Diagnosis and Treatment of Alzheimer’s Disease
Case Study and Commentary, Terri Edwards-Lee, MD, and Victor W. Henderson, MD, MS

Alzheimer’s disease (AD), the leading cause of dementia, is a devastating degenerative disease of the brain that results in progressive cognitive impairment and functional disability. Dementia prevalence among the elderly doubles about every 5 years [1]. The worldwide prevalence of dementia is estimated as 0.3% to 1% for persons aged 60 to 64 years but rises to 42% to 68% for those aged 95 years or older [2]. In North America, 6% to 10% of persons aged 65 years and older have dementia [3], with approximately two thirds of cases due to AD. In the United States, an estimated 4.5 million persons have AD, and this number is projected to increase to 13.2 million by 2050 [4]. The annual direct and indirect costs of AD may be as high as $88 billion [5].

AD affects not only patients but also family members and caregivers, who are called upon to support a loved one who over time less and less resembles the person they once knew. Fortunately, effective therapies are available to improve cognition, behavior, and function in patients with AD. However, benefit from these agents is often modest, and there is no treatment to reverse cognitive symptoms or halt disease progression. Because AD is most often diagnosed and managed by primary care physicians, these physicians must be able to make an accurate diagnosis, distinguishing among other common causes of dementia, and initiate and monitor therapies that address the cognitive, behavioral, and psychosocial needs of the patient.

CASE STUDY
Initial Presentation

A 69-year-old woman is brought by her daughter for evaluation of progressive memory problems. The patient’s daughter reports that mild forgetfulness, which she first noticed 3 years ago, has worsened noticeably over the past year.

- How is the presence of dementia determined?
- What are common causes of dementia?
Dementia

Dementia refers to disorders of the brain that affect cognition to a degree that impairs the ability to perform usual daily activities. The key symptom of dementia is impairment in memory associated with deficits in at least one other cognitive domain, such as language, skilled motor movements, recognition, or executive functioning (ie, planning, organizing, sequencing, or abstracting) [Table 1] [6]. These deficits must represent a decline in abilities and be severe enough to interfere substantially with work or usual social activities. In the context of this definition, memory represents the ability to learn new information and then recall this information after an interval of time, which can range from 1 to 2 minutes or more. Clinically, memory is assessed by presenting a patient with new information (eg, a short story or a list of words) and later asking the patient to recall as many story details or as many words as possible (delayed recall). Of note, a confusional state (delirium) can occur in older persons with infections, metabolic abnormalities, or adverse reactions to medications. Cognitive deficits in this situation do not represent dementia, and evaluation for possible dementia should be postponed until the confusional state has resolved. Less severe cognitive impairment, particularly that characterized by isolated memory deficits not severe enough to interfere substantially with daily activities, is often referred to as mild cognitive impairment, sometimes representing an early “preclinical” phase of AD [7].

The most common dementing illness is AD, but dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), and vascular dementia (VaD) are frequently encountered. In a dementia brain bank series, 77% of brains had AD pathology, 26% had DLB, 5% had FTD, and 18% had VaD [8]. In addition, mixed pathologies were common, with the total percentage in this study exceeding 100%. These other dementing disorders can usually be distinguished from AD on clinical grounds.

Alzheimer’s Disease

The key clinical feature in AD is the gradual loss of the ability to recall recent events or information, eventually accompanied by declines in other cognitive skills [Table 2] [9,10]. Cognitive loss generally reflects the malfunction of brain regions severely affected by intraneuronal neurofibrillary tangles and extracellular neuritic plaques, the characteristic histopathological changes of AD. Symptom onset is insidious, often recognized only in retrospect. Common early behavioral manifestations include apathy and delusions, such as delusions of theft or infidelity. Unlike their family members, many patients fail to recognize there is a problem. For some patients, depression, agitation, aggression, and sleep problems complicate the course of the disease. Visual or auditory hallucinations occasionally occur but typically not in the early disease course; elementary motor and perceptual functions are preserved until quite late in the course of AD. Life expectancy is reduced in the AD patient compared with persons without dementia [11]. During terminal stages of the disease, patients may be confined to bed and may be unable to walk, care for themselves, or recognize close family members. They experience complications of limited mobility, including contractures and susceptibility to pressure sores. Eating and even swallowing may be problematic, and the patient often succumbs to infections associated with immobility or to coexisting medical illnesses.

Dementia with Lewy Bodies

DLB is characterized by symptoms associated with both AD and Parkinson’s disease. The defining pathologic hallmark is the cortical Lewy body, an intraneuronal inclusion first described in the substantia nigra of patients with Parkinson’s disease. In addition, many patients with cortical Lewy bodies have tangles and plaques more typical of AD, although the burden of these changes in DLB is frequently less than that with AD. Not surprisingly, DLB shares symptoms and signs suggestive of both Parkinson’s disease and AD. The dementia is progressive and characterized by the presence of parkinsonism (especially extrapyramidal rigidity), fluctuating attention, and well-formed visual hallucinations; 2 of these 3 features are required for clinical diagnosis [12]. Disruptive motor behaviors occasionally occur during the rapid eye movement stage of sleep and can be a heralding symptom [13]. DLB patients are more likely to have depression and delusional misidentification (eg, believing that someone on the television screen is actually in the room) than are patients with AD [14].
### Frontotemporal Dementia

FTD refers to syndromes associated with selective atrophy of the frontal and temporal lobes. Histopathological features of FTD are variable, ranging from nonspecific changes to several types of intracellular inclusions to hippocampal sclerosis [15,16]. The clinical picture is typically dominated more by behavioral symptoms than by cognitive deficits, particularly marked alterations in personality and social conduct [17]. Symptom onset commonly occurs before age 65 years. The essential feature is an early and progressive change in personality characterized by difficulty in modulating behavior [18]. Patients can show profound apathy and loss of initiation or distractibility and behavioral disinhibition. Memory impairment is usually mild. A distinct subset of FTD patients predominately show language alterations (ie, a progressive aphasia), which can be fluent or nonfluent, and others have parkinsonian signs or motor features of amyotrophic lateral sclerosis [15]. Patients formerly classified as having Pick’s disease fall into the FTD spectrum.

### Vascular Dementia

As the term implies, VaD represents dementia attributed to vascular disease of the brain, which is usually (but not necessarily) cerebral infarction (ischemic stroke) as documented by history, neurologic examination, or brain imaging findings [19,20]. VaD is characterized by impairment in multiple areas of neurologic and cognitive function. The course is generally stepwise due to periodic declines associated with acute strokes, followed by symptom stabilization or mild improvement. However, gradual progression is sometimes seen, perhaps related to ischemic damage to the subcortical white matter. On occasion, a single strategically placed stroke (eg, in the thalamus) can cause dementia. Thought processes are typically slowed, and errors are made when integration of different cognitive abilities is needed. Movement is also slow, and the neurologic examination almost always shows focal increases in tone, focal weakness, and brisk or pathologic reflexes. When VaD is caused by discrete infarcts, the clinical assessment reflects the brain areas involved. The course of the dementia can often be substantially stabilized if stroke risk factors such as hypertension or hyperlipidemia are adequately controlled and stroke prophylaxis (eg, with an antiplatelet agent) is initiated. The main goal of therapy is to reduce stroke risk factors, and management of cognitive and behavioral symptoms is similar to that of AD.

### What is the approach to diagnostic evaluation in patients with suspected dementia?

When a patient is first seen for suspected dementia, the physician’s most important diagnostic resources are the informant interview and the office-based clinical assessment. Recommended evaluation of a patient with dementia typically includes a clinical history, physical and neurologic examination, cognitive screen, screening laboratory blood tests, and brain imaging [21]. The clinical history should involve both the patient and a knowledgeable informant, focusing on the mode of onset, initial symptoms, pattern of progression, and accompanying neurologic and behavioral symptoms. Identifying behavioral symptoms is important because changes in personality and behavior dominate the
initial presentation of FTD and because such symptoms can often be treated adequately. Successful treatment of behavioral symptoms can improve quality of life for caregivers as well as patients, often more so than treatment of cognitive symptoms.

Screening blood tests for dementia typically include tests for thyroid function, vitamin B_{12} level, electrolytes, serum glucose, renal and liver function tests, and a complete blood count [21]. In select populations, a screen for HIV or syphilis is appropriate, and other laboratory tests are warranted in particular clinical settings. Screening tests focus on conditions that can contribute to cognitive dysfunction, even when the primary cause of dementia is likely a degenerative brain disease. Although such screening infrequently identifies a specific cause of dementia, it often uncovers exacerbating conditions, which when treated may improve cognition, behavior, and function. Additional screening tests may be warranted in atypical cases, such as genetic testing for presenilin-1 mutations (linked to early-onset AD) in a relatively young patient with a strong family history of dementia.

Structural brain imaging with a non-contrast CT or magnetic resonance imaging (MRI) scan is appropriate in the initial evaluation of dementia [21]. The MRI scan provides better spatial resolution and may be more specific for certain disorders (recent infarction, inflammatory disorders). Generalized atrophy is common in AD but nonspecific. When assessed at research centers, marked atrophy of the hippocampus may be predictive of the presence of dementia due to AD [22].

The cognitive screen for dementia can be as simple as administering the Mini-Mental State Examination (MMSE) [23], the Orientation-Memory-Concentration test [24], or the 7-Minute Screen [25], but the clinician may wish to include other brief tasks such as verbal fluency [26] or clock drawing [27]. A more exact determination of the pattern of cognitive deficits can be obtained through comprehensive neuropsychological testing, which is especially helpful in cases of very early or questionable dementia.

Additional screening tests that are not part of the standard evaluation of dementia may increase diagnostic certainty in atypical cases [21]. There may be a limited role for functional imaging. For example, single photon emission computerized tomography or positron emission tomography may show patterns of blood perfusion or metabolic deficits that help distinguish AD from FTD [28]. Patients with an unusually rapid dementia course, seizures, pronounced myoclonus, or decreased consciousness may need a lumbar puncture to help rule out infection. Measurement of tau protein and amyloid-β_{1-42} concentrations in the cerebrospinal fluid can increase diagnostic certainty of AD in patients with an atypical presentation or comorbid conditions that adversely affect cognition, such as stroke or substance abuse [29].

**History**

The patient’s daughter reports that her mother’s memory problems initially consisted of inconsistent recall of recent conversations, but she now has trouble remembering appointments and frequently misplaces her glasses, purse, and other personal belongings. Two years ago, she assumed control of her mother’s finances “to prevent mistakes” after several bills were unpaid and others were paid twice. In contrast, basic activities of daily living such as dressing, bathing, toileting, and feeding are intact. The patient continues to garden, do light housework, and fix simple meals for herself. However, she had trouble preparing a large dinner when the family gathered for a recent holiday. She has no difficulty driving to familiar nearby locations (eg, hair salon, church) but once became lost while returning home from her daughter’s house. The daughter is particularly concerned that her mother argues with her and accuses her of stealing her money. There has been no physical aggression. Although there has been some day-to-day variability, symptoms have not fluctuated markedly. There are no hallucinations, and mood is normal.

Past medical history is unremarkable. The patient has been hospitalized only for childbirth. She does not use prescription or nonprescription medication on a regular basis. There is no history of stroke, hypertension, heart disease, diabetes, or thyroid disease. She does not smoke and drinks wine only on special occasions. She is educated through high school, was a textile worker for several years prior to her marriage, and has successfully raised 2 children. She has lived alone since the death of her husband 8 years ago. There is no family history of dementia or of other neurologic or psychiatric disease.

The patient presents neatly groomed with pleasant but bland, empty conversation. Affect is normal. She denies memory problems beyond those experienced by “everyone my age.” She is vague in reporting details of her medical history and repeats anecdotes during the interview.

**Further Evaluation and Diagnosis**

The patient scores 24 points on the MMSE (out of a possible 30 points); she loses points for orientation (did not know the exact date and named the preceding year rather than the current year), attention (omitted 1 letter in spelling the word WORLD backward), and recall (unable to remember 3 words whose names she had been asked to remember). She is able to produce 12 animal names in 60 seconds (normal is generally 15 or more), and she makes errors when asked to draw a clock. Her elementary neurologic examination is normal. In particular, gait is intact, and there are no signs of parkinsonism (no bradykinesia, rigidity, or tremor) and no focal neurologic abnormalities. The physician determines that the patient is demented and suspects AD as the underlying
cause. The results of the following blood tests are normal: complete blood count, electrolytes, glucose, creatinine, alanine aminotransferase, vitamin B12, and thyroid stimulating hormone. A noncontrast CT scan of the brain shows mild cerebral atrophy without signs of masses or stroke.

- What findings support a diagnosis of AD in this patient?

The patient clearly meets the criteria for dementia (Table 1). Impairments in several cognitive domains and functional impairments (paying bills, preparing a large meal) indicate a disturbance more severe than so-called mild cognitive impairment [7]. Insidious onset and gradual progression, prominent early memory deficits, and the absence of visual hallucinations, fluctuations in attention, parkinsonian features, or focal neurologic signs all point to a diagnosis of AD. The AD diagnosis is further substantiated by normal results of screening blood tests and the brain imaging study.

- How is mild to moderate AD managed initially?

**Treatment of Mild to Moderate AD**

The mainstay of pharmacologic treatment of AD is use of acetylcholinesterase inhibitors (AChEIs), which are approved by the U.S. Food and Drug Administration (FDA) for treatment of mild to moderate dementia due to AD (roughly corresponding to MMSE scores of 10 to 26). AChEIs block the breakdown of acetylcholine, a neurotransmitter whose concentration is decreased in the AD brain. Three AChEIs are in common use: donepezil, rivastigmine, and galantamine (Table 3). AChEI treatment can improve cognition, function, and some problematic behaviors [30–33], although therapeutic efficacy is generally modest. Treatment is probably cost-effective, with savings estimated at approximately $1100 per year in a randomized Swedish trial where caregiver time as well as health care costs were included [34] and at approximately $3900 per year in a case-control study analysis of a Medicare managed care plan [35]. The cost-effectiveness of these drugs, however, has been challenged [36]. For patients receiving an AChEI, functional decline is delayed by approximately 5 months [37]. Cognitive stabilization or mild cognitive improvement is common during the first months after AChEI initiation [38], but test-retest variability suggests caution in interpreting small increases or decreases in the MMSE or other cognitive scores.

At therapeutic doses, the AChEIs show similar efficacy and side-effect profiles. The most frequent side effects are related to peripheral cholinergic actions on the gastrointestinal system, including anorexia, nausea, vomiting, diarrhea, and weight loss. Other occasional side effects include headache, insomnia, dizziness, and muscle cramps. AChEIs are relatively well tolerated if given as directed with food and dosage elevations occur no more often than monthly. Because of peripheral cholinergic effects, AChEIs are contraindicated or should only be used with caution in patients with certain medical conditions (Table 4). Cholinergic deficits are present in DLB and VaD as well as AD, and AChEIs are possibly efficacious in these disorders [39,40]; less is known about the effects of AChEIs in patients with FTD. Note that use of AChEIs is not approved by the FDA for disorders other than AD.

Behavioral strategies targeting patients and their caregivers can improve functional and behavioral outcomes in AD [41]. Caregiver education and caregiver respite are important. The Alzheimer’s Association (1-800-272-3900; www.turner-white.com

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**Table 3. Commonly Used Acetylcholinesterase Inhibitors Approved for Mild or Moderate Dementia Due to Alzheimer’s Disease**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Usual Starting Dose (Total Daily Dose)</th>
<th>Usual Dosing Interval</th>
<th>Usual Therapeutic Dose (Total Daily Dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil</td>
<td>5 mg/day</td>
<td>Daily</td>
<td>5–10 mg/day</td>
</tr>
<tr>
<td>Galantamine*</td>
<td>8 mg/day</td>
<td>Twice daily</td>
<td>16–24 mg/day</td>
</tr>
<tr>
<td>Rivastigmine*</td>
<td>3 mg/day</td>
<td>Twice daily</td>
<td>6–12 mg/day</td>
</tr>
</tbody>
</table>

*In addition to being acetylcholinesterase inhibitors, rivastigmine is a butyrylcholinesterase inhibitor and galantamine is a nicotinic receptor modulator. It is unknown whether these additional actions contribute to clinical effects of these drugs.*

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**Table 4. Medical Conditions in Which Acetylcholinesterase Inhibitors Are Contraindicated or Should Be Used with Caution**

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Symptomatic bradycardia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sick sinus syndrome</td>
</tr>
<tr>
<td></td>
<td>Heart block greater than first degree</td>
</tr>
<tr>
<td></td>
<td>History of congestive heart failure</td>
</tr>
<tr>
<td></td>
<td>Unexplained episodes of syncope or presyncope</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td></td>
<td>Asthma</td>
</tr>
<tr>
<td></td>
<td>Pulmonary conditions requiring regular use of oxygen besides obstructive sleep apnea</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Untreated gastrointestinal bleeding in the previous 6 months</td>
</tr>
<tr>
<td></td>
<td>Active peptic ulcer disease</td>
</tr>
</tbody>
</table>
www.alz.org) is a valuable educational resource for all aspects of the disorder. Local support groups provide emotional support as well as practical insight on managing medical, behavioral, social, and legal aspects of the disease.

For many adults, operating a motor vehicle is essential to independent living, and the loss of driving privileges can represent a loss of autonomy. Complex motor, perceptual, and cognitive skills required for safe driving can be affected even in mild AD [42,43]. Driving skills are better preserved if cognition is only mildly impaired and if the presence of dementia is questionable [42,43]. Legal requirements vary by state regarding physician reporting of dementia. Confidential reporting to the county health department is mandated, for example, in California. Guidelines from the Quality Standards Subcommittee of the American Academy of Neurology suggest that driving discontinuation should be strongly considered even for mild AD [42]. When dementia is very mild or questionable, evaluation of driving performance by a qualified examiner can be helpful. Any decision not to discontinue driving should be reassessed in 6 months [42].

### Initial Management

The patient is started on an AChEI with titration of dosage at 1 month. Her daughter is referred to a local chapter of the Alzheimer’s Association and to a geriatric social worker. The patient is persuaded to discontinue driving, and her daughter arranges her own schedule to provide transportation for her mother. After 3 months, the patient’s daughter reports minor improvement in daily functioning and a decrease in delusions of theft. The patient’s MMSE score has improved by 2 points.

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**Table 5. One-Month Prevalence of Behavioral Symptoms in Demented Patients in the Cardiovascular Health Study**

<table>
<thead>
<tr>
<th>Behavioral Symptom</th>
<th>Alzheimer's Disease, %</th>
<th>Other Causes of Dementia, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delusions</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Agitation or aggression</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>Depression</td>
<td>31</td>
<td>35</td>
</tr>
<tr>
<td>Anxiety</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>Euphoria</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Apathy</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Irritability</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>Aberrant motor behavior</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>26</td>
<td>32</td>
</tr>
<tr>
<td>Eating disturbance</td>
<td>18</td>
<td>24</td>
</tr>
</tbody>
</table>

*Prevalence is based on 362 persons classified as having dementia with informant-based behavioral data from the Neuropsychiatric Inventory [44].

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**2-Year Follow-up**

Two years later, the patient is still able to perform activities of daily living and undertake some light housework, but she can no longer use a microwave oven, sometimes forgets to turn off the stove, and often leaves the lights on when going to bed. Her daughter notes that she has experienced crying spells over the past several months and seems not to enjoy visits with her grandchildren. She is also more irritable, sometimes yelling at her daughter when she reminds her to turn off the stove or return food containers to the refrigerator. When asked about her mood, the patient begins crying and says she cannot stop thinking about her deceased husband. She is not suicidal. Her MMSE score is 19, and her neuropsychologic examination is normal.

The physician notes that the patient has worsened during the 2 years after her diagnosis, although the magnitude of cognitive decline is within the range of that commonly seen in AD. Given the patient’s prominent depressive symptoms, the physician starts her on a selective serotonin reuptake inhibitor (SSRI), and the dose is titrated according to standard guidelines. Over the next 3 months, her mood improves, and she argues less often with her daughter. Functional skills are essentially unchanged.

### What pharmacotherapies are used to manage the behavioral symptoms of dementia?

Behavioral symptoms are common in all dementias. These include apathy, depression, problems with sleep, irritability, and agitation or aggression (Table 5) [44]. Some symptoms may respond to AChEI therapy [32,33], but if AChEI treatment and behavioral intervention do not satisfactorily diminish distressing symptoms, other classes of psychotropic medicines should be considered. Unfortunately, few psychotropic agents have been evaluated specifically for demented patients in randomized controlled trials.

Three types of medications are frequently used to treat the behavior symptoms associated with dementia: AChEIs, antidepressants, and antipsychotics. Apathy often responds to treatment with an AChEI, although not necessarily to the extent desired. Unfortunately, treatments specific for apathy are not well studied in dementia. For depression, antidepressants with substantial anticholinergic side effects should be avoided. The SSRIs are generally well-tolerated by patients with AD, and other behavioral symptoms may respond as well [45-47]. Sedating side effects of some antidepressants (eg, trazodone, a triazolopyridine, or mirtazapine, a tetra cyclic piperazinoazepine) may be exploited when depression is accompanied by insomnia, anxiety, or agitation. Although depressive symptoms are common in AD and depression by
How should patients with more severe AD be managed?

The principles for treatment of mild to moderate AD discussed above also apply to the more advanced stages of the disease. Although AChEIs are not approved by the FDA for patients with advanced dementia, some studies suggest that more severely impaired patients continue to benefit from these agents [25,59]. Memantine is approved for use in moderate to severe AD (roughly corresponding to MMSE scores of 5–17) [60,61]. Memantine is an uncompetitive antagonist of the N-methyl-D-aspartate (NMDA) class of glutamate receptors. NMDA receptors play a crucial role in learning and memory, but sustained receptor activation is implicated in processes leading to programmed cell death (apoptosis) [62]. In clinical trials, memantine compared with placebo [60] or memantine plus donepezil compared with donepezil alone [61] provided modest improvement in global severity, cognition, behavior and functional activities, and it decreased care-giving burden. The side effect profile is favorable, and there are few interactions with other medications. Memantine is contraindicated in patients with renal failure, and dosage should be titrated more slowly in patients with renal insufficiency.

Are there measures that might help prevent AD?

The costs of AD are enormous [5]. Current therapeutic approaches to AD, which rely heavily on AChEIs, can improve quality of life for patients and caregivers by improving cognition, behavior, and function. There is real hope that specific and highly effective treatment for AD will eventually be developed. Innovative therapies under development include those that seek to alter fundamental metabolic pathways culminating in AD pathology [63,64].

Prevention is of critical public health importance. Observational studies link a number of different factors to AD or to dementia in general, and by inference these associations suggest lifestyle modifications or interventions that might reduce the risk of developing dementia. However, there is as yet no clinical trial evidence that any intervention lowers AD risk in healthy persons. Initiating estrogen-containing hormone therapy after age 65 years is known to increase dementia risk [65], but clinical trial data are lacking for younger women, who are more likely to consider hormone therapy [66]. Observational studies have linked prior use of non-steroidal anti-inflammatory drugs to reduced AD risk [67]. However, long-term use of these agents is associated with potentially serious renal and gastrointestinal side effects, and treatment trials to date have failed to confirm therapeutic benefit in AD patients [68]. Other factors hypothesized to protect against AD include maintaining good blood pressure control, treating hyperlipidemia with a statin, staying

4-Year Follow-up

Four years after her initial assessment and approximately 7 years after the first appearance of memory difficulty, the patient can perform most basic activities of daily living, but she tends to wear the same dress each day and requires prompting to bathe or brush her teeth. Over the past several weeks, she has been awake much of the night fearful that her house will be burglarized, repeatedly checking locks on doors and windows. After particularly bad nights, she is more confused during the day. Her daughter is visibly tired and frustrated. Regular medications include an AChEI and an SSRI.

On examination, she is less interactive with the physician and with her daughter. Her speech output is limited, and she does not appear to follow much of the conversation. However, she supplies fluent, socially appropriate responses to simple questions (eg, How are you feeling today?). Her elementary neurologic examination remains essentially normal, and her MMSE score is 12. Memantine is started at an initial dose of 5 mg daily and increased by 5 mg per day each week in 2 daily doses to a maximum dose of 10 mg twice daily. At the office visit 6 weeks later, the daughter says that she believes her mother is more interactive and tends to speak a little more readily.

• How should patients with more severe AD be managed?
mentally and physically active, not smoking, consuming alcoholic beverages in moderation, and adhering to a healthy diet containing foods high in antioxidants and B vitamins (folic acid, vitamin B₆ and vitamin B₁₂ can reduce homocysteine levels) [69–76]. A number of clinical trials are underway to evaluate interventions in older persons with poor memory. In the presence of mild cognitive impairment, there is preliminary evidence that an AChEI may postpone the onset of AD in this situation [77]. As a cautionary note on vitamin E, prolonged use of high-dose supplements is linked to increased mortality [78].

Conclusion

Most cases of AD are diagnosed and managed by community-based physicians, often by the primary care provider. As evidence-based therapeutic options expand, it is increasingly important for physicians to achieve an accurate diagnosis, to identify comorbid disorders and other potentially contributing factors, and to offer individualized treatments based on patients’ specific diagnoses, cognitive and behavioral symptoms, and psychosocial needs. It is not yet possible to cure AD, but it is almost always possible to improve patients’ symptoms and quality of life and to diminish the burden assumed by their caregivers.

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Diagnosis and Treatment of Alzheimer’s Disease

DIRECTIONS: Each of the questions below is followed by 4 possible answers. Select the ONE lettered answer that is BEST in each case and circle the corresponding letter on the answer sheet.

1. The gradual onset and progression of impairment is characteristic of which of the following disorders?
   (A) Alzheimer’s disease
   (B) Dementia with Lewy bodies
   (C) Frontotemporal dementia
   (D) Each of the above

2. What is the most common initial impairment in the patient with Alzheimer’s disease?
   (A) Altered personality and social conduct
   (B) Difficulty learning and recalling new information
   (C) Aphasia
   (D) Visual hallucinations

3. Rigidity is a relatively common presenting symptom in which of the following disorders?
   (A) Alzheimer’s disease
   (B) Dementia with Lewy bodies
   (C) Frontotemporal dementia
   (D) Vascular dementia

4. A relatively common side effect of acetylcholinesterase inhibitors is:
   (A) Nausea
   (B) Liver enzyme abnormalities
   (C) Myalgias and muscle enzyme abnormalities
   (D) Weight gain

5. Memantine is most likely to be beneficial in which of the following?
   (A) Mild cognitive impairment in the absence of dementia
   (B) Mild Alzheimer’s disease
   (C) Severe Alzheimer’s disease
   (D) Frontotemporal dementia
EVALUATION FORM: Diagnosis and Treatment of Alzheimer’s Disease

Participants may earn up to 1 hour of category 1 credit by reading the article named above and correctly answering at least 70% of the accompanying test questions. A certificate of credit and the correct answers will be mailed within 6 weeks of receipt of this page to those who successfully complete the test.

Circle your answer to the CME questions below:

1. A  B  C  D
2. A  B  C  D
3. A  B  C  D
4. A  B  C  D
5. A  B  C  D

Please answer the following questions:

1. How would you rate this educational activity overall?
   ___ Excellent  ___ Good  ___ Fair  ___ Poor

2. Please rate the clarity of the material presented in the article.
   ___ Very clear  ___ Somewhat clear  ___ Not at all clear

3. How helpful to your clinical practice was this article?
   ___ Very helpful  ___ Somewhat helpful  ___ Not at all helpful

4. Please tell us how well the article achieved each of the following objectives.

   Participants will be able to:
   Apply criteria for dementia in the patient with memory problems
   ___ Achieved  ___ Partially achieved  ___ Not achieved

   Distinguish Alzheimer’s disease (AD) from other common disorders that cause dementia
   ___ Achieved  ___ Partially achieved  ___ Not achieved

   Recognize both behavioral and cognitive impairments in the patient with dementia
   ___ Achieved  ___ Partially achieved  ___ Not achieved

   Describe management options for mild to moderate AD
   ___ Achieved  ___ Partially achieved  ___ Not achieved

   Describe management options for moderate to severe AD
   ___ Achieved  ___ Partially achieved  ___ Not achieved

5. What changes will you make in your practice as a result of reading this article?
   ___________________________________________________________
   ___________________________________________________________

6. What topics would you like to see presented in the future?
   ___________________________________________________________
   ___________________________________________________________

Please print clearly:

Name: ______________________________________________________
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Physicians are required to report the actual amount of time spent on the activity, up to the maximum designated 1 hour. The actual time spent reading this article and completing the test was ____________________.

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101 Alexandrine, Lower Level
Detroit, MI 48201
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