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**NEW CRITERIA AND GUIDELINES FOR THE DIAGNOSIS OF  
ALZHEIMER'S DISEASE PUBLISHED FOR FIRST TIME IN 27 YEARS**

*- Research Agenda Suggested for Detecting Pre-Symptomatic Alzheimer's -  
- New Alzheimer's Definition Moves Researchers Closer to Early Detection and Intervention -*

**(Cedar Rapids, IA)** – For the first time in 27 years, new criteria and guidelines for the diagnosis of Alzheimer's disease have been published by three expert workgroups spearheaded by the Alzheimer's Association and the National Institute on Aging (NIA) of the National Institutes of Health (NIH).

Currently, 69,000 Iowans are living with Alzheimer's disease. "The new diagnostic criteria are exciting developments in the scientific process," said Joel Schmidt, Alzheimer's Association East Central Iowa Board President. "This moves us another step closer to our goal of eventually detecting and treating Alzheimer's disease before people experience the devastating symptoms of loss of memory and thinking abilities."

The workgroups published four articles including ready-to-use clinical diagnostic criteria for Alzheimer's disease dementia and mild cognitive impairment (MCI) due to Alzheimer's. A research agenda was proposed for preclinical Alzheimer's. The use of biomarkers in Alzheimer's dementia and MCI due to Alzheimer's was also proposed as a research agenda only, and is not intended for application in clinical settings at this time.

The articles – collectively, the National Institute on Aging/Alzheimer's Association Diagnostic Guidelines for Alzheimer's Disease – expand the definition of Alzheimer's to include presymptomatic and mildly symptomatic but pre-dementia stages of the disease. This reflects current thinking that Alzheimer's begins creating distinct and measurable changes in the brains of affected people years, perhaps decades, before memory and thinking symptoms are noticeable.

"It is our hope that incorporating scientific knowledge gained and technological advances made over the past quarter century will improve current diagnosis, bring the field closer to earlier detection and treatment, and ultimately lead to effective disease-modifying therapies," said William Thies, Ph.D., Chief Medical and Scientific Officer at the Alzheimer's Association. "Development and publication of these articles is a major landmark in the field. That said, publication of these articles is not yet the end of the process of developing new diagnostic criteria for Alzheimer's, but is another major step in the process."

The proposed new Alzheimer's disease diagnostic guidelines were published online today by *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*. Hard copy publication is scheduled for the May 2011 issue of the journal.

### **Three Stages of Alzheimer's Disease**

The current diagnostic criteria for Alzheimer's\*, for the most part, focus on reliable diagnosis when signs of problems in thinking, learning, and memory are noticeable to an individual, family, and friends. But research tells us that Alzheimer's likely begins years, maybe even decades, prior to symptoms appearing.

The new articles refer to three phases of Alzheimer's disease progression over time:

- Preclinical Alzheimer's Disease – Measurable changes in biomarkers (such as brain imaging and spinal fluid chemistry) that indicate the very earliest signs of disease, before outward symptoms are visible. Currently, there are no clinical diagnostic criteria for this phase, but the group provides a scientific framework to help researchers better define this stage of Alzheimer's.
- Mild cognitive impairment (MCI) due to Alzheimer's Disease – Mild changes in memory and thinking abilities, enough to be noticed and measured, but not impairment that compromises everyday activities and functioning.
- Dementia due to Alzheimer's Disease – Memory, thinking and behavioral symptoms that impair a person's ability to function in daily life.

According to the authors, in order to facilitate the possibility of future presymptomatic treatment of Alzheimer's, it was important to define the disease from the earliest changes in the brain, not only the observable, symptomatic stages of the disease. The authors propose that Alzheimer's begins with a long asymptomatic period during which detrimental changes are progressing in the brain, and individuals with biomarker evidence of these changes are at increased risk for developing cognitive and behavioral impairment and progression to Alzheimer's dementia.

A biomarker is a naturally occurring, measurable substance or condition in the body that reliably indicates the presence or absence of disease or the risk of later developing a disease; for example, blood glucose levels are a biomarker of diabetes, and cholesterol levels are a biomarker of cardiovascular disease risk. Both fluid and imaging measures are being tested as possible biomarkers for Alzheimer's.

There was a broad consensus within the workgroups that much additional research needs to be done to validate the application of biomarkers as they are proposed in the newly-published articles. According to the authors, "The definitive studies ... are likely to take more than a decade to fully accomplish. Thus, we must move quickly ... and adjust our models and study designs as new data become available."

"If we can definitively determine the risk of developing Alzheimer's dementia in people who have biomarker evidence of brain changes but are not showing outward symptoms, we will open

an important window of opportunity to intervene with disease-modifying therapies, once they are developed,” said Thies.

“In addition, the new criteria give us powerful tools to accelerate our knowledge in the fight against Alzheimer’s disease. They give us guidelines for getting a more accurate assessment of Alzheimer’s prevalence. In that way we can better assess the need for everything from research dollars to care services, to patient and caregiver education materials, to nursing home beds, to the number of gerontologists and nurses that we need. And, they give us a basis for creating the next generation of Alzheimer’s treatments that will be effective in each stage of the disease,” Thies said.

### **Moving the Field Toward Earlier Diagnosis and Treatment of Alzheimer’s**

The Alzheimer’s Association, in its 2010 report titled “Changing the Trajectory of Alzheimer’s Disease: A National Imperative,” showed that a hypothetical intervention that delayed the onset of Alzheimer’s dementia by five years would result in a nearly 45 percent reduction in the number of people with Alzheimer’s by 2050, and reduce the projected Medicare costs of Alzheimer’s from \$627 billion to \$344 billion dollars.

The authors of the newly-released articles write, “It is our hope that the advances in preclinical detection of Alzheimer’s will enable earlier, more effective treatment, just as nearly all of therapeutic gains in cancer, cardiovascular disease, osteoporosis, and diabetes involve treatment before significant clinical symptoms are present. Screening and treatment programs instituted for other diseases ... have already been associated with a decrease in mortality due to these conditions.”

Thies adds, “Currently, Alzheimer’s therapies are in development that may be able to slow or stop the progression of the disease. By improving early detection and risk evaluation, we will better be able to test potential therapies and eventually prescribe them for people at increased risk. Ultimately, this approach envisions for Alzheimer’s what is now common practice in cardiovascular disease, where early signs of risk – for example, in genetic markers or in blood cholesterol and/or blood pressure levels – can be treated to reduce the likelihood of heart attack or stroke later on.”

The challenge for Alzheimer’s now is that there is currently no single, generally accepted way to identify the disease in the earliest stage – before symptoms are evident. It is hoped that the research agenda outlined in the new preclinical Alzheimer’s article will correct this deficit.

### **Presymptomatic Disease Detection and Treatment – Not a New Idea, Except in Alzheimer’s**

According to the authors, “The concept of a preclinical phase of disease should not be too foreign. Medical professionals readily acknowledge that cancer can be detected at the stage of ‘carcinoma in situ’ and that hypercholesterolemia and atherosclerosis can result in narrowing of coronary arteries that is detectable prior to myocardial infarction. It is widely acknowledged that symptoms are not necessary to diagnose human disease. Type II diabetes, hypertension, renal

insufficiency, and osteoporosis are frequently detected through laboratory tests, and effective treatment can prevent the emergence of symptoms.”

“We should be open to the idea that Alzheimer’s could one day be diagnosed preclinically by the presence of biomarker evidence, which may eventually guide therapy prior to the onset of symptoms. We treat people with diabetes, elevated cholesterol, hypertension and a variety of other illnesses – we do not wait for strokes, heart attacks or other long term complications that we know will occur in significant numbers of those affected. Similarly, our intention is to use these criteria to better determine an individual’s risk of developing Alzheimer’s disease. This diagnostic research will help us discover the drugs of the future and prepare for the day when we can administer them to those at risk in order to prevent or delay the emergence of symptoms,” wrote the authors.

### **What Was Published**

The proposed new diagnostic criteria and research agenda for Alzheimer’s disease are presented in three documents, plus an introduction.

- One workgroup updated the 1984 diagnostic criteria for the dementia due to Alzheimer’s disease. Guy McKhann, M.D., Johns Hopkins University School of Medicine, Baltimore, and David Knopman, M.D., Mayo Clinic, Rochester, Minn., co-chaired this panel.
- A second workgroup focused on refining the criteria for the symptomatic, pre-dementia phase, referred to as Mild Cognitive Impairment due to Alzheimer’s disease. Marilyn Albert, Ph.D., Johns Hopkins University School of Medicine, Baltimore, chaired this workgroup.
- The third workgroup proposed a research agenda (NOT criteria for clinical diagnosis; this is an important distinction. See supplement 4.) for the asymptomatic, preclinical phase of Alzheimer’s. Reisa Sperling, M.D, Brigham and Women’s Hospital, Harvard Medical School, Boston, chaired this group.
- The introduction provides an overview of the changes that have occurred in the Alzheimer’s field since the first diagnostic criteria were published in 1984, and outlines future challenges that need to be addressed. Clifford Jack, M.D., Mayo Clinic, Rochester, Minn., is lead author of this article.

Preliminary recommendations were announced in July 2010 at the Alzheimer’s Association International Conference on Alzheimer’s Disease (AAICAD). These early drafts were then made available for comment on the Alzheimer’s Association website, along with further presentation and discussion at a variety of medical and scientific meetings.

The three sets of recommendations differ in terms of relevance to current clinical practice.

- The clinical diagnostic criteria for Alzheimer’s dementia and MCI due to Alzheimer’s are intended to guide diagnosis in the current clinical setting, such as a doctor’s office, including settings where no access to testing for biomarkers exists.
- The use of biomarkers in both Alzheimer’s dementia and MCI due to Alzheimer’s disease is intended only for research at this time. However, some biomarkers, especially those using advanced imaging techniques, could enter clinical practice in the near future, though much remains to be learned about their utility in this setting.

- The recommendations of the preclinical Alzheimer's workgroup are intended for research purposes only, and do not have any clinical utility at this time.

A fourth workgroup has been organized to examine the postmortem, pathological criteria for Alzheimer's. The results of their deliberations are expected to appear later in 2011.

### **Alzheimer's Association**

The Alzheimer's Association is the world's leading voluntary health organization in Alzheimer's care, support and research. Our mission is to eliminate Alzheimer's disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health. For more information, please visit [alz.org](http://alz.org), or call 800-272-3900.

### **National Institute on Aging (NIA)**

NIA, part of the National Institutes of Health, a component of the U.S. Department of Health and Human Services, leads the federal government effort conducting and supporting research on aging and the health and well being of older people. For information on age-related cognitive change and neurodegenerative disease, go to the NIA's Alzheimer's Disease Education and Referral (ADEAR) Center at [www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers). For more on health and on aging generally, go to [www.nih.nia.gov](http://www.nih.nia.gov). Media contact is Peggy Vaughn, Office of Communications and Public Liaison, at 301-496-1752 or [nianews3@mail.nih.gov](mailto:nianews3@mail.nih.gov).

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\* McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;34,939-44.