

# Georgetown University Medical Center

## Memory Disorders Program Newsletter



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### Many Things You Always Wanted to Know About Research But Were Afraid to Ask

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The GUMC Memory Disorders Program evaluates, diagnoses, treats and cares for persons with Alzheimer's disease (AD) and related disorders. Additionally, we provide opportunities for participation in research studies. We recruit persons who have mild, moderate or severe AD, those with mild cognitive impairment, and people with no memory problems to participate in clinical trials. Although many different types of clinical trials exist, this article will consider treatment trials, where promising medications or interventions are being tested.

Most of our studies involve both a subject and a study partner, a person who is the subject's family member, friend, or professional caregiver. The study partner generally accompanies the subject to all study visits; and that person is called on to answer questions and to provide input on how the subject is doing.

It is my goal in a series of articles to unravel some of the mysteries behind research, to explain to you what we do and why we do it, and how you and your family can be informed participants in this process. In this

first article, I will discuss the Guiding Principles in Human Research. In future editions of this newsletter, I will address such topics as: Why Participate in Research?; Understanding the Nuts and Bolts of Study Participation; Elements of the Consent Form.

#### Guiding Principles

Let me start by outlining some of the Guiding Principles we observe in conducting research on our fellow human beings. The needs of the subject come first, prior to study participation and involvement. Our focus has to be what is best for the subject, independent of the requirements of the trial. The majority of studies we conduct allow persons with Alzheimer's disease to be on such medications as Aricept, Exelon or Razadyne, Namenda and Vitamin E. As new drugs are approved for use with Alzheimer's disease, those will most likely be allowed in many studies as well. For those studies that do not allow people to be on these kinds of medications, we would not recruit subjects who use

and benefit from these medications. That would be contrary to our focus on the needs of the subject and contrary to Good Clinical Practice.

For those with memory problems, we require consent of the individual along with that of a "legally authorized representative" for health care matters. This is done to ensure that a subject is not coerced into participating in a study. While consent is required before a subject can participate in a clinical trial, if for any reason a subject no longer wishes to participate in a study, the person and the legally authorized representative can withdraw consent at any time in the process. Also, if the physician feels that the subject is unable to comply with study requirements, or if the person has other problems that impede participation, the physician may suggest that the subject end study participation.

Story continued on pg.3

### The Director's Column:

#### The Search for Treatments to Slow Alzheimer's Progression: Targeting Amyloid

It is good news for the millions of families affected by Alzheimer's disease that huge efforts are under way at pharmaceutical companies and academic medical centers to discover, develop and test new treatments. Even better is the reason for optimism about the prospects for success: the cause of Alzheimer's disease is now known. The cascade of events that occurs in the Alzheimer's disease brain leading to the symptoms of dementia can be traced back to a single molecule called beta-amyloid, or A $\beta$ .

Many different types of research point to A $\beta$  as the culprit in AD. A $\beta$  is the most important constituent of the amyloid plaques that accumulate in the AD brain; the molecule is highly toxic to brain cells. Perhaps most convincing is that every known genetic cause of AD has been directly linked to this molecule. There is still substantial debate about the precise mechanisms by which A $\beta$  damages brain cells, but a majority of scientists now agree that the most exciting strategies to control the disease process aim directly at reducing the accumulation of A $\beta$  in the brain.

A number of different approaches to attacking the A $\beta$  molecule show promise. Some candidate drugs reduce the activity of the enzymes (called secretases) that release A $\beta$  from its larger parent molecule. Other new drugs bind to A $\beta$  leading to its clearance from brain. Examples of both strategies are now being tested at Georgetown and elsewhere. Flurizan is a secretase inhibitor developed by Myriad Pharmaceuticals, and Alzhemed is an amyloid binding drug developed by Neurochem Inc.; both are being tested in large Phase III clinical trials.

Story continues on pg.2

*The Director's Column continued...**The Search for Treatments to Slow Alzheimer's Progression: Targeting Amyloid*

Two new studies now recruiting subjects at Georgetown use antibodies to attack A $\beta$ . Antibodies are proteins generated by immune cells to fight invading organisms such as viruses and bacteria. Vaccines work by stimulating the production of antibodies by an individual's own immune cells. But antibodies can also be created in the laboratory and infused intravenously into patients; this process is called passive immunization. Two studies, one sponsored by Elan Pharmaceuticals and the other by Ely Lilly and Company, are testing infusions of different antibodies directed against A $\beta$  as treatments for AD.

Each of these anti-amyloid strategies has been effective in reducing the accumulation of A $\beta$  in brain in animal studies. If they show similar activity in humans with AD, we expect them to slow disease progression. The process of testing new drugs is unfortunately a slow one, taking years. But with the causative molecule identified, and many promising therapies now in clinical trials, important advances in the treatment of AD can be expected. (For a more detailed scientific review of the anti-amyloid drug development process, please read my recent article "the Development of Anti-Amyloid Therapy for Alzheimer's Disease: From Secretase Modulators to Polymerization Inhibitors" published in the journal *CNS Drugs*. It can be downloaded from our web site: (memory.georgetown.edu) *Written by Paul S. Aisen, MD*

**ADNI Update:**

We are currently enrolling individuals with AD, individuals with MCI and those without memory complaints to participate in the Alzheimer's Disease Neuroimaging Initiative. This study aims to recruit 800 people at research centers across the country, and involves MRI scans every six months, optional LPs (lumbar punctures) and PET scans if individuals are willing, and 6-8 clinic visits that include physical and cognitive exams. ADNI is funded by NIH and industry sponsors and compensation (\$100/clinic visit and \$200/LP) is provided. The goal of ADNI is to be able to detect brain and biological changes that occur before memory decline and other symptoms appear, which would allow researchers to evaluate the effectiveness of drugs at the earliest possible time. Keep an eye out for ADNI's national media campaign that features Maya Angelou, who has donated her time to encourage participation in this research study.

For more information about this study please contact Kelly Behan 202-687-0413

**Defining "Dementia"**

Words used to define disorders characterized by memory loss and thinking changes can be intimidating and are frequently misunderstood by patients and families, and even health care providers. This is not surprising as our understanding of these types of illnesses is evolving and has expanded considerably in recent years. Perhaps the two most commonly misunderstood words encountered by patients and family members receiving care through the Memory Disorders Program are the words that we use most often, **dementia** and **Alzheimer's**. Taking a moment to clarify these terms will help to reduce confusion and may alleviate fears grounded in the unknown.

Dementia is a diagnostic term used to describe disorders characterized by a gradual decline in thinking abilities (most commonly memory loss) and causing diminished function. Diminished function is reflected by a decreased ability to manage affairs or care for oneself. The word gradual is emphasized because dementia does not usually occur suddenly and this makes early detection of symp-

toms difficult. This has also contributed to the false belief that major cognitive impairment is a part of normal aging, as growing old is also a gradual process. Reassuringly, dementia is not a part of normal aging. It does, however, occur increasingly with age and is rarely encountered in individuals under the age of 50. Approximately 6-8% of individuals over the age of 65 suffer a dementing illness.

Alzheimer's disease is the most common form of dementia comprising the majority of cases. Vascular dementia, caused by cerebrovascular disease (stroke) is the second most common form of dementia. The prevalence of vascular dementia is approximately 1/5 that of Alzheimer's disease. Mixed dementia occurs when both conditions are present and is also fairly common. There are many other types of dementia that are far less common and together comprise less than 25% of dementias.

Alzheimer's disease is the primary focus of treatment and research conducted by the Memory Disorders Program. The disease derives its name from a German physician

named Alois Alzheimer who identified the pathologic hallmarks of this most common form of dementia in the early 1900s. In the past, Alzheimer's disease was often referred to as "senile dementia," a misnomer reflecting confusion about the relationship between Alzheimer's and aging. In fact, it is a specific disease with a specific cause: we now understand that malformation of proteins in the brain, referred to as tangles and plaques, are the abnormalities that cause the manifestations of Alzheimer's disease. Short term memory loss is the most common early symptom of these pathologic changes. As in all forms of dementia, symptom progression in Alzheimer's disease is gradual and leads to functional decline. The staff at the Memory Disorders Program is always happy to answer your questions. If we use terminology that does not make sense please do not hesitate to ask us to explain. Effective communication is important as we work together to optimize treatment.

*Written by Brigid Reynolds, RN, MSN, NP*

## Research Opportunities at Georgetown's Memory Disorders Program

### Currently Enrolling Studies:

Study Name	Required Diagnosis	Key Inclusion/Exclusion	Study Duration/ Number of Visits	Who to contact
<b>Flurizan</b> (drug study)	Mild Alzheimer's Disease	Patient must be able to have an MRI or CT Scan	7 visits over 12 months	Dana at 202/687-3355
<b>Elan</b> (antibody study)	Mild to Moderate Alzheimer's Disease	Patient must be able to have an MRI	25 visits over 27 months	Carolyn at 202/784-6671
<b>Huperzine</b> (drug study)	Mild to Moderate Alzheimer's Disease	Patient cannot currently be taking Aricept, Exelon, or Reminyl/Razadyne	9 visits over 24 weeks	Kelly at 202/687-0413
<b>Valproate</b> (drug study)	Moderate Alzheimer's Disease	Patient cannot be experiencing any agitation or psychosis	12 visits over 26 months	Dana at 202/687-3355
<b>Nicotine</b> (drug study)	Mild Cognitive Impairment	Patient needs to be a non-smoker	11 visits over 12 months	Kelly 202/687-0413
<b>ADNI</b> (imaging study)	Normal Elderly/MCI/Mild to Moderate Alzheimer's Disease	Patient must be able to have an MRI	8 visits over 18 months	Kelly 202/687-0413
<b>Lilly</b> (antibody study)	Mild to Moderate Alzheimer's Disease/Normal Controls	Patient must attend visits once a week for 12 weeks.	12 visits over 12 weeks	Dana at 202/687-3355
<b>Caregiver Communications Study</b>	Mild Alzheimer's Disease /Normal Controls	Patient must live with someone who can also participate.	2 visits over 12 months	Kris at 202/687-9078

### *Many Things You Always Wanted to Know About Research But Were Afraid to Ask Continued...*

Staff members discuss the consent form in great detail with potential subject participants and their legally authorized representatives before consent forms are signed. Our goal is to see that all questions are answered. If a staff member is unable to provide subjects and their legally authorized representatives with the information they need, other staff, including the Principal Investigator, may be called in to respond to the questions.

Before testing of medications takes place in human subjects, be they healthy individuals or persons with specific health conditions, many steps must take place in order for the United States Food and Drug Administration (US FDA) to provide its approval for such an effort. Laboratory testing and animal testing must occur and the sponsor of the study must report these results to the FDA for consideration. The next article in this series will address the approval process for conducting a research study and reasons to participate in research. *Written by Carolyn Ward, MSPH*

### Caregiver Communication Study

We are currently recruiting healthy volunteer subject pairs to participate in the Caregiver Communication Study. The aim of this study is to develop a new way to observe communication behaviors used by persons with Alzheimer's disease in the home environment. The Communicative Coping Behavior Checklist (CCBC) is an observation checklist to be completed by the caregiver or knowledgeable informant. With this research we hope to improve the communicative relationship between the caregiver and the care receiver. The study requires two visits for both the patient and the caregiver. Each visit will last 2 to 2 1/2 hours. For more information please contact Kris at 202-687-9078 or Pamela Saunders, PhD at 202-784-4771.

## Have You Been Seen by a Nurse Practitioner?

The Nurse Practitioner (NP) role evolved in the 1960s as registered nurses advanced their training to meet the demand for primary care in rural areas where family practice physicians were scarce. Currently, there are approximately 116,000 NPs in the U.S. providing high-quality, cost-effective and individualized care throughout a patient's lifespan. NPs practice in a variety of settings that include geriatrics, pediatrics, family/primary care and women's health.

Nurse practitioners typically complete two additional years of graduate level training and a clinical practicum under a physician or an experienced nurse practitioner, usually leading to a Master's degree in Science. NPs are governed by their state's Board of Nursing and each state's scope of practice is different. In the District of Columbia, NPs can independently, or in collaboration with a physician, diagnose, treat and prescribe medications for patients who are within their scope of practice. Other titles used to describe the NP profession are: APRN (advanced practice registered nurse), CNP (certified nurse practitioner), CRNP (certified registered nurse practitioner).

A landmark study in the Journal of the American Medical Association (JAMA, Jan. 2000) showed that patients in an ambulatory care setting who received care from both physicians and nurse practitioners reported the same level of satisfaction with both physicians and NPs, and had the same health outcomes. In our Memory Disorders Program, nurse practitioners evaluate new and returning patients and are actively involved with patients and caregivers who decide to participate in research studies. The next time you're in, ask to see the nurse practitioner! *Written By Patrycja Zielinska, RN, MSN, NP*

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**Please visit our website at <http://memory.georgetown.edu>**

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