Hormone Replacement Therapy in Perimenopausal Women

Sanjay Asthana, M.D., Department of Medicine (Geriatrics), has received grant funding to initiate KEEPS (the Kronos* Early Estrogen Prevention Study). This study will address the following questions:

◆ Which is the best time in a woman’s reproductive history to initiate hormone therapy?
◆ What is the preferred form of estrogen therapy?
◆ Which is the most effective route for administration of estrogen?
◆ Which is the best progestin to counteract the adverse effects of estrogen on the lining of the uterus?
◆ What are the most sensitive measures to look at the effects of estrogen on cognition and mood?
◆ Which hormone therapy regimen is most relevant and mimics the menstrual cycle?

Specifically, KEEPS will evaluate the efficacy of four years of hormone therapy on measures of cognition and mood in 720 healthy, nonhysterectomized perimenopausal women (ages 42-58 years). This study also seeks to establish the relationship between estrogen-induced changes in markers of atherosclerosis, heart disease, inflammation, and blood hypercoagulability. It also seeks to determine if the Alzheimer’s ApoE genotype will influence cognitive responsivity to hormone therapy.

This will be the first multi-site, randomized, placebo-controlled, double-blind, parallel-group design study to address major hormone therapy related issues raised in recent years. The study will be administered at the University of Wisconsin-Madison and the William S. Middleton Memorial Veteran’s Hospital, Madison, WI. Enrollment will also occur at Yale University, University of Washington School of Medicine, University of Utah School of Medicine, and University of California at San Francisco, Montefiore Medical Center, Mayo Clinic, Harvard Medical School, and Columbia University.

*Kronos is the name of the Longevity Research Institute (KLRI) that conducts state-of-the-art clinical translational research on the prevention of age-related diseases and the extension of healthier human life.

Alzheimer’s Research Focuses on Early Intervention and Prevention Strategies

Mark Sager, M.D., Director of the Wisconsin Alzheimer’s Institute (WAI) at the UW School of Medicine and Public Health has received funding from the National Institute on Aging for a new study entitled, “Wisconsin Registry for Alzheimer’s Prevention: Biomarkers of Preclinical AD.” The purpose of this research is to develop early detection and intervention strategies to aid in preventing Alzheimer’s Disease (AD) in a population at increased risk; namely, adult children of persons with AD.

The WAI will study cognitive and neurobiological changes occurring in middle-aged individuals without dementia, who share hereditary as
Advances in Aging Health  (continued from page 1)

Alzheimer’s Research Focuses on Early Intervention and Prevention Strategies

well as environmental and health risk factors with affected parents. Study participants will be selected from the University of Wisconsin Registry for Alzheimer’s Prevention (WRAP). WRAP has collected DNA, plasma, and serum samples, and has conducted extensive assessments on more than 825 adult children of persons with AD and participants without this family history.

This prospective cohort (longitudinal) study will conduct a second wave of laboratory and neuropsychological testing and structural and functional magnetic resonance imaging (fMRI) to define patterns and predictors of cognitive change over a four-year interval. The investigators hypothesize that adult children of persons with AD will exhibit signs of abnormal cognitive aging with deterioration in learning, memory, and executive function and volumetric and fMRI abnormalities. They expect that these deficits will be predicted by specific genetic, vascular, and lifestyle risk factors for AD.

The specific aims of this study are to:

◆ determine the effects of family history of AD and the apolipoprotein E4 (APOE4) gene, an Alzheimer’s risk factor, on the cognitive aging of participants.

◆ determine the effects of vascular and lifestyle risk factors on the cognitive aging of participants.

◆ examine the effect of family history of AD and the APOE4 gene on brain aging as determined by rates of longitudinal decline in brain volume and fMRI activation during episodic memory tests.

The investigators intend to use this information to identify health and lifestyle variables that are associated with abnormal cognitive aging and the development of AD. These findings can then be used to develop interventions that may prevent or delay the onset of this disease.

Singer Brings Expertise to IOA Projects

Burton Singer has been a collaborating investigator on projects at the Institute on Aging since 1995. His academic career was divided among Columbia University (1967-1984), Yale University (1984-1993), Princeton University (1994-present), and the University of Wisconsin (2004-present). He served as Chair of the National Research Council Committee on National Statistics and Chair of the Steering Committee for Social and Economic Research in the World Health Organization Tropical Disease Research (TDR) program. He was elected to the National Academy of Sciences (1994), the Institute of Medicine of the National Academies (2005) and was a Guggenheim fellow in 1981-1982. He received his Ph.D. in Statistics at Stanford University (1967).

Dr. Singer has centered his research in three principal areas: (1) identification of social, biological, and environmental risks associated with vector-borne diseases in the tropics; (2) integration of psychosocial and biological evidence to characterize pathways to alternative states of health; and (3) development of analytical methods for analysis of longitudinal survey data, including the integration of qualitative and quantitative evidence. His research pertaining to aging has focused on forecasting the health status of elderly populations, assessment of the decline in disability among older Americans and its implications for the Medicare Trust Fund, and quantitative characterization of the health status of elderly populations at the community level. He is a co-principal investigator on the Midlife in the United States (MIDUS) study with primary responsibility for analysis that links biomarker assessments and medical histories with psychosocial experience, personality profiles, and measures of well-being. This work will be expanded over the next several years to include studies of gene-environment interactions and their relationship to psychological phenotypes. Comparative analysis between the U.S. and Japan will be facilitated by a companion study to MIDUS, Midlife Health in Japan (MIDJA), recently funded by the National Institute on Aging.
Molly Carnes, M.D., M.S. is the 2006 Joseph T. Freeman Award recipient. This award is a lectureship presented by the Gerontological Society of America (GSA) in honor of a prominent physician in the field of aging. Dr. Carnes will present a lecture at the November 2007 GSA meeting in San Francisco, CA. Dr. Carnes is a University of Wisconsin Professor in the Department of Medicine, Section of Geriatrics; Director of the Center for Women’s Health Research; Affiliate Professor in the Department of Psychiatry and the School of Engineering; affiliate of the Institute on Aging; an Affiliate Faculty of the Women’s Studies Program; and the Jean Manchester Biddick Professor of Women’s Health Research. She is also the Founder and Director of the Women’s Health Program and Osteoporosis Clinic at the Middleton Veteran’s Administration Hospital.

Age-Related Websites
Find valuable information at these websites:

PROFILES OF OLDER AMERICANS
The 2005 “Profile of Older Americans” is a report produced by the Administration on Aging. It includes statistical information about older Americans, such as marital status, living arrangements, racial and ethnic composition, poverty, education, health care, caregiving and more.

SENIOR HEALTH
http://www.nihseniorhealth.gov
The National Institutes of Health Senior Health website features information about a wide variety of health issues, including Alzheimer’s, arthritis, diabetes, dry mouth, eye diseases, falls, heart problems, stroke, and much more. This easy-to-use site features the ability to hear as well as view the text.

FEDERAL INTERAGENCY FORUM ON AGING-RELATED STATISTICS
www.agingstats.gov
“Older Americans Update 2006: Key Indicators of Well-Being” is the third in a series of reports that provide data on the overall status of the U.S. population age 65 and over, present a broad summary of national indicators of well-being for this population, and monitor changes in these indicators over time. By following these data trends, more accessible information will be available to target efforts to improve the lives of older Americans. This website includes complete statistical information, instructions for ordering a hard copy of the report, and other websites of interest.
**MIDUS II Progress Report:**

**Sleep and Daily Well-Being - MIDUS**

Researchers are beginning to assess how the amount and quality of sleep affect daily life. Using information from the Daily Diary Study, led by David Almeida (Penn State University), here are some initial findings:

- Across the week, Americans sleep, on average, 7.09 hours per day (SD=1.02), wake up at 6:40 am (SD=1.31) and go to bed at 10:23 pm (SD=1.15).
- People who sleep more report feeling happier and less grumpy throughout the day. Moreover, going to bed later was associated with a greater likelihood of experiencing stressors, such as arguments and work deadlines.

- The relationship between sleep and spending time on leisure activities (e.g., reading, socializing) varies by age. Younger adults who go to bed later spend less time on leisure activities, whereas older adults who go to bed later spend more time on leisure activities.

- Sleep was also related to how people balance work and family responsibilities. People who slept more reported that family life actually enhances work experiences and that work life benefits family experiences.

- Future analyses will examine the causes of sleep patterns as well the psychological and physical consequences of a good night’s sleep.

Visit our website at www.midus.wisc.edu, which now includes over 180 publications from the original study!
Emotional Support - This study examined whether adults are more likely to abuse alcohol if they believe that their parents did not provide them with enough care, attention, and emotional support during childhood. The findings showed evidence of a link between deficiencies in early parental support (especially maternal support) and adult alcohol problems, suggesting that even moderate deficiencies in parental support during childhood are associated with elevated risk. The association does not appear to be explained by the early initiation of alcohol use among individuals who received poor parental support. Instead, the findings suggest that the experience of poor parental support during childhood has long-lasting, negative, psychological effects that can lead to alcohol abuse. [Shaw, BA (2006). Lack of emotional support from parents early in life and alcohol abuse later in life. International Journal of Aging and Human Development, 63, 49-72].

Body Weight and Social Relationships - Some sociologists have argued that obesity is a stigmatized characteristic and that heavy people are treated poorly by others, even their loved ones. This study compared underweight, normal weight, overweight, and obese persons to see how they differ from one another in terms of the love and support they receive from significant others, as well as the criticism that they receive. Findings revealed that the quality of relationships with significant others (usually spouse) was not affected by body weight, however, relationships with parents and siblings were poorer for obese people than for normal weight persons. Obese persons reported high levels of criticism from their family members, with the criticism reflecting problems associated with weight, such as maintaining a strict diet, or difficulties with daily physical activities. The level of warmth and love received from family members was also linked to weight history. Men and women who were overweight as adolescents and were still obese in adulthood reported the lowest levels of warmth and support. The findings suggest that overweight young people may internalize the idea that they are less attractive or competent than their thinner peers, and such beliefs may create problems for personal relationships even into adulthood. [Carr, D.S. & Friedman, M. (2006). Body weight and interpersonal relationships. Social Psychology Quarterly, 69(2), 127-149].

Parenting and Well-Being - This study included MIDUS respondents who had grown children and found that people who recall warm, supportive relationships with their own parents in childhood also are more likely to report good parenting with adult children, as well as greater engagement in helping or volunteering roles in the community. However, the study also found that neither the quality of relationships with one’s own adult children nor participation in community roles was a more important influence on reported well-being. Therefore, the research reported that those who have less favorable family experiences may be able to compensate and maintain positive well-being by engaging in helping activities outside the family in the community. Finally, the study found that participation in helping and volunteer activities was more important for women’s than men’s positive adjustment. [An, J.S. & Cooney, T.M. (2006). Psychological well-being in mid to late life: The role of generativity development and parent-child relationships across the lifespan. International Journal of Behavioral Development, 30(5), 20-31].

New Findings from MIDUS I:

- Emotional Support - This study examined whether adults are more likely to abuse alcohol if they believe that their parents did not provide them with enough care, attention, and emotional support during childhood. The findings showed evidence of a link between deficiencies in early parental support (especially maternal support) and adult alcohol problems, suggesting that even moderate deficiencies in parental support during childhood are associated with elevated risk. The association does not appear to be explained by the early initiation of alcohol use among individuals who received poor parental support. Instead, the findings suggest that the experience of poor parental support during childhood has long-lasting, negative, psychological effects that can lead to alcohol abuse. [Shaw, BA (2006). Lack of emotional support from parents early in life and alcohol abuse later in life. International Journal of Aging and Human Development, 63, 49-72].

- Body Weight and Social Relationships - Some sociologists have argued that obesity is a stigmatized characteristic and that heavy people are treated poorly by others, even their loved ones. This study compared underweight, normal weight, overweight, and obese persons to see how they differ from one another in terms of the love and support they receive from significant others, as well as the criticism that they receive. Findings revealed that the quality of relationships with significant others (usually spouse) was not affected by body weight, however, relationships with parents and siblings were poorer for obese people than for normal weight persons. Obese persons reported high levels of criticism from their family members, with the criticism reflecting problems associated with weight, such as maintaining a strict diet, or difficulties with daily physical activities. The level of warmth and love received from family members was also linked to weight history. Men and women who were overweight as adolescents and were still obese in adulthood reported the lowest levels of warmth and support. The findings suggest that overweight young people may internalize the idea that they are less attractive or competent than their thinner peers, and such beliefs may create problems for personal relationships even into adulthood. [Carr, D.S. & Friedman, M. (2006). Body weight and interpersonal relationships. Social Psychology Quarterly, 69(2), 127-149].

- Parenting and Well-Being - This study included MIDUS respondents who had grown children and found that people who recall warm, supportive relationships with their own parents in childhood also are more likely to report good parenting with adult children, as well as greater engagement in helping or volunteering roles in the community. However, the study also found that neither the quality of relationships with one’s own adult children nor participation in community roles was a more important influence on reported well-being. Therefore, the research reported that those who have less favorable family experiences may be able to compensate and maintain positive well-being by engaging in helping activities outside the family in the community. Finally, the study found that participation in helping and volunteer activities was more important for women’s than men’s positive adjustment. [An, J.S. & Cooney, T.M. (2006). Psychological well-being in mid to late life: The role of generativity development and parent-child relationships across the lifespan. International Journal of Behavioral Development, 30(5), 20-31].

Longitudinal data from MIDUS II are now publicly available through the University of Michigan. Interested users can download data and documentation by logging onto the ICPSR website at https://www.icpsr.umich.edu/ticketlogin.

MIDUS II (2004-05) involved data collection from 75% of original eligible MIDUS I (1995-96) respondents. The result is a longitudinal sample consisting of 4,963 adults ranging in age from 35 to 84. Extensive information was obtained from these individuals about work and family life, psychological outlooks, social relationships, and health.
The Biology of Aging and Age-Related Diseases Training Grant, funded by the National Institute on Aging, is a multidisciplinary program that provides annual support for four predoctoral students and four postdoctoral fellows. Following are profiles of two trainees.

**Patrick Bradshaw**

joined the Biology of Aging and Age-Related Diseases Training Grant as a postdoctoral trainee in August, 2005. He completed his Ph.D. in biochemistry at Ohio State University in 2001 followed by two postdoctoral positions in bioinformatics at the University of Missouri and Virginia Tech. He is currently working with Drs. Richard Weindruch and Tomas Prolla on studies of the relation between mitochondrial dysfunction and aging. Mitochondria are the tiny powerhouses within the cell that utilize nutrients and oxygen to fuel the body’s energy needs. During this process they also release potentially dangerous reactive oxygen species that lead to cell damage and aging. Mitochondria contain their own DNA. When this DNA is mutated in mice, as the result of an error-prone copying mechanism, premature aging is observed. Dr. Bradshaw hopes to determine if slowing the accumulation of these DNA errors will increase the healthy lifespan of normal animals.

Dr. Bradshaw stated that “The Institute on Aging is a very valuable resource on campus. It provides a friendly, nurturing environment that fosters world-class research.” He indicated that the training grant has allowed him to interact and exchange ideas with many individuals across campus at bi-monthly training grant meetings. He also feels that the travel funding provided by the grant provides the opportunity for trainees to exchange ideas with the international aging community at large, that would not have otherwise been possible.

Dr. Bradshaw hopes to find a faculty position to continue his research after finishing the training grant.

**William Simonson**

became interested in biomedical research as an undergraduate at the University of Washington, where he studied the immunology of Type I diabetes. Mr. Simonson subsequently joined the Medical Scientist Training Program at UW-Madison, which provides integrated graduate training in scientific research and clinical medicine, leading to both the M.D. and Ph.D. degrees. He completed two years of medical training and is currently working toward his Ph.D. in Cellular and Molecular Biology in the laboratory of Dr. Anna Huttenlocher, M.D., Professor of Pharmacology. After receiving his Ph.D., he will complete his M.D. training.

Mr. Simonson became a predoctoral trainee in August of 2003 on the UW Institute on Aging Biology of Aging and Age-Related Diseases Training Grant. He studies how white blood cells function during the immune response; specifically, how T lymphocytes are able to migrate quickly through the body to sites of inflammation, then stop rapidly and become activated when they recognize foreign molecules on the surface of target cells. The goal is to identify the factors involved in these processes in hopes that they will serve as targets for the development of improved drugs. For example, a drug that interferes with T lymphocytes stopping at a site of inflammation could be used to treat autoimmune conditions like rheumatoid arthritis, multiple sclerosis, and lupus.

Mr. Simonson indicated that training grant opportunities, such as support for attendance at scientific conferences and bimonthly seminars with other trainees and faculty, have broadened his knowledge of research in the field of aging. He said, “My participation on the training grant has been invaluable in allowing me to pursue my goal of conducting immunology research while also seeing patients in a clinical setting.”

Trainees Supported by NIA Grant
Margaret Gatz, Ph.D.

Professor, University of Southern California, Departments of Psychology, Gerontology and Preventive Medicine; Foreign Adjunct Professor, Karolinska Institute, Stockholm, Sweden, Department of Medical Epidemiology and Biostatistics

Dr. Gatz directs the Study of Dementia in Swedish Twins, a large longitudinal investigation of genetic and environmental factors in Alzheimer’s disease. Author of over 200 scholarly papers, she was named by the Gerontological Society of America as the 2006 recipient of the Donald P. Kent Award, given to a person who displays the highest standards for professional leadership in gerontology through teaching, service and interpretation of gerontology to the larger society. Dr. Gatz currently chairs her department and serves as coordinator of the graduate track in clinical psychology and aging, one of a handful of programs of its kind nationwide.

Neil Binkley, M.D.

Associate Professor, UW Department of Medicine (Endocrinology and Geriatrics); Associate Director, UW Institute on Aging

Dr. Binkley’s research efforts focus on osteoporosis diagnosis, osteoporosis in men and the role of nutrition in bone loss. He has published over 80 articles, contributed to numerous textbooks and has authored over 130 abstracts. He is a member of the American Geriatrics Society, American Society for Bone and Mineral Research, International Society for Clinical Densitometry, Gerontological Society of America, International Bone and Mineral Society and the Wisconsin Bone Club.

Richard Davidson, Ph.D.

Vilas Professor, UW Departments of Psychology and Psychiatry

Dr. Davidson’s work examines the biological substrates of emotion, affective style and affective disorders throughout the lifespan. He is a William James and Vilas Research Professor of Psychology and Psychiatry at the University of Wisconsin-Madison. He has received the NIMH Research Scientist Award, the William James Fellow Award from the American Psychological Society, and the Distinguished Scientific Contribution Award from the American Psychological Association. He is on the editorial board of numerous major journals and is founding editor of the new APA journal, Emotion. He directs the NIMH-funded Wisconsin Center for Affective Science, the Wisconsin Center for Mind-Body Interaction, and the NIMH Training Program in Emotion Research. His research focuses on the neural substrates of emotion and emotional disorders.

Ross L. Levine, M.D.

Associate Professor, UW Department of Medicine (Neurology and Radiology); Senior Clinician, WI Comprehensive Stroke Center

Dr. Levine’s work in the field of aging includes age-related cerebral blood flow changes; successful aging and the neurological examination; positron emission tomographic imaging and brain degenerative states; neuroimagining and memory failure; dysphagia and aging; and many age-related issues in stroke victims.

Health Fair Information
◆ Alzheimer’s Disease ◆ Immunizations
◆ Alternative Medicine ◆ Osteoporosis
◆ Swallowing Disorders ◆ Memory Disorders ◆ Stroke Prevention
◆ Volunteer Opportunities ◆ Falls Prevention ◆ Housing Options

Screening Assessments
◆ Bone Density ◆ Blood Pressure

Poster Session
UW researchers are invited to showcase information about their research in aging.

Award Presentations
The Institute on Aging makes three awards each year to recognize outstanding achievement in the areas of biomedical, psychosocial and clinical/applied research in aging or life course studies. The recipients are current students or advanced trainees at the UW-Madison.

2006 New Investigator Award Recipients
From left to right: Janice Jou, Clinical Applied, Tetyana Pudrovksa, Sociobehavioral and Philipp Raess, Biomedical.
Calendar of Events

April 26-27, 2007
Emotion Symposium
608-263-6161

September 13, 2007
Current Concepts in Nutrition and Aging
608-265-9101

October 18, 2007
19th Annual Colloquium on Aging
608-261-1493