The Middleton Award was established by VA in 1960 to honor William S. Middleton, MD, an educator and physician-scientist who served as VA’s chief medical director from 1955 to 1963. The award is given each year to a senior VA biomedical investigator for major scientific contributions. It comes with \$50,000 for three years in additional research support. ■

Career milestones

Jonathan B. Perlin, MD, PhD, MSHA, and **Kilmer S. McCulley, MD,** were honored at the 2003 Association of Military Surgeons of the United States (AMSUS) awards conference. Perlin, VA's deputy undersecretary for health and acting chief research and development officer, won the Richard A. Kern Award for his lecture titled "Prevention: Using Advanced Technologies to Improve the Effectiveness, Efficiency and Humanity of Health Care." McCulley, chief of pathology and laboratory services at the Boston VA Medical Center, received the Edward Rhodes Stitt Award for his lecture on homocystine, vitamins and the prevention of vascular disease.

Gail A. Bishop, PhD, research health science specialist at the Iowa City VAMC and a microbiology and immunology professor at the University of Iowa, received the Outstanding Mentor Award from the University of Iowa Graduate College.

Herman S. Cheung, PhD, research career scientist at the Miami VAMC and professor of biomedical engineering at the University of Miami, received the Researcher of the Year Award from the school's College of Engineering. Cheung studies tissue engineering and pathogenical biomineralization.

Kenneth M. Heilman, MD, chief of neurology at the Malcom Randall VAMC in Gainesville, Fla., and distinguished professor and program director in the Department of Neurology at the University of Florida College of Medicine, received a 2003 Distinguished Service Award from the American Speech-Language-Hearing Association.

Janet A. Mulcare, PhD, research health specialist at the Dayton, Ohio, VAMC and associate professor of physical therapy, Andrews University, was named the William Evans Visiting Fellow at the University of Otago in New Zealand. This appointment recognizes research contributions in the area of exercise for persons with multiple sclerosis.

APA award to pioneer of constraint-induced therapy

Edward Taub, PhD, a researcher at the Birmingham VA Medical Center who developed new ways to train stroke patients to use their affected limbs, has received the 2004 Distinguished Scientific Award for the Application of Psychology from the American Psychological Association (APA).

Taub, also a professor of psychology at the University of Alabama, developed a set of methods he terms Constraint Induced Movement therapy, or CI therapy. The main technique involves restriction of a stroke patient's less-affected arm for two weeks, using a sling, along with intensive training of the more-affected arm during that time. The therapy, which has shown promise in several small trials, is longer in duration and more intensive than standard physical therapy. Taub and colleagues have also explored CI therapy for other disorders, such as spinal cord injury and hip fractures. ■

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