CURRENT STANDARDS FOR ASSESSMENT AND DIAGNOSIS OF ALZHEIMER’S DISEASE: A NURSE’S PERSPECTIVE

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Dementia is defined as a general loss of intellectual abilities involving impairment of memory, judgment, and abstract thinking in addition to changes in personality. It does not include delirium (loss of intellectual functioning because of clouded consciousness) or loss of intellectual abilities caused by depression or another psychiatric disorder. Dementia is defined as “an organic mental syndrome” in which potential causes are numerous. Clinically, dementia is defined as the decline of memory and other cognitive functions in comparison to the patient’s previous level of function. Dementias have many different causes, some of which are reversible (e.g., adverse medication effects, infections, stroke, and vascular malformation). The dementias share some common characteristics and the challenge is to determine what type and its cause.

Alzheimer’s disease (AD) is characterized by progressive memory loss and cognitive decline. Over the past several years, leading medical organizations have published practice guidelines on the diagnosis and management of AD, based primarily on sets of criteria developed by the American Psychiatric Association (in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, [DSM-IV-TR]) and the National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA). AD is primarily a diagnosis of exclusion because AD cannot be definitively diagnosed until autopsy, when the characteristic pathology (plaques and neurofibrillary tangles) can be observed. Although AD may be confused with vascular dementia, clinical diagnosis of AD is now 85% to 90% accurate with these diagnostic criteria. The nurse plays a leading
role in the early identification and assessment of AD or other types of dementia and the apparent precursor of AD, mild cognitive impairment (MCI).

**Clinical Assessment**

The American Academy of Neurology (AAN), in their practice guidelines, indicates that the DSM-III-R or the NINCDS-ADRDA criteria are reliable and should be used to diagnose AD (the DSM has now been updated to the fourth edition, text revision). The DSM-IV-TR and NINCDS-ADRDA criteria are summarized and outlined in Tables 1 and 2.2,3,6 The DSM-IV-TR criteria are broader than the NINCDS-ADRDA and are more often used in a research setting. The NINCDS-ADRDA criteria are “user friendly” and are more specific; they include classification of definite, probable, or possible AD. It is important to note that these criteria

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**Table 1. Summary of DSM-IV Criteria for Diagnosis of Alzheimer’s Disease**

- Gradual onset and continuing decline of cognitive function from a previously higher level, resulting in impairment of social and occupational function
- Memory impairment (decreased ability to learn new information or recall previously learned information) and at least one of the following:
  - Aphasia (language disturbance)
  - Apraxia (inability to carry out motor activities, despite intact motor function)
  - Agnosia (failure to recognize or identify objects, despite intact sensory function)
  - Disturbances of executive function, including abstract reasoning, concentration, planning, organizing, and sequencing
- Cognitive deficits are not because of other psychiatric, neurologic, or systemic diseases
- Cognitive deficits do not exclusively occur in the setting of delirium

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

Data from American Psychiatric Association.3

**Table 2. NINCDS-ADRDA Criteria for the Clinical Diagnosis of Alzheimer’s Disease**

<table>
<thead>
<tr>
<th>Criteria for Diagnosis</th>
<th>Possible (Atypical onset, presentation, or clinical course of dementia in the absence of other neurologic, psychiatric, or systemic causes)</th>
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<tbody>
<tr>
<td></td>
<td>Presence of second systemic or brain disorder sufficient to produce dementia, but not considered to be the cause of the dementia</td>
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<td></td>
<td>Single, gradually progressive, severe cognitive deficit identified in the absence of other identifiable cause</td>
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<td>Probable</td>
<td>Dementia established by clinical examination, documented by mental status testing, and confirmed by neuropsychological tests</td>
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<td></td>
<td>Deficits in 2 or more areas of cognition</td>
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<td></td>
<td>Progressive worsening of memory or other cognitive functions</td>
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<td></td>
<td>No disturbance of consciousness</td>
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<tr>
<td></td>
<td>Onset between ages 40 and 90 years</td>
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<td></td>
<td>Absence of systemic or other brain disease that could account for dementia</td>
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<tr>
<td>Definite</td>
<td>Clinical criteria for probable AD</td>
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<td></td>
<td>Histopathologic evidence obtained from a biopsy or autopsy</td>
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</tbody>
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Of note, a diagnosis of probable AD is supported by the following:
- Progressive deterioration of specific cognitive functions, such as language, motor skills, and perception
- Impaired activities of daily living and altered patterns of behavior
- Family history of similar disorders, particularly if confirmed neuropathologically
- Laboratory results of normal lumbar puncture as evaluated by standard techniques, normal pattern or nonspecific changes in electroencephalogram, and evidence of progressive cerebral atrophy on computed tomography by serial observation

Other features consistent with probable AD include:
- Plateaus in the course of illness progression
- Associated symptoms of depression, insomnia, incontinence, delusions, illusions, hallucinations, catastrophic verbal, emotional, or physical outbursts, sexual disorders, and weight loss
- Other neurologic abnormalities, especially with more advanced disease and including motor signs, such as increased muscle tone, myoclonus, or gait disorder
- Seizures in advanced disease (rarely seen)
- Computed tomography normal for age

Symptoms that make a diagnosis of probable AD unlikely include:
- Sudden onset
- Focal neurologic findings
- Seizures or gait disturbances early in the course of the illness

AD = Alzheimer’s disease; NINCDS-ADRDA = National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer’s Disease and Related Disorders Association.

Data from McKhann et al.2
reserve a diagnosis of definite AD only for histopathologic proof of AD pathology at autopsy.2

Possible AD is characterized primarily by progressive cognitive decline when no other cause can explain it. Probable AD is defined as progressive worsening of memory and decline in areas of cognitive functioning, with dementia established by mental status testing with neuropsychological tests. AD has certain clinical hallmarks including progressive decline (as opposed to stepwise decline), gradual onset, absence of neurologic deficits that suggest only one area of the brain is involved, and impairment of activities of daily living (ADLs).2 However, no single symptom is unique to AD.5,7 Although patients are often referred for neuropsychological testing, the primary care nurse is frequently the healthcare professional who administers assessments of mental status, behavior, and ADLs. Several tests are frequently used, including the Mini-Mental State Examination (MMSE), the Clock Drawing Test, and the AD Assessment Scale–Cognitive Decline, in addition to assessment of ADLs and behavior tools. Each test evaluates different areas of cognition, including recall, language, spatial orientation, and learning.2 These tools are described in detail elsewhere in this monograph.

Alzheimer’s disease can also be characterized as mild, moderate, or severe based on MMSE scores, as outlined in Table 3.1 Primary care nurses may interact with patients with AD at all 3 stages of severity, although those patients with severe AD generally need specialized healthcare facilities. Often, it is the primary care nurse who will recognize mild AD, with the patient (or the family member) reporting symptoms of short-term memory loss, confusion in historically familiar routines and environments, or personality changes, such as apathy or depression. However, many patients may use humor or deflection to hide their symptoms.

Laboratory testing also plays an important role in AD diagnosis, often to rule out other possible causes of dementia. The AAN recommends magnetic resonance imaging (MRI) or computed tomography (CT) scanning in the initial evaluation of a patient with dementia. MRI is used to detect and analyze changes in brain size and volume. An MRI scan may reveal evidence of stroke, a brain tumor, or a buildup of fluid, all of which can also cause dementia. CT scans can identify areas of poor blood flow, tumors, strokes, or other brain defects. MRI and CT scanning are standard procedures for the evaluation of patients with AD, but positron emission tomography (PET) and single positron emission computed tomography (SPECT) are also being studied. PET and SPECT detect changes in brain function (ie, blood flow and/or metabolism), not just brain structure, by injecting a radiolabelled tracer into the patient. Areas with abnormal functioning show reduced use of sugar. Of note, Medicare may cover a PET scan after a thorough evaluation has determined cognitive decline in a person but has not clearly pinpointed a specific disease or other cause for symptoms.9 However, as of yet, PET and SPECT are not recommended by the AAN in the routine evaluation of patients with possible or probable AD.6

The National Institute of Aging has launched a neuroimaging and biomarker initiative using serial MRI and PET scans to examine changes in brain structure and function with AD progression. The changes will be recorded along with clinical, neuropsychological, and biological marker information to determine when and where brain degeneration occurs with disease progression.10 It is currently known that the brain atrophies with AD, losing as much as 30% of its volume by death (approximately 2.4%–3% per year).11,12 The areas most affected are widespread regions of the cerebral cortex, where the neurons that use acetylcholine primarily reside, and the symptoms reflect the many areas of damage in the brain. Several current treatments act by help-
ing to keep levels of acetylcholinesterase activity in the brain synapses stable.

Depression is a frequent comorbidity with AD. Depression, along with vitamin B₁₂ deficiency and hypothyroidism, must be excluded in patients with dementia because their symptoms can mimic AD in the early stages. These blood tests are a standard part of the evaluation of patients with dementia and are recommended by the AAN, along with a complete blood cell count and a chemistry panel. Depending on the specific clinical circumstances, other tests could include erythrocyte sedimentation rate, urinalysis, toxicology, chest X-ray, heavy metal screen, human immunodeficiency virus testing, cerebral spinal fluid examination, and electroencephalography, although they are not formally recommended. Testing for syphilis, although a possible cause of dementia, is not recommended unless clinical suspicion warrants it.

The first case study describes the assessment of a patient at risk for AD in a primary care practice, and includes a discussion of the nurse’s role in this situation.

**Mild Cognitive Impairment**

Mild cognitive impairment has attracted much attention in the past several years as researchers have realized that MCI appears to be a precursor to, or the very earliest stages of, AD. In its broadest definition, MCI is impairment in a single cognitive domain that is beyond what one would expect for the patient’s age, or a mild degree of impairment in multiple cognitive domains. In 2001, the AAN published practice guidelines for the early detection of memory problems. The AAN workgroup of specialists identified criteria for an MCI diagnosis, as outlined in Table 4. Diagnostic criteria for amnestic MCI include memory complaint, preferably corroborated by an informant, essentially normal cognition, largely normal ADLs, and objective memory impairment for age. Importantly, these individuals do not show signs of dementia. There are 4 types of MCI: amnestic, multiple domains, mild impairment, and single nonmemory domains. Amnestic MCI is the most common type and it is highly prevalent in the elderly. In the Cardiovascular Health Study—Cognition Study of 3068 patients, MCI was present in 22% of those patients aged 75 years and older. Patients with MCI convert to AD at a rate of approximately 10% to 15% per year.

Several lines of evidence point to MCI as the earliest clinical manifestations of AD. For example, mem-

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**Case Study**

**Assessment of a Patient at Risk for Alzheimer’s Disease**

**Background**

Mr. S is a 72-year-old widower and retired mechanical engineer. His wife died 5 years ago from a stroke. Mr. S is seeing his primary care physician at the urging of his daughter (age 35 years). He has noticed some “mental fuzziness” in the past year, mostly during casual conversation (forgetting the names of recently seen movies) and forgetting social appointments (despite having them written on his calendar). He has been reluctant to see his physician because he does not consider the mental lapses to be serious, just embarrassing. However, the daughter reports that the father recently got lost driving to her house for dinner—a route he has taken countless times during the past 7 years. With that incident, the daughter insisted that her father see his physician, if only to “prove her wrong,” and he ultimately agreed.

During the history taking, Mr. S appeared to be in a pleasant mood and was open and talkative about his condition. However, as his daughter continued to provide greater detail of his mental dysfunction, he became increasingly reticent.

**Physical Examination**

Mr. S has slightly elevated blood pressure (130 mm Hg/95 mm Hg) and slight dyslipidemia (total cholesterol 210 mg/dL; high-density lipoprotein cholesterol 45 mg/dL; low-density lipoprotein cholesterol 140 mg/dL). His heart rate and pulse are normal. His weight is normal for his age and height (5’10” and 180 pounds). He reports good physical health overall and walks 3 miles daily.

He is currently taking an over-the-counter pain reliever when needed for occasional stiffness.

**Social History**

Mr. S retired approximately 12 years ago, after which he and his wife had pursued their many hobbies—college courses to learn German, joining a book club, volunteer work in the community and church, social outings with friends, and Elderhostel vacations. Following his wife’s death, Mr. S attends social outings less frequently and has only attended 1 Elderhostel vacation. However, he does continue with college courses in other areas of interest and with his volunteer work.

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Memory impairment is more similar in patients with mild AD than normal patients of the same age, but their cognitive impairment resembles healthy patients.\textsuperscript{17} Studies measuring atrophy of the hippocampus (Figure 1) show that those patients with MCI, particularly those with declining abilities, have significantly greater volume reductions after 3 years, approaching that of patients with AD, compared to controls (Figure 2).\textsuperscript{10,18} Very recently, Bennett et al followed 180 Catholic clergy from the Religious Orders Study and found at autopsy that those patients with MCI had intermediate levels of AD pathology (plaques and neurofibrillary tangles) and cerebral infarction compared to those patients without cognitive impairment and those with dementia.\textsuperscript{19}

### Table 4. AAN Practice Guidelines for the Early Detection of Memory Problems

The AAN workgroup of specialists identified the following criteria for an MCI diagnosis:

- An individual’s report of his or her own memory problems, preferably confirmed by another person
- Measurable, greater-than-normal memory impairment detected with standard assessment tests
- Normal overall thinking and reasoning skills
- Ability to perform normal daily activities

AAN = American Academy of Neurology; MCI = mild cognitive impairment. Data from Petersen et al.\textsuperscript{13}

### Figure 1. Diagram of the Major Brain Regions

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**Assessment**

The nurse discusses the possibility of cognitive decline with aging and other possible causes of his poor memory, such as a vitamin B\textsubscript{12} deficiency (especially because he cooks for himself, and his meals consist mostly of sandwiches or frozen dinners) or depression, even though it has now been several years since his wife’s death. The nurse then tells Mr. S that she will ask him a few questions to see how his memory is and how things are going for him today. She proceeds with the Mini-Mental State Examination (MMSE); his score is 24.

The nurse also asks Mr. S about other aspects of his life—who handles his finances, who takes care of his laundry and cleaning the house, and whether anyone else has noticed the types of changes that he and his daughter describe. The nurse indicates that she would like to speak with the daughter alone for a few moments. The nurse queries her on any personality changes Mr. S may be showing (none) or changes in hygiene, such as bathing, dental hygiene, or wearing clean neat clothes (none).

**Discussion**

The primary care nurse is often the confidante for patients. Nurses are often considered to be more approachable than physicians and have more time to spend with the patient to engage the patient in conversation and ask questions about difficult issues (eg, depression and social embarrassment). The patient and the daughter clearly want to discuss the cognitive problems of Mr. S and are concerned, despite his waning participation in the evaluation. As the daughter describes her father’s social life, Mr. S looks away but appears to be listening to the conversation. Thus, he is able to concentrate but is embarrassed to discuss all of his symptoms.

The nurse should also engage family members or other informants especially at early stages of a dementia. Their insight helps to corroborate the medical staff’s evaluation. Based on the National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) criteria, Mr. S may have probable Alzheimer’s disease (AD), but the physician must first order some blood tests to rule out other possible causes and will most likely also order a computed tomography scan. Based on the NINCDS-ADRDA criteria, he is showing signs of cognitive decline based on his MMSE score, with deficits in at least 2 areas of cognition (poor recall of new information, dysnomia, and difficulty driving), and progressive worsening of his cognitive status. If he does have probable AD, his MMSE score suggests mild severity. Once the diagnosis is confirmed by the physician, the nurse can then inform the patient (and preferably also his daughter) about the resources available to them and the short-term and long-term issues they will need to consider.
Making the diagnosis of MCI is perhaps the greatest challenge. Petersen et al, in their practice guidelines, recommend considering the use of general cognitive screening instruments, such as the MMSE. A detailed neuropsychological battery of instruments that focus on limited aspects of cognition may also be useful, such as the Clock Drawing Test or the Time and Change Test, described elsewhere in this monograph. Importantly, for a diagnosis of MCI, the decline in cognitive function must progress over time. Informants can provide important information during the history taking and assessment of patients at risk for dementia. Petersen et al suggest several tools that emphasize history from an informant, such as the Informant Questionnaire on Cognitive Decline in the Elderly, the Blessed Dementia Rating Scale, and the Clinical Dementia Rating Scale. Similarly, patient interviews may also be considered, especially in a population at increased risk for cognitive impairment, such as the elderly. However, caution must be exercised because of the limited scope of these tools.

Case Study

A Patient Who May Be Showing Signs of Mild Cognitive Impairment

Background
Mrs. G, a 65-year-old woman, presents to her primary care physician to have a full medical examination, as required by her insurance company. She has been a regular patient at this practice for the past 30 years.

Physical Examination
Heart rate and blood pressure are normal, as is her lipid profile. She is currently taking daily vitamin E and a daily multivitamin, hormone replacement therapy (estrogen only), and hydrochlorothiazide 25 mg. Her medical history is unremarkable except for severe arthritis, requiring one knee replacement (last year). She will most likely have the second knee replaced in the next 1 to 2 years. Mrs. G is obese, and has been for most of her adult life. Her lifestyle is sedentary (mostly because of the arthritic pain), but she maintains an active social life.

Social History
She had been married for 20 years, but she was divorced 20 years ago and never remarried. Her children and grandchildren do not live close by. She is a retired schoolteacher and principal, having spent 40 years in her profession. She holds college- and graduate-level degrees and has continued personal educational endeavors since retiring (book clubs, lectures, and adult education courses at a local college).

Assessment
The nurse has known Mrs. G for many years and attended school with one of her daughters. She begins by engaging in casual conversation with Mrs. G, asking about her daughter and Mrs. G’s mood in recent weeks and months, to which Mrs. G indicates that her mood is “fine,” although she does admit to having less patience with people and more trouble sleeping at night. She attributes this to “getting old.” The nurse asks Mrs. G about some events in the local news, of which Mrs. G appears to be unaware. The nurse then asks about some of the national news (eg, an educational bill signed by the President of the United States), and Mrs. G offers a perfunctory, general answer, which is uncharacteristic of her. The nurse is concerned about her response, thus asks Mrs. G some of the questions from the Mini-Mental State Examination (MMSE), such as

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Once deficits extend beyond a single cognitive domain, the diagnosis of probable AD can be considered. Ongoing research is evaluating whether the current treatments for AD can be initiated as early as the MCI stage. A large study reported at the April 2005 annual meeting of the AAN, and published online in the April 14, 2005, New England Journal of Medicine, was the first clinical trial ever to demonstrate that a treatment could delay transition from MCI to AD. The 3-year study enrolled more than 750 older adults with “amnestic MCI,” the chief feature of which is memory difficulties greater than would be expected for an individual's age and education. Participants were randomly assigned to 1 of 3 daily regimens: 10 mg donepezil, 2000 IU vitamin E, or a placebo. Participants receiving donepezil had a reduced risk of developing AD during the first year of the trial, but by the end of the 3-year study their risk was the same as those participants taking vitamin E or the placebo. Vitamin E showed no significant benefit at any time. Study authors said the results were not strong enough to support a clear recommendation to treat MCI with donepezil, but they could prompt a discussion between a physician and patient on an individual basis. Donepezil is currently approved by the US Food and Drug Administration to treat mild to moderate AD.21

The second case study describes a patient who may be showing signs of MCI and the tools the nurse uses to develop and evaluate a differential diagnosis.

CONCLUSIONS

Based on years of extensive research, it is now possible to diagnose AD with a high degree of accuracy with a careful and thorough history, measurement of cognition over time, laboratory tests to rule out other possible causes, and, when possible, corroborating evidence from family members or other informants. MCI appears to be an early manifestation of AD and can also be diagnosed using the tools for AD diagnosis, although the degree of impairment is much more subtle. As we continue with research into more detailed neuroimaging and a biomarker for AD (beyond the plaques and neurofibrillary tangles at autopsy), we will hopefully be able to diagnose this disorder at its very earliest stages, more fully understand its pathophysiologic processes, and thus be led to more precise and preventive treatments for this disease.

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as “What is the date today?”; “What is this (pointing to a pencil)” Mrs. G is able to name the date, after several seconds of concentration, but she is unable to say the word pencil. She simply says, “Oh, you know. You write with it.”

DISCUSSION

Mrs. G is showing some signs of cognitive impairment and memory loss; however, the severity is mild and could be explained away by any number of causes. For example, Mrs. G may not be aware of local news events because she does not watch the local news or has been away on vacation. She may have struggled with the date because of a recent hectic schedule. However, failure to name a common object, such as a pencil, suggests an early sign of dementia, and the inability to discuss major national news on a topic of interest to her is unlikely given her educational status and career as an educator. The nurse has deftly taken advantage of her long-standing relationship with Mrs. G to surreptitiously assess for mild cognitive impairment (MCI) or another type of dementia in its early stages with questions from the MMSE.

Given Mrs. G's medical history, vascular disease would not be the most likely cause. Although age is a significant risk factor for vascular disease, her blood pressure and lipid profile are normal for her age. Given her educational level and her daily multivitamin, a vitamin B12 insufficiency is not a likely cause but still must be ruled out. Also, obtaining her thyroid hormone levels would be warranted to determine if she has hypothyroidism, especially because she is obese. Adverse medication effects would be unlikely given her current medications, an unusually low number for someone her age. She may be exhibiting symptoms of MCI (eg, insomnia, personality changes, poor recall of new information, and dysnomia).

Although the symptoms are mild, the case makes a prudent point that the symptoms are significant for an individual with such a background. Mental status testing would absolutely be warranted, in addition to a complete neuropsychological battery, because it will serve as the gauge for further progression. It is always important to rule out medical causes, thus the blood workup should be ordered. Because there appears to be no informant, it would be interesting to include an occupational therapy consultation to evaluate the "test of life" (ie, situations that copy the daily tasks and routines from home and work life). Finding other social interactions may provide further data for corroboration (ie, church, bank account, and grocery store).
REFERENCES