If you live long enough, chances are that changes in your health &/or functional status will require you to retire from driving. For persons diagnosed with Alzheimer’s disease (AD), it is not a question of if retirement from driving will be required, but when.

Concerned family members often turn to physicians and other health providers for answers. Few physicians have specific training in this area, however, and it can take time for patients, families and health providers to agree on an appropriate course of action.

A new 2-year ADRC project funded by the American Automobile Association (AAA) Foundation for Traffic Safety will explore this situation from the perspective of driver licensing in Missouri. Education Core Leader, Dr. Tom Meuser, will serve as Principal Investigator and Coordinator of the project, entitled Medical Fitness to Drive & A Voluntary State Reporting Law.

Two other Washington University faculty, Drs. David Carr (Medicine/Geriatrics) and Gudmundur Ulfarsson (Civil Engineering) will participate significantly in the project. Other co-investigators include Marla Berg-Weger, PhD (Saint Louis University), Pat Niewoehner, OTR/L, CDRS (St. Louis VAMC), & Peggy Barco, MS, OTR/L (Center for Head Injury Services).

In 1998, through a joint lobbying effort of the AAA, Concerned Americans for Responsible Driving, Alzheimer’s Association, Washington University, and other organizations, the Missouri Legislature passed a voluntary reporting law for potentially unsafe drivers. House Bill 1536 allows physicians, other health professionals, law enforce-

ment and license office personnel, social service professionals, family members, and others to report potentially unsafe drivers for retesting and possible license revocation (see www.drivingsafe.org). The law grants immunity from prosecution for breach of confidentiality, is non-specific with regards to age (although the majority of those reported are older), and includes a Medical Advisory Board for review of complex cases. HB-1536 is administered through the Drivers License Bureau, Missouri Department of Revenue (MDOR), in cooperation with the Missouri State Highway Patrol (MSHP) which provides all on-road testing.

Most individuals reported under HB-1536 are asked to submit a physician’s statement documenting their health status. Depending on what’s in this report, some may be required to take on-road testing through the Highway Patrol, while others may lose the privilege to drive immediately.

A State-University Partnership

Although 43 of 50 states in the US have voluntary reporting laws like HB-1536, to date, none of these laws have been evaluated for efficacy. Do such laws actually remove unsafe drivers from the road? What medical conditions are of the greatest concern?

With strong support from officials at MDOR and MSHP, Dr. Meuser, Dr. Carr, and the rest of the team will gather the data necessary to answer these and other important questions.

Since 1999, over 7,000 individuals have been reported under the provisions of HB-1536. Thousands of professional and family reports and health statements are available for analysis. These data will be combined with citation records (e.g., speeding tickets, moving violations) and crash data to provide a comprehensive characterization of the medically impaired older driver in Missouri. Updates will be provided in future issues of HORIZONS.
**A Short, Valid Assessment for Dementia?**

One of the many exciting projects underway at the ADRC focuses on developing a brief, valid, and culturally appropriate screening tool to detect dementia in the community. Starting in 2004, Center Director, Dr. John C. Morris, and colleagues, have worked to develop and validate such a tool, called the Brief Inventory for Dementia Detection (BIDD). The BIDD includes questions for a family informant and specific tests for the person with suspected dementia. Preliminary validation data suggests that the BIDD works. Those found to have a score in the impaired range go on to receive a dementia diagnosis following a more detailed clinical assessment.

Validation of the BIDD involves fruitful collaborations with Saint Louis University (SLU) and the St. Louis County Health Department (SLCHD). Participants from a SLU Study—Physical Frailty in Urban African Americans—are administered the BIDD along with a more detailed assessment at our Center. Through the dedicated efforts of MAP nurse clinician, Pamela Jackson, physicians and nurses from the SLCHD are learning to administer the BIDD as part of care they provide to older adults in our community. Data from both of these collaborative efforts will confirm the validity and culturally sensitivity of this new screening tool.

**Volunteers Needed for ADRC Studies**

Do you know of someone that might consider volunteering for a research project on cognitive aging?

Two primary projects of the ADRC are in need of new volunteers this year. The Memory & Aging Project enrolls persons aged 65+ with mild memory problems. The Adult Children Study needs a few additional adult volunteers, age 55 or older, with a family history of Alzheimer’s disease (AD) in at least one parent, as well as adult volunteers 45 and older for whom neither parent had AD.

If you know of a potential volunteer, please ask that person to call the ADRC at 314-286-2863. Thank you!
A combination of brain scanning with a new imaging agent and cerebrospinal fluid (CSF) analysis has left neuroscientists encouraged that they may finally be moving toward techniques for diagnosing Alzheimer's disease before its clinical symptoms become apparent.

"When clinical symptoms start, the disease process has already been at work in the patient for many years and possibly even decades," explains Anne Fagan, Ph.D., research associate professor of neurology at Washington University School of Medicine in St. Louis. "Up to 30 percent of neurons in vulnerable areas are already dead, and you can't get them back. So finding markers that can help us identify patients prior to symptoms is really our big push now."

With colleagues Mark Mintun, M.D., professor of radiology, and David Holtzman, M.D., the Andrew B. and Gretchen P. Jones Professor and head of the Department of Neurology, Fagan studied a group of 24 people that included individuals diagnosed with very mild and mild Alzheimer's disease and cognitively normal subjects. As expected, in patients with cognitive impairments believed to be attributable to Alzheimer's disease, researchers found low CSF levels of amyloid beta 42 (A-beta 42), the principal ingredient of the brain plaques that are characteristic of Alzheimer's disease. In the same individuals, brain scans with a new imaging agent that reveals the presence of amyloid plaques in the brain were positive.

What scientists didn't anticipate was that three cognitively normal subjects would have both low CSF levels of A-beta 42 and positive results from the brain scans. Fagan stressed that although this aspect of their findings was very intriguing, it doesn't prove that the three normal subjects will one day develop clinical Alzheimer's disease.

"For now, definitive diagnosis of Alzheimer's disease still cannot be made until autopsy," she says. "It's going to take a number of years for us to fully assess these results, because all we can do now is follow the participants closely to see if they eventually develop Alzheimer's dementia."

Fagan presented the result of the study at the November 2005 annual meeting of the Society for Neuroscience in Washington, D.C. The study also appeared in the March 2006 issue of Annals of Neurology.

Many prior studies have found that A-beta 42 levels drop in the cerebrospinal fluid of Alzheimer's disease patients. A-beta 42 is naturally produced in the brain, and researchers suspect that the creation of amyloid plaques may be linked to breakdowns of the processes that normally clear A-beta 42 from the brain via the CSF and the bloodstream.

However, natural variations occur in CSF A-beta 42 levels in healthy subjects, and the amount this level drops in Alzheimer's patients also varies. This left no distinct level scientists could identify as a diagnostic marker characteristic of Alzheimer's disease.

Fagan wanted to see if useful distinctions could be made by combining data on CSF A-beta 42 levels with results from brain scans with a new imaging agent, PIB (for Pittsburgh compound B). Developed by researchers at the University of Pittsburgh, PIB temporarily sticks to amyloid plaques in the brain but washes clean in 30 to 60 minutes. Scientists can detect this sticking with a PET scanner.

Using PIB data available from ongoing studies of research volunteers at the Memory and Aging Project at the Alzheimer's Disease Research Center at Washington University, Fagan compared PIB scan results and levels of CSF A-beta 42.

"When I realized that everyone who was PIB positive also had lower CSF A-beta 42 levels, I had one of those 'aha!' moments that makes it so exciting to be a scientist," Fagan says.

Other CSF factors, such as levels of another form of A-beta and of a molecule found in the brain cell tangles created by Alzheimer's disease, did not correlate with positive PIB scan results.

Story by Michael Purdy, Medical Public Affairs, Washington University School of Medicine.

Brain Donation

Did you know that over 60% of MAP-ADRC participants agree to donate their brains to science upon death? Brain autopsy is the one sure way to confirm a dementia diagnosis given in life.

At Washington University, our specialists can diagnose Alzheimer's disease (AD) with ~93% accuracy. Other forms of dementia are more challenging to get right, however. The autopsy plays a critical role in the research process, paving the way for studies connecting data collected in life with confirmed diagnoses. Many studies, in fact, now require the use of autopsy-confirmed cases.

The final act of volunteering for research on AD is brain donation. We are deeply grateful to our participants and their family members for supporting this aspect of the research process. Family members play an especially important role, as they are responsible for notifying the Center of the death within a few hours and working with our Autopsy Nurse to make sure the process goes smoothly.

If you haven't decided on brain donation as yet, please consider this possibility. Call 314-286-2683 if you have any questions about the autopsy process. Thank you.

Dr. Anne Fagan

Would you like to make a gift in support of the ADRC? You may support our research, education and service goals by joining the Friends of the ADRC. Members of the Friends are entitled to attend periodic Friends Receptions featuring presentations on research findings from Dr. John C. Morris, Director of the ADRC, and other investigators, and also receive free admission to various ADRC-sponsored conferences. Friends are encouraged to make an annual gift in support of the ADRC.

Donations from Friends support both the infrastructure upon which the ADRC depends, as well as specific research and educational projects of the Center. Private donations help to fund promising pilot research projects (i.e., small projects to test out new ideas), educational conferences such as the Leonard Berg Symposium series, the training of medical students and fellows, and other worthwhile projects.

To join, simply call (314-286-241) or e-mail (adrcfriends@abraxas.wustl.edu) the Friends Coordinator.
Millions of prescriptions are written each year in the US for benzodiazepines. Those who take medications in this class (see list below) need to know about side effects and alternatives. This article provides a brief summary.

Why are these drugs prescribed?
Benzodiazepines are prescribed most often for anxiety and insomnia problems. The risk of experiencing one of these conditions may increase as we age. Benzodiazepines are indicated for short-term control of these conditions, commonly defined as no more than 10 days with the first attempt to control symptoms and no more than four months on the second attempt to control symptoms. Longer-term use may be appropriate in some instances.

How do benzodiazepines work?
These drugs work within the central nervous system, that is, the brain and spinal cord. They mimic the action of a neurotransmitter which is in charge of depressing certain areas of the central nervous system to produce feelings of relaxation and drowsiness. They are efficacious when used for the correct indication, with the appropriate dosage, and under the supervision of the doctor.

What are the common side effects?
Because these drugs work to depress the brain and spinal cord, patients may experience effects such as:

- Decreased mental alertness
- Drowsiness, Confusion
- Blurred Vision
- Impaired Judgment
- Dizziness, Disorientation
- Depression, Emotional Problems
- Impaired Learning & Recall
- General Forgetfulness
- Uncontrolled Muscle Movements
- Addiction / Withdrawal

Are they safe for older adults?
Benzodiazepines can cause and/or worsen cognitive problems, especially in older adults. Memory loss is a common side effect. Even though every individual taking this medication will not experience side effects, it is important to realize that they can occur and the elderly are more susceptible to experiencing them. Recent studies indicate that cognitive impairment may also develop gradually as a late complication of long-term benzodiazepine use. Most experts agree that benzodiazepines should be avoided in patients with memory loss or dementia.

What about negative drug interactions?
Benzodiazepines interact negatively with a number of medications used by older adults. Alcohol use can worsen such interactions even further. For example, Digoxin is a drug commonly prescribed for heart failure, and when taking it simultaneously with a benzodiazepine, the level of Digoxin in the blood may increase resulting in toxic effects. Other drugs that may interact with benzodiazepines are:

<table>
<thead>
<tr>
<th>Brand / Trade Name</th>
<th>Generic Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ativan</td>
<td>lorazepam</td>
</tr>
<tr>
<td>Xanax</td>
<td>alprazolam</td>
</tr>
<tr>
<td>Valium</td>
<td>diazepam</td>
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<tr>
<td>Klonopin</td>
<td>clonazepam</td>
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<tr>
<td>Restoril</td>
<td>temazepam</td>
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<tr>
<td>Halcion</td>
<td>triazolam</td>
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<tr>
<td>Serax</td>
<td>oxazepam</td>
</tr>
<tr>
<td>Dalmane</td>
<td>flurazepam</td>
</tr>
<tr>
<td>Librium</td>
<td>chlordiazepoxide</td>
</tr>
<tr>
<td>Traxene</td>
<td>clorazepate</td>
</tr>
</tbody>
</table>

Barbiturates        Propranolol
Narcotics           Scopolamine
Cimetidine          Theophylline
Oral Contraceptives Levodopa
Prozac (fluoxetine) Ketoconazole
Probenicid          Valproic Acid
Ranitidine          Metoprolol
Isoniazid           Darvocet

Are there any medical conditions that are adversely affected by benzodiazepines?
In addition to memory loss and dementia, benzodiazepines may be harmful for persons with respiratory/lung diseases, such as chronic obstructive pulmonary disease (COPD), bipolar mood or addiction disorders, closed angle glaucoma, hepatic or renal impairment, Parkinson’s disease, and certain seizure disorders.

Are there any alternatives for anxiety / insomnia?
Benzodiazepines differ in the ways they are metabolized in the body. Lower doses of oxazepam, lorazepam, and temazepam are safer in the elderly population than other benzodiazepines. Ambien (zolpidem) is an alternative that may have fewer side effects. However, the safest alternative would be nonpharmacologic, behavioral measures. For controlling insomnia, such measures include avoiding substances that can affect alertness / drowsiness at bedtime (caffeine, alcohol, nicotine, stimulants), establishing a regular time to wake up and go to sleep, avoiding naps during the day, avoiding excessive fullness or hunger before bed, and creating a comfortable sleep environment. For controlling anxiety, nonpharmacologic measures include exercising regularly, avoiding stimulants like caffeine, eating a well balanced diet, meditating, and avoiding alcohol.

Lastly, many medications have side effects or drug interactions which result in anxiety or insomnia. The first thing a person should do when experiencing one of these symptoms is to check with a doctor or pharmacist to see if the anxiety or insomnia may be a result of a medication he or she is currently taking.

A special contribution from Laura Reukert, Pharm.D, a recent graduate of the St. Louis College of Pharmacy. Ms. Reukert produced this summary as part of a dementia elective during her last semester.
Aging, Healthcare & Dementia in Rural Missouri

by Tom Meuser, PhD

Missouri is a rural State in terms of geography and population distribution. According to the Office of Social and Economic Data Analysis (OSEDA), University of Missouri, 91 of Missouri’s 113 counties are considered rural/non-metropolitan by US Census criteria. A meaningful portion of Missouri’s population in 2000 (32%) resided in these 91 rural counties. Four metropolitan areas (St. Louis, Kansas City, Columbia, Springfield—where our four Alzheimer’s Association chapters are based) and nearby areas accounted for the majority of state residents (68%).

Missouri’s total population of older adults in 2000 was 13.5%, higher than the national average of 12.4%. A substantial number of households in rural counties included one or more older adults. As shown in Figure 1, the rural counties of north central and south central Missouri had particularly high percentages (dark blue, up to 41%) of elder households in 2000.

Why is this? According to OSEDA, overall population in many rural counties declined over the past 20 years. One explanation is that older adults are “aging in place” whereas younger adults are moving elsewhere and fewer children are born to remaining residents. Adults aged 85 and over, in fact, represented the second highest growing population group in Missouri (next to baby boomers aged 35-54) between 1990 and 2000. The number of older adults in this 85+ cohort rose 21.4% during this period.

Although a substantial number of older adults reside in rural counties, relatively few physicians practice in these counties. Only 16% of all licensed physicians in Missouri practiced in rural counties in 2000. Rural Knox County in northeastern Missouri (circled in red in Figure 1), for example, had a total population of 4,300 when the census was taken in 2000, with 21% of residents over the age of 65 years. Only five licensed physicians practiced in Knox County at that time!

In Knox County, as in probably most rural counties across the US, older adults must often travel many miles to other counties or metropolitan areas to access healthcare services. This situation is likely to complicate care for older adults with Alzheimer’s disease (AD) who must rely on others (family, friends, social service organizations) to facilitate and otherwise follow-up on medical appointments and general care needs.

Approximately one third of Missouri’s estimated 125,000 persons with AD reside in rural counties. Changing demographics suggest that a substantial portion of these live alone, and thus may face even greater healthcare challenges.

What’s being done?

Community service organizations, such as the Alzheimer’s Association and Area Agencies on Aging, are doing a lot to serve the needs of rural elders. Rural hospitals, such as Audrain Medical Center in Mexico, Missouri, serve as important hubs for dementia care, drawing patients from many miles.

The Washington University ADRC supports rural dementia care through educational outreach. Our Rural Clinician Partners Program (RCPP) seeks to improve dementia care in rural areas by enhancing the knowledge base of the physicians and other healthcare professionals that practice there.

The RCPP uses a “mini-residency” educational model, involving select groups of clinicians in 3-day intensive training experiences in St. Louis. Many ADRC faculty and staff volunteer their time and expertise to participate in RCPP sessions — provided to small groups of 4-5 trainees up to six times per year.

Primary care physicians, advanced practice nurses, and physician assistants are the primary targets for the program. Clinicians may apply for entry, or individuals may be nominated by a colleague, local organization, or even a patient.

Since 2000, the RCPP has trained over 85 clinicians from across Missouri. As shown in Figure 2 below, trainees have come from rural counties across the state (red stars). Counties in cream have just 8-102 persons per square mile. For comparison, St. Louis County has over 2,000 persons per square mile. The counties of far northwest and west central Missouri are important RCPP targets for the next few years.

Initial planning is underway for the ADRC to co-sponsor a Rural Dementia Care conference in the Spring of 2008. The goal of the conference will be to document the challenges associated with providing quality dementia care in rural areas and to propose practical improvements. More details will follow in future issues of HORIZONS.

COMING SOON
Missouri Senior Report 2006
A Joint Project of OSEDA & Aging Organizations across Missouri
Obtain your copy at:
www.oseda.missouri.edu

Figure 1

Figure 2
<table>
<thead>
<tr>
<th>Study Coordinator</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angela Oliver, MS, RN</td>
<td>&lt;br&gt;Eligible in &lt;br&gt;double-blind, placebo-controlled study.</td>
<td>&lt;br&gt;Men with PSA greater than 25.</td>
</tr>
<tr>
<td>Wendy Overman, BA</td>
<td>&lt;br&gt;Eligible for &lt;br&gt;study.</td>
<td>&lt;br&gt;Women with history of &lt;br&gt;cancer.</td>
</tr>
<tr>
<td>Chrysler Tomson, MSN, RN</td>
<td>&lt;br&gt;Eligible for &lt;br&gt;study.</td>
<td>&lt;br&gt;Men with &lt;br&gt;PSA levels greater than 25.</td>
</tr>
<tr>
<td>&lt;br&gt;Referring patient:</td>
<td>&lt;br&gt;Study Design</td>
<td>&lt;br&gt;Investigational Agent</td>
</tr>
</tbody>
</table>

*Informational Table – Active Clinical Trials through MAP-ADRC (May, 2006)*
New Faces

Benita Austin, MSN, APRN-BC, ANP, joined MDC as a nurse clinician in April. Prior, she managed bone marrow transplant care at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University School of Medicine in Baltimore.

Joy Kurz, MSN, RN, GNP-BC, joined MAP and MDC as a nurse clinician in April. Prior, she served as Director of the Senior Care/Wound Care Center at Des Peres Hospital. Joy also has a criminal justice degree and worked as a juvenile probation officer years ago.

Abbey DeWeese joined MAP as a psychometrician in May. Abbey just received her BA in Psychology from UM-St. Louis and hopes to eventually pursue a PhD. Right now, much of her energy is devoted to her young daughter, Corrine, and getting ready for a June wedding.

Karolina K. Piotrowicz joined MAP as a clerk in January. A native of Poland and an accomplished linguist, Karolina is working towards her BA in Managerial Economics. She and her husband, Jarek, will soon celebrate their first wedding anniversary.

Sherry Ellis joined MAP as a secretary in February. Prior to starting at Washington University four years ago, Sherry worked in the travel industry. A native of St. Louis with her husband, a pet supply salesman, she keeps busy raising three teenagers.

Jessica C. Lester will join the ADRC as a project coordinator in July. She received her BA in Sociology from the University of Chicago in 2003, hopes to attend medical school in the future. Her fiancé, Kevin Germino, is a Pediatric Resident at SLU.

Fond Farewells

Ebru Karakoc, MD, Fellow — Returned to Turkey to complete her residency in Neurology.

Linda Ding, Psychometrician — Starts Medical School at the University of Missouri-Columbia in July.

Angie Berry, MSN, Nurse Clinician — Joined the Human Studies Committee as a Senior Research Review Specialist.

Lea Grinberg, MD, PhD, Fellow — Returned to Brazil to open a Neuropathology Lab at the University of Sao Paulo.

Rajka Liscic, MD, PhD, Fulbright Fellow — Returned to Croatia to continue her career as an academic neuroscientist.

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