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# The Differential Diagnosis and Treatment of Mild Cognitive Impairment and Alzheimer Disease

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The substantial clinical heterogeneity seen among patients with Alzheimer disease (AD) makes the associated differential diagnosis difficult, even for experienced clinicians. In addition to memory and learning impairment, an AD diagnosis requires demonstrated impairment in another cognitive domain, namely complex attention, executive function, language, perceptual-motor, and/or social cognition.<sup>1</sup> Of these deficits, cognitive decline has the largest impact on day-to-day living.

It is essential that clinicians exclude alternative causes for changes in cognitive functioning, as the correct treatment plan for an individual depends on the underlying condition. Psychiatric disorders, such as depression and schizophrenia, can resemble dementia and can cause executive dysfunction or thought disorders. Medical issues such as thyroid disease and vitamin deficiencies can similarly mimic AD. Findings

from comprehensive patient assessments and laboratory work can assist with the differential diagnosis.

Frontotemporal dementia, Parkinson disease, primary progressive aphasia, vascular dementia, dementia with Lewy bodies, and other dementias often present similarly to AD.

Relative to AD, frontotemporal dementia usually has a younger age at onset and causes personality changes and impulsive behaviors. Parkinsonian features, namely tremor and rigidity, accompany Parkinson disease, whereas a patient experiencing early language difficulties may be experiencing fluent or non-fluent primary progressive aphasia. Patients with a risk of vascular disease, a history of cerebrovascular disease, or vascular lesions present on a magnetic resonance imaging scan could have vascular dementia. Early visual hallucinations, fluctuating attention,

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This COMMENTARY section of *The Journal of Clinical Psychiatry* presents the highlights of the teleconference series "Screening, Diagnosing, and Treating Mild Cognitive Impairment and Mild Alzheimer Disease," which was held on February 25, 2022. This report was prepared and independently developed by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Biogen MA Inc.

The teleconference was chaired by **Dr Allan Anderson, MD, MMM, CMD, DLFAPA**, Banner Alzheimer's Institute, Tucson, Arizona. The faculty was **Dr Matthew Malone, DO, MBA**, Banner Alzheimer's Institute, Tucson, Arizona.

## CME Objective

After completing this educational activity, you should be able to:

- Diagnose patients with mild cognitive impairment or mild Alzheimer dementia
- Facilitate prompt treatment initiation for patients with mild cognitive impairment or mild Alzheimer dementia

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Marlene P. Freeman, MD, Editor in Chief, Boston, Massachusetts, has received research funding from JayMac and Sage; has been a member of the Independent Data Safety and Monitoring Committee for Janssen (Johnson & Johnson), Novartis, and Neurocrine; and has served on advisory boards for Eliem and Sage. As an employee of Massachusetts General Hospital (MGH), Dr Freeman works with the MGH National Pregnancy Registry, which receives funding from Alkermes, Aurobindo, AuroMedics, Johnson & Johnson/Janssen, Otsuka, Sage, Sunovion, Supernus, and Teva, and works with the MGH Clinical Trials Network and Institute, which receives research funding from multiple pharmaceutical companies and the National Institute of Mental Health. Dr Freeman has also received royalties through MGH for the Massachusetts General Hospital Female Reproductive Lifecycle and Hormones Questionnaire.

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**Financial Disclosure**

**Dr Anderson** has served on the speakers/advisory boards for Biogen. **Dr Malone** has no financial disclosures.

**Review Process**

The author agreed to provide a balanced and evidence-based presentation and discussed the topic and CME objective during the planning sessions. The author's submitted content was validated by CME Institute staff, and the activity was evaluated for accuracy, use of evidence, and fair balance by a peer reviewer who is without conflict of interest.

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REM behavioral sleep disorder, and/or Parkinsonism are all highly suggestive of dementia with Lewy bodies.<sup>2</sup>

Cholinesterase inhibitors, memantine, and other historical treatments for AD target symptoms of the disease, rather than the condition's underlying causes.<sup>3</sup> However, there is much excitement surrounding recent advances and research regarding efforts to target the pathology of the disease. After data from a pair of double-blind, randomized, and placebo-controlled trials, EMERGE and ENGAGE, showed reduction in amyloid burden in the brain in patients with stage 3 AD, or mild cognitive impairment (MCI), and patients with stage 4, or mild Alzheimer dementia, aducanumab became the first disease-modifying therapy to be approved by the US Food and Drug Administration.<sup>4</sup> Amyloid-related imaging abnormalities (ARIA), edema (-E) and/or hemosiderin (-H), were detected in 41% of patients<sup>4,5</sup> treated with aducanumab versus 10% placebo. Clinicians should be aware of and watch for ARIA symptoms when treating patients with aducanumab.

Researchers are now looking toward preventative treatments for AD capable of interrupting the biological cascades that lead to dementia. In the future, testing for biomarkers could play an outsized role in preventative treatment and may help clinicians stratify patients by risk and identify the most appropriate targeted therapy.

Individuals often want to know measures they can take in the present to prevent or delay the onset of dementia. According to dementia expert James Ellison, MD, MPH, to address this common question, clinicians can use the acronym DANCERS to provide their patients with helpful preventative tips.<sup>6</sup> DANCERS stands for disease management, activity, nutrition, cognitive training, engaging with others, relaxation, and sleep. **Disease management** of diabetes, hypertension, hyperlipidemia, and obesity can help

reduce risk. **Activity**, particularly aerobic exercise, benefits the brain as well as the heart. **Nutrition**, such as the MIND diet (a combination of Mediterranean and DASH diets), can lower the likelihood of dementia. **Cognitive training**, such as crossword puzzles or Sudoku, and engaging in new activities are helpful. Activities that "stress" the brain may be more beneficial, such as learning to play a new instrument or learning a new language. **Engaging with others** also benefits the brain. **Relaxation** through activities such as meditation, yoga, and deep breathing, additionally plays an important role in promoting brain health. And lastly, adequate **sleep** is important as deep sleep helps to clear out amyloid in the brain.<sup>6,7</sup>

Finally, clinicians should not forget about the second patient commonly in the room—the caregiver. Checking in with caregivers and asking them questions is an important part of a multifaceted treatment approach. Caregivers experience loss during the Alzheimer trajectory, including the loss of a relationship, a partner, a way of life, and even a career.<sup>8</sup>

As advances continue in the field of AD, identifying patients at risk for developing MCI and AD is becoming more possible. Improvements in AD diagnoses will help clinicians initiate treatment earlier in the disease trajectory and thereby optimize patient outcomes. Earlier intervention can lead to individuals living in their own home longer, being with their families, and maintaining their independence to greatest extent possible.

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1. Which of the following forms of dementia, relative to Alzheimer disease, has an earlier age at onset and causes personality changes and impulsivity?
  - a. Frontotemporal dementia
  - b. Lewy body dementia
  - c. Vascular dementia
  - d. Primary progressive aphasia
  
2. Which acronym, according to Dr Ellison, can be used to remember patient actions that can prevent or delay the development of Alzheimer disease?
  - a. PRISMS
  - b. DOCTORS
  - c. DANCERS
  - d. PRINCES

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