Reinsurance Group of America, Incorporated®

Volume 13, May 2004

Re·FLECTIONS

RGA's Medical Underwriting Newsletter

LETTER FROM THE EDITOR

This edition of *Re-flections* is dedicated solely to the topic of Alzheimer's disease.

The increased focus on older-age underwriting in the life insurance industry makes the ability to recognize and appropriately underwrite age-related entities like Alzheimer's disease even more important than ever before. I hope that you will find this article informative and thought provoking.

J. Carl Holowaty, M.D.

cholowaty@rgare.com

ALZHEIMER'S DISEASE

Life insurers are familiar with the signs, symptoms, and diagnostic criteria of most of the common medical conditions encountered on a daily basis in the course of evaluating mortality risk. When underwriters evaluate the risk associated with coronary artery disease, for instance, there is usually no shortage of attending physician statements, often containing multiple diagnostic test results that help stratify mortality risk. The available information, including lab screenings such as lipid profiles, family history, blood pressure readings and build figures allow underwriters to confidently quantify the risk associated with this serious condition and to offer an insurance policy in many cases.

For many years insurers have required life insurance applicants to supply a medical history, blood and urine samples, as well as electrocardiograms or other diagnostic tests when the financial risk and client profile justify the expense. These tests are designed to clearly detect or screen for the more prevalent life-shortening conditions. It may now be time to consider, under certain circumstances, the need to expand screening tests to capture conditions that until now may have 'fallen through the cracks'. In doing so, insurers hope to more accurately stratify risk, thus providing more affordable life insurance for the general population and improving life insurers' claims experience.

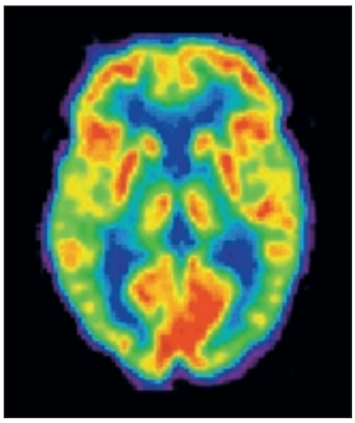
continued on page 2

In the U.S. insurers are issuing policies to increasingly older individuals. This reflects both the need of the elderly to preserve their often quite substantial estates, as well as the changing demographics of the insurance market. People are living longer (and often healthier) than ever before. Although the elderly are certainly still prone to diseases that insurers have already developed much expertise in evaluating, there remains a deficiency in the ability to screen for some of the diseases that are quite common in this group. I refer specifically to Alzheimer's Disease (AD).

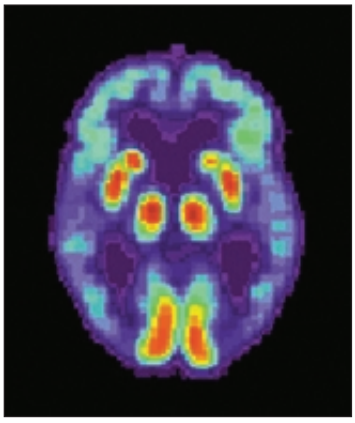
AD is a sub-category of dementia, which is a clinical syndrome characterized by multiple cognitive deficits sufficient to interfere with daily activities and quality of life. It is a condition associated with excess mortality. AD is still often not well-recognized in its early stages by primary clinicians and it needs to be distinguished from other, less serious causes of cognitive decline.

AD is the most common cause of dementia in people age 65 and older. Current estimates are that four million Americans suffer from some degree of Alzheimer's. It is estimated that by the year 2050, 14 million people will have AD. This assumes that medical science is not able to find a cure or adequate prevention by that time. The National Vital Statistics Report lists AD as the seventh-leading cause of death for all races and both sexes age 65 and over.[1] It is the fifth-leading cause of death in those 85 years and older. Underwriters currently screen in some fashion for all of the other non-infections and non-accidental top ten causes of death. The usefulness of a screen for AD would depend on the prevalence in the population being tested, accuracy of the screen, and the test's cost and physical impact on the applicant. Fortunately, public awareness of this condition has increased to the point where there is a great social and personal interest in such a screen.

The estimated annual incidence of probable AD in a Boston, Massachusetts population was 0.6 percent for persons age 65-69, 1.0 percent for persons age 70-74, 2.0 percent for persons age 75-79, 3.3 percent for persons age 80-84, and 8.4 percent for persons age 85 and older[2]. Although these incidence rates are only directly reflective of a specific general population, it is probably safe to assume that the incidence rate within the insurance population is not trivial, and that the rate can be expected to increase significantly in older age groups. This study can be used to form some rational basis for determining when it is best to start screening. The prevalence of AD is most concerning when underwriting the elderly. The Alzheimer's Disease and Related Disorders Association estimates that one in ten persons over age 65, and nearly half of those over age 85 have some degree of AD[3].

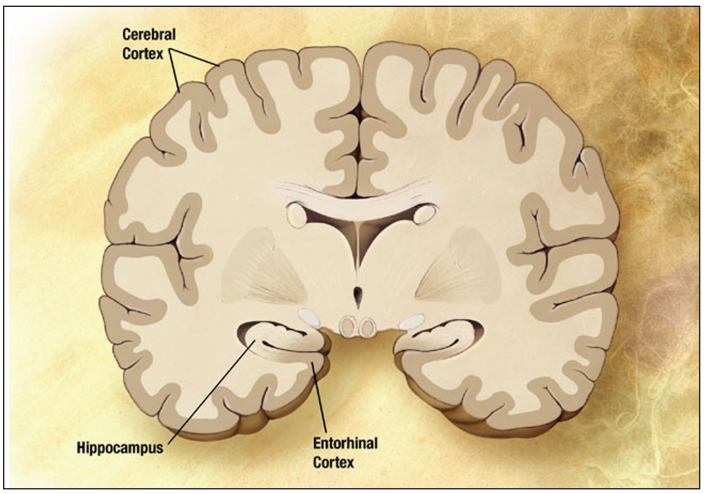


Pet Scan of Normal Brain
reference:
www.alzheimers.org/
unraveling/07.htm

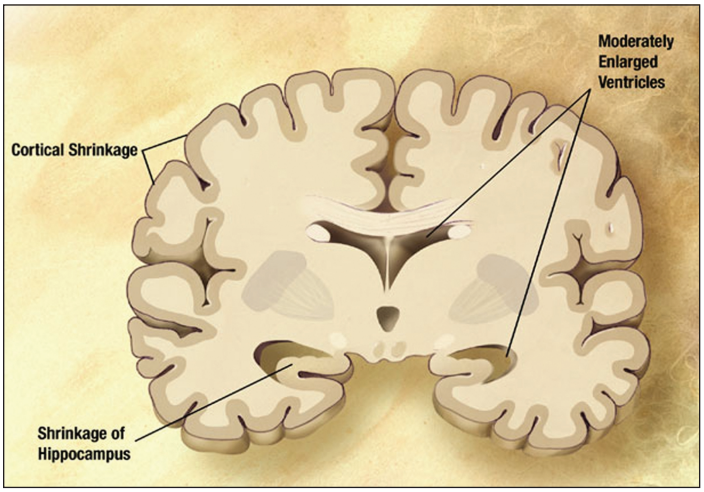


Pet Scan of Alzheimer Disease Brain
reference:
www.alzheimers.org/
unraveling/07.htm

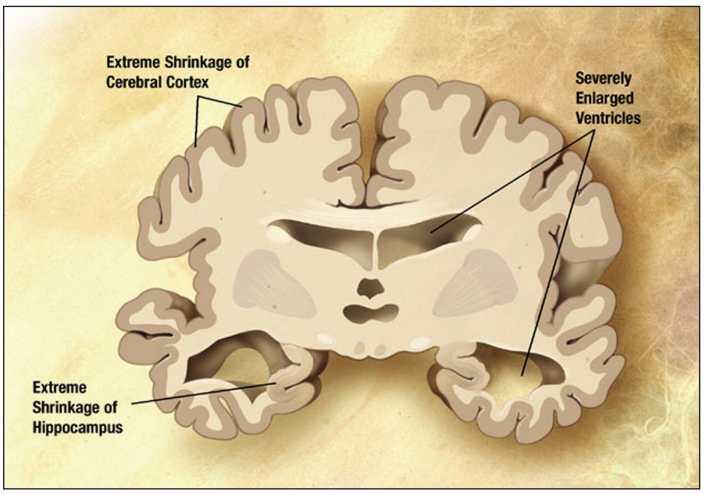
AD is a condition with serious survival implications. The median survival time following a diagnosis of AD depends largely on the patient's age at time of diagnosis. This ranges from 8.3 years of survival when diagnosed at age 65, to 3.4 years of survival when diagnosed at age 90. Diagnosis of AD at age 65 or 90 was associated with a 67 percent and 39 percent reduction in median life span[4], with pneumonia, malignancy and heart disease



Preclinical AD



Mild AD



Severe AD

reference: www.alzheimers.org/unraveling/07.htm

being the leading causes of death. These figures make the underwriting of AD difficult to justify. However, as with most diseases, it may be possible to stratify the risk and select the better risks. Some studies have suggested that–at least in a Swedish population aged 85–the survival time in individuals with mild AD was no different from that in individuals without dementia.[5]

One of the most problematic issues with AD is that it may not be well-differentiated clinically from 'normal' cognitive deterioration, at least in its early stages. It is all too common to see a brief entry in an attending physician's statement questioning the possible diagnosis of AD. It is difficult for an underwriter to ignore such a tentative diagnosis and its dire mortality implications. On the other hand, it is equally hard to just assume that the memory or other cognitive deficits are 'normal' aging signs. As usual, a good working knowledge of AD may help discriminate between the two entities.

When evaluating cognitive function, it is important to remember that changes in memory function are seen in the normal aging process and do not seriously interfere with daily activities. In some cases they may be related to co-existing medical conditions and treatment. Normal age-related cognitive deterioration involves a decrease in the speed of encoding and retrieving information. Although cognitive processing time is delayed, in most cases the accuracy of the memory-dependent response is not significantly affected. While there may be a gradual continuum between normal aging of the brain and AD, this is not certain. The distinction between normal aging and very early AD is critical since the conversion rate to probable AD in the first group is only 1-2 percent annually, and in the second group is ten-to-fifteen percent annually.[6]

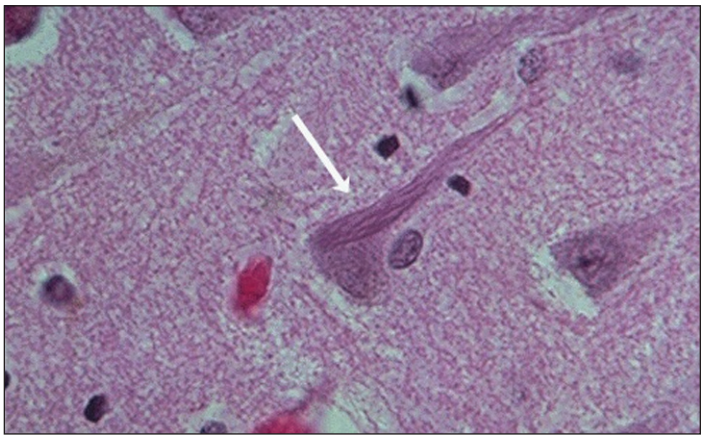
The terms 'benign senescent forgetfulness' and 'age-associated memory impairment' (AAMI)

describe mild memory problems that are worse-than-expected for normal aging, but do not yet meet AD diagnostic criteria. Some researchers feel that there is an increased risk of development of overt AD in these groups. Another at-risk group are those described as having a 'mild cognitive impairment' (MCI). MCI is also sometimes known as 'age-associated cognitive decline', 'isolated memory impairment', 'incipient dementia', 'dementia prodrome' or 'questionable dementia'. MCI is a transitional state between the cognitive changes of normal aging and dementia where there is history of memory impairment (corroborated by an informant), but otherwise normal cognitive function and intact activities of daily living. The overall prevalence in the general population age 60-76 is about five percent. The progression to AD is estimated to be about 6-25 percent per year.[7]

A diagnosis of possible AD is made when a person has a dementia syndrome in absence of other neurological, psychiatric or systemic disorders that could cause dementia. Probable AD is diagnosed when dementia is established by clinical examination and confirmed by neuropsychological testing, with deficits in two or more areas of cognition. There is usually a history of progressive worsening of memory and other cognitive functions but no significant disturbance of consciousness. Once again, there should be an absence of other known or suspected causes of dementia. Definitive AD is diagnosed when there are clinical criteria for probable AD as well as histopathologic evidence from biopsy or autopsy.

The clinical diagnosis of AD is reached when[8]:

1. There is memory impairment *and* one or more of the following cognitive disturbances:
    a. Aphasia (impaired communication in speech, writing or signs)
    b. Apraxia (impaired ability to carry out motor activities in spite of intact motor function)
    c. Agnosia (failure to recognize or identify objects despite intact sensory function)
    d. Disturbance in executive functioning such as planning, organizing, sequencing and abstracting
2. The cognitive deficits are severe enough to cause social or occupational impairment and a significant decline from previous levels of functioning.
3. The cognitive deficits are not due to other known causes of dementia, including drug or medication use.
4. The dementia is not accounted for due to psychiatric disorders such as depression or schizophrenia.



Alzheimer's disease neurofibrillary tangle. The neurons demonstrate intracytoplasmic proliferation of twisted filaments producing the visible "neurofibrillary tangle" under the microscope.
reference: www-medlib.med.utah.edu/WePath/TUTORIAL/CNS/CNSDG006.html

While the DSM-IV criteria described above provide the criteria for probable AD, they really don't provide primary care diagnosticians enough help in deciding when a person has progressed beyond the types of cognitive changes typically seen with normal aging. Lay organizations such as the Alzheimer's Association have outlined useful warning signs of AD that are much easier to understand in everyday terms. These tips may also be useful in interpreting an Attending Physician's statement, since they relate directly to the types of comments described by average people. This checklist may be useful to underwriters as well[9]:

Memory loss. It is normal to occasionally forget appointments, names or telephone numbers, but most people will eventually recall this information—it is not irretrievably lost. People with AD typically will not be able to recall recently learned information. They usually will not remember this information, even with cuing.

Disorientation to time and place. Everyone occasionally forgets the day of the week or gets temporarily confused when distracted or tired, but people with AD can get lost on their own street or in their home, forget where they are and how they got there.

Poor or decreased judgment. People with AD exhibit poor judgment well outside the norm. They may give away large sums of money without thinking of the consequences, or dress very inappropriately for the occasion.

Problems with abstract thinking. People with AD may have difficulty with concepts such as what numbers are for and their relationship to each other.

Misplacing things. People with AD typically put items in unusual places such as their house keys in the refrigerator, compounding their inability to recall what they did with the item.

Changes in mood or behavior. People with AD often show rapid and unexplained mood swings.

Changes in personality. There is usually some change in personality with aging, but people with AD often become confused, suspicious, fearful or dependent. These changes may be partially explained by some of their other cognitive changes.

Loss of initiative. People with AD often sit passively for hours in front of the television, sleep more than usual and lose interest in former activities such as hobbies or social activities. Depression may also lead to this problem as well.

AD is a diagnosis of exclusion. Even when clinical history and cognitive changes suggest a diagnosis of AD, it is important to eliminate other potential causes of dementia. This would include a review of medications, to ensure that the changes in cognition cannot be attributed to medication side effects. It is also important to evaluate the individual for organic conditions such as hypothyroidism, B12 deficiency or systemic illness. Occasionally, consideration may be given to investigative tests such as the CT or MRI that can detect causes of dementia such as hydrocephalus, tumors, subdural hematoma or vascular dementia. Lastly, a psychiatric evaluation may be needed to determine if the symptoms of dementia may be due to common disorders such as depression.

One of the biggest challenges for clinicians as well as insurers is to be able to quickly, accurately, and cost effectively determine if a person has the early symptoms of AD. It is relatively simple with tests such as the Mini-Mental State Examination (MMSE) to determine if a person has a probable dementia. Unfortunately this simple and easily administered test has limited value in identifying the early stages of AD as well as MCI. This is an important group that insurers need to identify, since it is a fairly common condition and could have deleterious mortality implications if it has not been correctly underwritten or priced adequately within the affected population.

continued on page 6

Several clinical rating systems have been created to help stratify the severity of AD. The Global Deterioration Scale (GDS) was developed as a seven-stage system to qualify the severity of dementia[9].

Global Deterioration Scale

Stage	Example of Deficit
No cognitive decline	N/A
Very mild cognitive decline	Subjective complaints of memory loss only. No objective evidence of loss on interview.
Mild cognitive decline	Decreased performance during difficult social or occupational tasks. Objective evidence is slight.
Moderate cognitive decline	Moderate cognitive loss.
Moderately severe cognitive decline	Unable to recall major current memories. Needs assistance to survive. Dresses inappropriately.
Severe cognitive decline	Largely unaware of recent events. Emotional and personality changes. Unable to bathe or dress self.
Very severe cognitive decline	Loss of all effective communication abilities. Incontinent. Psychomotor loss.

Another common rating system for AD is the Functional Assessment Staging (FAST) scale. This is a more detailed system that helps stratify the clinical stages of AD[10].

FAST Stage	Characteristics
1. (normal adult)	No decline in functions.
2. (normal adult)	Personal awareness of functional decline.
3. (early AD)	Deficits noticed in demanding employment situations.
4. (mild AD)	Requires assistance in complicated tasks, such as handling finances, or planning a dinner party.
5 (moderate AD)	Requires assistance in choosing proper attire.
6 (moderately severe AD)	
6a	Requires assistance dressing.
6b	Requires assistance bathing.
6c	Requires assistance with mechanics of toileting.
6d	Urinary incontinence.
6e	Fecal incontinence.
7 (severe AD)	
7a	Speech ability limited to about a half-dozen words.
7b	Speech limited to one word.
7c	Ambulatory ability lost.
7d	Ability to sit up lost.
7e	Ability to smile lost.
7f	Ability to hold head up lost.

A Clinical Dementia Rating (CDR) scale has been developed by Washington University in St. Louis to evaluate the staging of AD[11]. Trained physicians, nurses or other health professionals can reliably administer it. A structured interview is conducted with both the subject in question as well as an informant. This test evaluates six functional cognitive areas:

1. Memory
2. Orientation
3. Judgment
4. Community Affairs
5. Home and Hobbies
6. Personal Care

Each of these domains is assigned a rating:

0 = Normal
0.5 = Questionable Impairment (more than just normal aging)
1 = Mild Impairment (mildly impaired relative to peers)
2 = Moderate Impairment
3 = Severe Impairment

Scores of 1 or higher show clear signs of a dementing illness. Those who score 0.5 may be experiencing the very early manifestations of AD.

Research is also being done using investigative modalities such as the positron emission tomograph (PET)[12, 13]. AD is characterized by regional impairment of cerebral glucose metabolism in neocortical association areas. Perhaps this test will eventually be useful in distinguishing normal cognitive changes from that of MCI or early AD. As yet, this expensive test remains unlikely to be of use as a screening tool for AD.

Treatment of AD remains unsatisfactory. Within the last ten years, the U.S. Food and Drug Administration (FDA) has approved several cholinesterase inhibitors for treatment of AD. These are: donepezil (Aricept), rivastigmine (Exelon), galantamine (Reminyl), and tacrine (Cognex). These drugs do not appear to significantly alter the progressive loss of cognitive function, but they may help stabilize some symptoms. The FDA approved memantine (Namenda) in early 2004 for the treatment of moderate-to-severe AD. Although it may provide some symptomatic relief, it does not help with the underlying pathologic process.

Alzheimer's Disease is a common condition in the elderly. It is important for underwriters to recognize its existence, since it has excess mortality and is difficult to treat. AD is currently difficult to detect in its early stages, partially due to the lack of physician training in using existing clinical tools. It would benefit the insurance industry to encourage and fund research that will help develop simple screening tests that may be used within the at-risk population both by attending physicians and non-medical examiners, thereby increasing our effectiveness in risk selection in the elderly. ■

INFORMATION
Find current and past issues of *Re-flections* at www.rgare.com/media/re_flections.asp

REFERENCES

1. United States. National Center for Health Statistics. National Vital Statistics Report, Vol. 50, No. 16, 16 September 2002.

2. “Statistics about Alzheimer’s Disease”. 1 February 2003. Online. Internet. 1 August 2003. Available http://www.alz.org/AboutAD/Statistics.htm.

3. United States. National Center for Health Statistics. National Vital Statistics Report, Vol. 50, No. 16, 16 September 2002.

4. Brookmeyer, R., Corrada MM, Curriero FC, Kawas C. “Survival following a diagnosis of Alzheimer disease”. *Arch Neurol*. 2002 Nov, 59(11):1764-7.

5. Aevarsson O, Svanborg A, Skoog I. “Seven-year survival rate after age 85 years: relation to Alzheimer disease and vascular dementia”. *Arch Neurol*. 1998 Spe; 55(9):1226-32.

6. Petersen RC. “Mild cognitive impairment: transition between aging and Alzheimer’s disease”. *Neurologia*. 2003 Mar;15(3):93-101.

7. Reisberg Barry, MD. “GDS: what, why and how?” Alzheimer Insights Online Vol 4, No 2. Online. Internet. http://www.alzheimer-insights.com/vol4no2/vol4no2d.htm.

8. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition.*

9. “Ten Warning Signs of Alzheimer’s Disease”. Online. Internet. 31 July 2003. Available http://www.alz.org/AboutAD/10Signs.htm.

10. “The Stages of Alzheimer’s Disease”. Alzheimer’s Association. Online. Internet. 31 July 2003. Available www.alz.org/ResourceCenter/FactSheets/Fsstages.pdf.

11. “Clinical Dementia Rating Scale & NEW On-Line Training Protocol”. Washington University Alzheimer Disease Research Center. Online. Internet. 19 August 2003. Available http://www.adrc.wustl.edu/adrc/cdrScale.html.

12. Herholz K. “PET studies in dementia”. *Ann Nucl Med*. 2003 Apr;17(2):79-89.

13. Silverman DH, Small GW, Change CY, et al. “Positron emission tomography in evaluation of dementia: Regional brain metabolism and long-term outcome”. *JAMA*. 2001 Nov 7;286(17):2120-7.