In the Clinic

Dementia

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CME Objective: To review current evidence for prevention, screening, diagnosis, and treatment of dementia.

The information contained herein should never be used as a substitute for clinical judgment.

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Dementia is defined as a decline in 2 or more cognitive capacities, causing impairment in function but not alertness or attention. The decline in cognition distinguishes it from lifelong intellectual disability (previously called "mental retardation") and single learning disorders, both of which are present from birth and symptomatic in childhood. That 2 or more cognitive capacities must be impaired distinguishes dementia from amnestic mild cognitive impairment (MCI), the amnestic syndrome (previously called the Korsakoff syndrome), and single focal brain lesions. Requiring impairment in functional activity also distinguishes it from MCI, although this interpretation is controversial. The requirement for intact attention and alertness distinguishes it from delirium. The *Diagnostic and Statistical Manual of Mental Disorders, version 5*, has recently proposed replacing the word "dementia" with the phrase "neurocognitive disorder" to destigmatize the syndrome. However, opponents point out that the term "neurocognitive disorder" lacks specificity because it includes other categories of cognitive impairment, such as intellectual disability, learning disabilities, and delirium.

Dementia is a syndrome rather than a specific illness; the most common types are Alzheimer disease (AD), vascular dementia, Lewy body dementia, and frontotemporal dementia. One or 2% of these patients presenting with dementia has a potentially reversible disorder, such as normal pressure hydrocephalus, medication-induced cognitive impairment, hypothyroidism, or major depression.

Although it can begin at any age after childhood, dementia is predominantly a syndrome of later life, with the prevalence in persons older than 65 years estimated to be 9%–13%. The annual incidence rate is 0.25% at age 65 and doubles every 5 years, reaching approximately 15% at age 95 (1).

Caring for patients with dementia is a heavy emotional and financial burden for families and society as a whole. Patients can be cared for initially in the home, but institutionalization is ultimately required for many patients—67% die in nursing homes (2). Depending on the methods used to value informal care, the yearly per-person cost attributable to dementia ranged between $41 689 and $56 290 in 2010 (3).

Although most forms of dementia currently have no cure, research findings and accumulated clinical experience support a set of practices that maximizes the function and well-being of patients with dementia and their families. This approach incorporates a broad range of practices, including comprehensive diagnostic assessment, optimization of treatment for general medical conditions, attention to patient comfort and quality of life, pharmacotherapy, control of psychiatric symptoms, and education and support of the patient's family.

1. Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. Am J Public Health. 1998;88:1337-42. [PMID: 9736873]
2. Mitchell SL, Teno JM, Miller SC, Mor V. A national study of the location of death for older persons with dementia. J Am Geriatr Soc. 2005;53:299-305. [PMID: 15673356]
3. Hurd MD, Martorell P, Delavande A, Mullen KJ, Langa KM. Monetary costs of dementia in the United States. N Engl J Med. 2013;368:1326-34. [PMID: 23550670] doi:10.1056/NEJMsa1204629
4. Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. Lancet Neurol. 2011;10:819-28. [PMID: 21775213] doi:10.1016/S1474-4422(11)70072-2

Prevention

What medical interventions or health behaviors can help patients prevent dementia or cognitive decline?

Although the different types of dementia have several risk factors, data supporting the effectiveness of specific preventive measures to address them are limited.

A 2011 meta-analysis identified 7 potentially modifiable risk factors for AD and calculated a population attributable risk (PAR) and CI for each in the United States: physical inactivity (PAR = 21% [95% CI, 5.8–36.6]), depression (PAR = 14.7% [CI, 9.6–20.3]), smoking (PAR = 10.8% [CI, 3.0–19.8]), midlife hypertension (PAR = 8.0% [CI, 2.2–15.1]), midlife obesity (PAR = 7.3% [CI, 4.3–10.8]) , cognitive inactivity or low educational

attainment (PAR = 7.3% [CI, 4.4–10.3]), and diabetes mellitus (PAR = 3.3% [CI, 1.5–5.4]) (4).

However, the National Institutes of Health sponsored a panel report published in the same year concluding that "Currently, insufficient evidence exists to draw firm conclusions on the association of any modifiable factors with the risk of AD" (5). Because avoiding or ameliorating the risk factors for dementia provides other health benefits, it seems prudent to advise patients to address these risk factors for the potential benefit of lowering the risk for AD. Patients should also be advised to minimize risk for head trauma by using seat belts in automobiles and helmets for contact sports and riding a bicycle or motorcycle.

What medications can be used in patients presenting with signs of dementia?

Clinicians should regularly review the medications of elderly patients and minimize use of those that can cause cognitive impairment, particularly benzodiazepines, anticholinergics, barbiturates, and other sedative-hypnotics. Several studies have shown that elderly patients taking benzodiazepines or other sedative-hypnotics perform more poorly on cognitive tests than those not taking these medications (6).

Significant epidemiologic evidence links mid-life estrogen use to a lower incidence of dementia later in life (7). However, in prospective prevention trials, including the large Women's Health Initiative Memory Study (WHIMS), use of estrogen plus progestin for prevention of dementia was associated with an increased incidence of dementia and other medical complications (8).

*The WHIMS was a placebo-controlled, randomized, controlled trial of estrogen plus progestin (*n *= 2229) versus placebo (*n *= 2303) for prevention of dementia in women aged 65 years and older. Use of estrogen for a mean of 4 years was associated with a relative risk of 2.05 (CI, 1.21–3.48) for dementia during the study period.*

Ginkgo biloba did not prevent dementia in one prospective trial (9).

Screening

Should clinicians screen for dementia?

Universal screening for dementia is not recommended (10), but the disorder is prevalent and often goes undetected in the primary care setting (11).

In a study reviewing the primary care records of 297 patients, dementia in 65% of patients meeting the criteria was not noted on the patient's chart, including 20% of those with advanced dementia (11). In a retrospective review of 1489 patients referred to a memory disorders program, those referred from a dementia screening program had a mean Mini-Mental Status Examination (MMSE) score of 20.8 ± 5.7 compared with those referred from their physicians (18.8 ± 6.6), from families (16.8 ± 6.6), or from other sources (15.3 ± 7.1) (11).

As a result, the clinician should consider dementia in the differential diagnosis of adult patients of any age with symptoms of memory difficulty interfering with daily function, unexplained functional decline, deterioration in hygiene, questionable adherence to medication regimens, or new-onset psychiatric symptoms.

What methods should clinicians use when looking for dementia?

When elderly patients are being evaluated for dementia, clinicians should use a standardized screening instrument together with a brief history from the patient and a knowledgeable informant. The screening instrument should be easy to use, highly sensitive, widely available, and supported by

5. Daviglus ML, Plassman BL, Pirzada A, Bell CC, Bowen PE, Burke JR, et al. Risk factors and preventive interventions for Alzheimer disease: state of the science. Arch Neurol. 2011;68:1185-90. [PMID: 21555601] doi:10.1001/archneurol.2011.100
6. Larson EB, Kukull WA, Buchner D, Reifler BV. Adverse drug reactions associated with global cognitive impairment in elderly persons. Ann Intern Med. 1987;107:169-73. [PMID: 2886086]
7. Zandi PP, Carlson MC, Plassman BL, Welsh-Bohmer KA, Mayer LS, Steffens DC, et al; Cache County Memory Study Investigators. Hormone replacement therapy and incidence of Alzheimer disease in older women: the Cache County Study. JAMA. 2002;288:2123-9. [PMID: 12413371]
8. Shumaker SA, Legault C, Rapp SR, Thal L, Wallace RB, Ockene JK, et al; WHIMS Investigators. Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: the Women's Health Initiative Memory Study: a randomized controlled trial. JAMA. 2003;289:2651-62. [PMID: 12771112]
9. DeKosky ST, Williamson JD, Fitzpatrick AL, Kronmal RA, Ives DG, Saxton JA, et al; Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for prevention of dementia: a randomized controlled trial. JAMA. 2008;300:2253-62. [PMID: 19017911] doi:10.1001/jama.2008.683
10. U.S. Preventive Services Task Force. Screening for cognitive impairment in older adults. Rockville, MD: Agency for Healthcare Research and Quality; 2014. Accessed at www.uspreventiveservicestaskforce.org/uspstf14/dementia/dementiasumm.htm on 5 May 2014.

population data relevant to the patient in question. The MMSE (12) has been widely used but is now copyrighted. Alternatives include the Mini-Cog (13), the St. Louis University Mental Status Exam (SLUMS) (14), and the Montreal Cognitive Assessment (MoCA) (15). The Mini-Cog has the benefit of brevity, the SLUMS is most similar to the MMSE (16), and the MoCA has the best sensitivity but lower specificity (17). An alternative instrument is the Informant Questionnaire on Cognitive Decline in the Elderly (IQ CODE), which can be filled out by a family member or other informant who knows the patient well (18).

Prevention and Screening... Use of benzodiazepines, anticholinergics, barbiturates, and other sedative-hypnotics must be minimized in elderly patients. Screening for dementia in the elderly population is not recommended, but in selected patients a brief history from the patient and a knowledgeable informant together with a standardized instrument, such as the MMSE, the Mini-Cog, the SLUMS, or the MoCA, can be used to decide whether a more extensive evaluation is necessary.

CLINICAL BOTTOM LINE

Diagnosis

What elements of the history are especially important in evaluating patients with suspected dementia?

Clinicians should use the patient's history to characterize the cognitive deficits, generate a differential diagnosis, and determine the cause of the dementia. This goal is best accomplished by identifying medical, neurologic, and psychiatric signs and symptoms that may be clues to the cause of the cognitive problems and establishing their order of appearance, severity, and associated features. In the case of cognitive difficulties, it is most important to try to obtain collateral information from a knowledgeable informant, because cognitive dysfunction can impair the patient's ability to report accurately. It is often easier to collect this information without the patient present.

In taking the history, the physician must be knowledgeable about the differential diagnosis and natural history of the most common types of dementia (Appendix Table, available at www.annals.org). For example, in classic AD, early symptoms are dominated by difficulties with short-term memory, subtle language and visuospatial perceptual problems, and changes in executive function. Significant reductions in efficiency and organizational abilities that the patient may or may not recognize could also occur. Symptoms begin insidiously and are slowly progressive. The overall level of alertness remains unimpaired. Patients or families may not label these difficulties as memory problems but may instead report conversations when the patient has no recollection of previous discussions, increased forgetfulness that causes the patient to lose objects or become confused while shopping, or simply increased disorganization and decreased efficiency. Symptoms are often first noticed or reported at the time of a life change, such as the death of a spouse, a move into a new residence, or being in an unfamiliar place on vacation. Table 1 describes the diagnostic criteria of the National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer's Disease

11. Valcour VG, Masaki KH, Curb JD, Blanchette PL. The detection of dementia in the primary care setting. Arch Intern Med. 2000;160:2964-8. [PMID: 11041904]
12. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189-98. [PMID: 1202204]
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14. Saint Louis University School of Medicine. Saint Louis University Mental Status Examination. St. Louis: Saint Louis University School of Medicine. Accessed at http://aging.slu.edu/index.php?page=saint-louis-university-mental-status-slums-exam on 7 May 2014.

Table 1. Diagnostic Criteria for Different Kinds of Alzheimer Disease*

Probable Alzheimer disease is defined by:
Dementia established by clinical examination and documented by an instrument, such as the MoCA, SLUMS or Mini-Mental Status Examination
Deficits in 2 or more areas of cognition, one of which is usually memory
Progressive decline
No disturbance of consciousness
Onset between age 40–90 years
Absence of other disorders that could account for the deficits
Possible Alzheimer disease is defined by:
Dementia established by clinical examination and documented by an instrument, such as the Mini-Mental Status Examination
Absence of other conditions that would cause dementia
Variations in the clinical course from the typical course of Alzheimer disease; when another condition is present that could cause dementia but is not felt to be the primary cause; or when there is a single, severe, progressive cognitive deficit without an identifiable cause
Definite Alzheimer disease is defined by:
The presence of clinical criteria for probable Alzheimer disease combined with biopsy- or autopsy-confirmed histopathology.
The diagnosis of probable Alzheimer disease is supported by the presence of:
Specific cognitive deficits, such as executive dysfunction, aphasia, agnosia, and apraxia
Impaired activities of daily living
Positive family history
Supportive laboratory tests, such as normal lumbar puncture, normal electroencephalography, and cerebral atrophy on neuroimaging
The diagnosis of Alzheimer disease is unlikely when:
The onset is acute
Focal neurologic findings are present
Seizure or gait disturbance is present early in the disease course

**Adapted from reference 25.*

and Related Disorders Association Work Group (19, 20).

Clinicians evaluating a patient with a change in cognition or overall function must consider delirium. Delirium is characterized by cognitive impairment and an impaired level of alertness/attention/consciousness. In contrast to dementia, the onset of delirium is usually abrupt, and fluctuations over minutes or hours are prominent. Although some patients may be agitated and manifest psychotic symptoms, others are slow and drowsy and appear mildly depressed or withdrawn. Prompt diagnosis of delirium is critical because it usually reflects an underlying systemic condition, such as infection, metabolic derangement, medication effect, or cancer. Use of an instrument, such as the Confusion Assessment Method, increases identification of delirium in high-risk settings, such as the intensive care unit (21). It is important to remember that many elderly patients report minor cognitive problems, such as mild forgetfulness, difficulty remembering names, and reduced concentration. These problems are typically sporadic, do not worsen significantly over time, are easily compensated for, do not affect function, and are often judged to be worse by the patient than by others. In contrast, early dementia insidiously becomes a pattern; worsens over time; is difficult to offset; eventually interferes with routine activities, such as bill paying and meal preparation; and is often judged to be worse by others than by the patient. Patients with memory problems should be screened for

15. Nasreddine Z. Montreal Cognitive Assessment. Greenfield Park, Québec, Canada: Center for Diagnosis & Research on Alzheimer's Disease; 2014. Accessed at www.mocatest.org on 7 May 2014.
16. Tariq SH, Tumosa N, Chibnall JT, Perry MH 3rd, Morley JE. Comparison of the Saint Louis University Mental Status Examination and the Mini-Mental State Examination for detecting dementia and mild neurocognitive disorder—a pilot study. Am J Geriatr Psychiatry. 2006;14:900-10. [PMID: 17068312]
17. Roalf DR, Moberg PJ, Xie SX, Wolk DA, Moelter ST, Arnold SE. Comparative accuracies of two common screening instruments for classification of Alzheimer's disease, mild cognitive impairment, and healthy aging. Alzheimers Dement. 2013;9:529-37. [PMID: 23260866] doi:10.1016/j.jalz.2012.10.001
18. Jorm AF. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): a review. Int Psychogeriatr. 2004;16:275-93. [PMID: 15559753]
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20. McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement. 2011;7:263-9. [PMID: 21514250] doi:10.1016/j.jalz.2011.03.005

Laboratory Studies for Patients Being Evaluated for Cognitive Problems*

Comprehensive metabolic profile
Complete blood count
Thyroid-stimulating hormone level
Vitamin B_{12} level
In addition, patients may need to undergo additional tests, including the following:

- Rapid plasma reagin (fluorescent treponemal antibody can be checked in cases where concern for neurosyphilis is higher)
- HIV test
- Toxicology screen
- Erythrocyte sedimentation rate
- Heavy metal screen
- Thiamine level
- Paraneoplastic panel
- Chest radiograph or computed tomography of the chest
- Urinalysis

*Adapted from references 22 and 23.

dementia, but a complete evaluation should be reserved for those with measurable impairment in memory or other aspects of cognition.

How should clinicians evaluate the physical, mental, and cognitive status of patients with suspected dementia?

During the physical examination, the clinician should look for conditions that can cause or worsen cognitive symptoms (Appendix Table, www.annals.org), with an emphasis on vascular and neurologic disease. The examination should include a mental status evaluation that begins with an assessment of the patient's level of alertness, general appearance, and cooperation, which can provide clues to delirium, depression, or nutritional deficiencies. Speech should be evaluated for its content (grammatical or semantic errors) and form (rate, fluency, and volume); the patient's mood and affect should be assessed for depression, anxiety or mania, and the risk for suicide; and thought content and perception should be examined for delusions or hallucinations and obsessions or compulsions.

The cognitive examination should include a standard instrument, such as the SLUMS, which takes 5 minutes to administer, or the MOCA, which can take 10 minutes. Both tests have strengths and limitations. The MOCA emphasizes executive function and is more sensitive; the SLUMS evaluates orientation, immediate recall, concentration, naming, language function, praxis, and visual–spatial perception. Naming and praxis can be further tested by asking the patient to name a series of common and uncommon objects and by asking them to demonstrate tasks, such as brushing hair or teeth or slicing bread. Abstract reasoning and judgment should be tested by asking for solutions to real-life problems, such as what to do if one smells smoke in the house, or by having the patient interpret proverbs or similes. Asking the patient to draw a clock and put the hands at 10 minutes past 11 is a quick test of visual-spatial perception, praxis, and planning ability. Also, the patient should be evaluated for corticosensory deficits, such as neglect or left–right confusion.

What laboratory tests are helpful in the evaluation of any patient with cognitive dysfunction?

According to guidelines from the American Academy of Neurology, patients who are evaluated for cognitive problems should have a laboratory evaluation for common medical disorders, with selected additional studies depending on the specific clinical situation (see the Box: Laboratory Studies for Patients Being Evaluated for Cognitive Problems).

When should clinicians order imaging studies and other, more specialized laboratory studies?

Patients with cognitive difficulties less than 3 years in duration should have a neuroimaging study of the head using computed tomography or magnetic resonance imaging to exclude cerebrovascular disease, hemorrhage, tumor, abscess, Creutzfeldt-Jakob disease, and hydrocephalus. The yield is higher in patients with early age of onset; rapid progression; focal neurologic deficits; risk factors for cerebrovascular disease; recent falls; central nervous system (CNS) infection; unexplained fluctuation of consciousness; or symptoms atypical of AD, such as early and marked personality change. Routine use of glucose or amyloid positron emission tomography scanning is not recommended, although these tests may be useful in certain cases, such as differentiating frontotemporal dementia from AD and in assessing for early-onset dementia (24, 25).

Genetic studies are not indicated in the evaluation of dementia

21. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in mechanically ventilated patients: validity and reliability of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). JAMA. 2001;286:2703-10. [PMID: 11730446]
22. Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey-Bloom J, Relkin N, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56:1143-53. [PMID: 11342678]
23. Massoud F, Devi G, Moroney JT, Stern Y, Lawton A, Bell K, et al. The role of routine laboratory studies and neuroimaging in the diagnosis of dementia: a clinicopathological study. J Am Geriatr Soc. 2000;48:1204-10. [PMID: 11037005]

unless there is a specific concern about Huntington disease. Current evidence does not support routine testing for the *ApoE4* allele (26). Testing for the autosomal dominant gene mutations found in patients with familial AD or fronto-temporal dementia should be considered only if multiple family members are affected, the clinical picture and workup support one of these disorders, and the patient is younger than 60 years at onset. Genetic counseling is recommended before genetic testing (26).

Other tests should be reserved for specific situations. Electroencephalography may be useful if there is a question of delirium, seizures, encephalitis, or Creutzfeldt–Jakob disease. Lumbar puncture may be indicated in patients younger than 55 years and in those with rapidly progressive dementia; a positive rapid plasma reagin; and if acute or chronic CNS infection, the paraneoplastic syndrome, CNS cancer, or immunosuppression is possible. Neuropsychological testing provides the most comprehensive assessment of cognitive function and is particularly useful if the diagnosis of dementia is uncertain (27) or a precise characterization of the patient's cognitive impairment is necessary.

What other disorders should clinicians consider in the assessment of cognitive dysfunction?

During assessment of patients with cognitive disturbances, they should be evaluated for not only the most common disorders that cause dementia but also medications, depression, and MCI. Patients with MCI (28) have cognitive decline without impaired function and should be followed closely, because 7% to 15% "convert" each year and meet the criteria for dementia; after 5 years, nearly 50% of patients with MCI meet dementia criteria (28).

Diagnosis... Patients who report cognitive and functional decline should be evaluated through a detailed history of medical, neurologic, and psychiatric symptoms from the patient and a knowledgeable informant. They should also be given a thorough physical and mental status evaluation and a cognitive examination. Whether to obtain basic laboratory studies and additional studies, including structural neuroimaging, is dictated by the clinical presentation.

CLINICAL BOTTOM LINE

Treatment

What should clinicians advise patients and caregivers about general health and hygiene?

In the early stages of dementia, patients may have difficulty comprehending the details of their medical care, organizing care, and keeping track of appointments and medications. The clinician should be alert to these limitations and prepare a care plan that compensates for them. Later in the illness, patients may be unable to identify symptoms, such as constipation, dysuria, tooth pain, or diminished visual or auditory acuity, and the clinician should proactively look for these problems.

It is important to attend to general medical and preventive care as conscientiously as in patients without dementia. A stroke or heart attack due to uncontrolled

24. Foster NL, Heidebrink JL, Clark CM, Jagust WJ, Arnold SE, Barbas NR, et al. FDG-PET improves accuracy in distinguishing frontotemporal dementia and Alzheimer's disease. Brain. 2007;130:2616-35. [PMID: 17704526]
25. Johnson KA, Minoshima S, Bohnen NI, Donohoe KJ, Foster NL, Herscovitch P, et al; Amyloid Imaging Task Force of the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging. Update on appropriate use criteria for amyloid PET imaging: dementia experts, mild cognitive impairment, and education. Amyloid Imaging Task Force of the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging. Alzheimers Dement. 2013;9:e106-9. [PMID: 23809369] doi:10.1016/j.jalz.2013.06.001
26. Loy CT, Schofield PR, Turner AM, Kwok JB. Genetics of dementia. Lancet. 2014;383:828-40. [PMID: 23927914] doi:10.1016/S0140-6736(13)60630-3
27. Schmand B, Rienstra A, Tamminga H, Richard E, van Gool WA, Caan MW, et al. Responsiveness of magnetic resonance imaging and neuropsychological assessment in memory clinic patients. J Alzheimers Dis. 2014;40:409-18. [PMID: 24473187] doi:10.3233/JAD-131484
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hypertension is likely to impair a patient's function and quality of life as much as the dementia itself, at least in the early and middle stages of the disease. Thus, caring for patients with dementia includes careful attention to basic general health practices, including good control of hypertension, diabetes, and cholesterol; antiplatelet therapy where appropriate; and vaccinations. For patients with more advanced dementia, it becomes increasingly important to pay attention to nutrition, skin care (particularly of the perineum), toileting schedules, and dental care.

What should clinicians advise about safety issues, such as driving, cooking, and other activities that may require supervision?

Patients with progressive dementia ultimately lose the ability to drive, but predicting when an individual patient should stop driving is difficult, particularly if the restriction significantly burdens the patient or family members. Nonetheless, addressing the issue is imperative, as numerous studies have shown that driving ability becomes impaired in early stages of the disease.

The patient should be asked about recent motor vehicle accidents, near misses, and changes in driving ability. These inquiries should be made in a setting that facilitates an open exchange of information and may necessitate meeting with an informant without the patient present. Patients with early dementia whose driving ability has already deteriorated should be instructed to stop driving immediately. Those with early dementia who have no history of driving problems should undergo a driving evaluation through the local motor vehicle administration (MVA) or an occupational therapy program at a local hospital. If no impairment in driving is evident and the patient continues to drive, the history should be updated regularly to determine whether the capacity to drive has deteriorated. State laws differ in regard to reporting patients with a diagnosis of dementia to local MVAs, and the clinician should be familiar with the applicable regulations. The American Academy of Neurology Evidence-Based Practice Parameter outlines an approach to assessing driving in patients with dementia (29).

In a prospective, case–control study using the Washington University Road Test, which has an off-road and on-road component, only 3% of controls failed the test, 19% of patients with very mild AD failed, and 41% with mild AD failed (P< 0.001). Previous driving experience did not protect against failure (30).

A physician-directed recommendation can have beneficial and adverse outcomes. For example, a Canadian study of what happened when physicians recommended that patients discontinue driving for a variety of disorders reported a 45% reduction in road crashes (4.76 vs. 2.73) (P<0.001), a decrease in return visits to the physician, and an increase in visits to emergency departments for depression (31).

Clinicians should assess other safety issues with the patient and family on an ongoing basis. Patients with progressive dementia eventually are unable to administer medications; cook; or use power tools, lawnmowers, or firearms. Home-safety assessments by home therapists can determine which activities are still safe and which need to be limited or supervised. An activity can often be modified to allow ongoing participation in a safe fashion, such as cooking or gardening together with a family member or friend. Wandering from home is fairly common, presents significant safety concerns, and must be assessed regularly.

29. Iverson DJ, Gronseth GS, Reger MA, Classen S, Dubinsky RM, Rizzo M; Quality Standards Subcomittee of the American Academy of Neurology. Practice parameter update: evaluation and management of driving risk in dementia: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2010;74:1316-24. [PMID: 20385882] doi:10.1212/WNL.0b013e3181da3b0f
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What should clinicians advise about nonpharmacologic approaches to sleep problems, behavioral problems, and psychiatric manifestations of dementia?

Psychiatric symptoms, such as depression, anxiety, sleep problems, agitation, hallucinations, and delusions, are common and often require intervention (32). Various nonpharmacologic approaches are effective and should be tried first unless the symptoms are causing immediate danger or marked distress (33). These approaches emphasize the notion that many emotional and behavioral disturbances can be "decoded" or understood in terms of internal or environmental factors that make them more or less likely to occur. This decoding process should be done using systematic approaches, such as 4-D or DICE (34, 35) (Table 2). Decoding involves describing the behavior in detail and noting its characteristics, including the time of day, location, antecedent factors, people present and absent, proximity to eating or other key activities, and the consequences of the behavior. Common examples of environmentally driven behavioral disturbances include agitation when the patient is hungry, tired, under pressure to perform, in pain, or lonely. Common examples in the institutional setting include agitation when personal care is being provided, during shift changes, and in the presence of specific staff members. When patterns are recognized, targeted interventions can be developed, implemented, and refined. Approaching behavioral disturbances this way can often preclude the use of psychotropic medications.

Nonpharmacologic interventions were effective in reducing behavioral and psychological symptoms (overall effect size, 0.34 [CI, 0.20–0.48]; P=0.01) and improving caregiver reactions to these behaviors (overall effect size, 0.15 [CI, 0.040.26]; P=0.006) (33).

When should clinicians prescribe acetylcholinesterase inhibitors and memantine to slow cognitive decline?

Acetylcholinesterase inhibitors, such as donepezil, galantamine, or rivastigmine, can be prescribed to delay cognitive decline in patients with mild, moderate, or advanced AD. These drugs are better tolerated if they are slowly titrated to reach the target dose. Memantine is approved for use in moderate-to-advanced AD and can be used in conjunction with acetylcholinesterase inhibitors.

33. Brodaty H, Arasaratnam C. Meta-analysis of nonpharmacological interventions for neuropsychiatric symptoms of dementia. Am J Psychiatry. 2012;169:946-53. [PMID: 22952073] doi:10.1176/appi.ajp.2012.11101529
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Table 2. Approach for Assessing and Treating Behavioral and Psychiatric Disturbances*

	Define/Describe	*Decode (What Causes the Problem)*	*Devise a Treatment Plan*	*Determine Whether the Treatment Has Worked*
	What occurs and under what circumstances?	Cognitive impairment, psychiatric symptoms, medical condition, environment?		
Persistent yelling	What is being said and when is it said? What consequences result from the yelling (to the patient and others)?	Forgetfulness, fear—perhaps from psychotic symptoms, pain, shift changes, noise/other bothersome stimuli, presence/absence of particular individuals	Treat psychiatric or medical conditions, alter environment or patient placement within it, alter environment or patient placement within it, redirect, reassure, medicate	Monitor frequency of yelling following the interventions
Depressed mood	Describe patient's mood. What time of day is it exhibited? In what environment? Around which people? Are there clear precipitating events?	Frustration with forgetfulness, delirium, major depression, medications, general medical conditions, environment (recent move, departure of a caregiver, some trigger in the milieu)	Provide reassurance or distraction, treat depression—medications/electroconvulsive therapy, treat general medical conditions, adjust medications, improve patient activity regimen, adjust milieu	Monitor/document patient's mood after intervention; monitor/document side effects; identify barriers to implementation of the treatment plan

**Adapted from reference 35.*

When the benefit is unclear, the drug may be stopped but should be restarted if acute cognitive deterioration occurs. Patients and families may need help in developing realistic expectations for these agents. Side effects of cholinesterase inhibitors include nausea, diarrhea, bradyarrhythmia, syncope, weight loss, and ataxia.

One study followed 295 community-living patients who had been receiving donepezil for at least 3 months (36) and assessed outcomes at the end of 1 year. The primary outcome included standard measures of cognitive ability as determined by the Standardized MMSE and the ability to perform activities of daily living as measured by the Bristol Activities of Daily Living Scale (BADLS). Patients assigned to continue donepezil, compared with those assigned to discontinue the drug, had a score on the Standardized MMSE that was higher (indicating better cognitive ability) by 1.9 points (1.4 points is the minimum clinically important difference) (CI, 1.3–2.5) and a score on the BADLS that was lower (indicating less impairment) by 3.0 points (3.5 points is the minimum clinically important difference) (CI, 1.8–4.3). Patients assigned to receive memantine instead of placebo had a score on the Standardizes MMSE that was 1.2 points higher (CI, 0.6–1.8; P<0.001) and a score on the BADLS that was 1.5 points lower (CI, 0.3–2.8; P<0.02). The differences between donepezil and memantine were not statistically significant, and adding memantine to donepezil was not better than either drug alone.

Which other pharmacologic agents are helpful in treating specific types of dementia, and in what situations should clinicians consider prescribing these agents?

The acetylcholinesterase inhibitor rivastigmine has been shown to be effective in improving cognitive performance in patients with mild-to-moderate Parkinson disease in doses similar to those used in AD, and it is believed that this benefit occurs with the other acetylcholinesterase inhibitors (37). Several trials have also shown the benefits of acetylcholinesterase inhibitor treatment for cognition in dementia with Lewy bodies (38, 39). However, use of these drugs in patients with vascular dementia is not recommended. Vitamin E has been shown to have modest benefit on function but not cognition in 2 well-designed trials of patients with dementia, and concerns about increased mortality were not substantiated (40, 41).

Which pharmacologic agents are ineffective in treating specific types of dementia and should be avoided?

The herbal supplement ginkgo biloba does not slow progression of dementia (42). Also, nonsteroidal anti-inflammatory drugs, estrogen, and ergoid mesylates should not be prescribed for cognitive decline. Data on whether the widely used food supplements coconut oil and Axona can be recommended are inadequate.

When should clinicians prescribe antidepressants in patients with dementia?

Nearly one third of patients with dementia develop an episode of major depression after the onset of dementia (43), but evidence for the efficacy of antidepressant medications is mixed (44). One explanation is that some symptoms of major depression, such as weight loss and disturbed sleep, may be produced by dementia alone and complicate the diagnosis. Clinicians therefore need to have a high index of suspicion for major depression.

When should clinicians prescribe antipsychotic agents to treat behavioral disturbances or psychotic symptoms, and what are their side effects?

Absent a significant risk for harm, psychotic symptoms, such as hallucinations, delusions, and agitated behavior, should first be treated nonpharmacologically (33) because all drugs in this class carry a risk for elevated mortality (1.6–2.0 in the subsequent 12–52 weeks) (45-48). Pharmacotherapy is indicated if symptoms are causing significant

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42. Schneider LS, DeKosky ST, Farlow MR, Tariot PN, Hoerr R, Kieser M. A randomized, double-blind, placebo-controlled trial of two doses of Ginkgo biloba extract in dementia of the Alzheimer's type. Curr Alzheimer Res. 2005;2:541-51. [PMID: 16375657]

distress for the patient or creating a dangerous situation. The second-generation antipsychotic agents are usually recommended instead of first-generation agents because of a lower risk for tardive dyskinesia. Overall, the efficacy of these agents is modest (46). Although more evidence supports the use of risperidone and olanzapine, similar drugs also are used. These drugs should be prescribed at the lowest possible dose and for the shortest possible time. Ongoing use should be monitored regularly, and attempts should be made to decrease the dose and discontinue the drug within 3 months of starting. They should not be routinely used only for sleep due to toxicity (Table 3). The U.S. Food and Drug Administration requires black-box warnings for second-generation antipsychotics because of increased rates of death and cerebrovascular events. The reasons for these bad outcomes are unclear, but falls, infections, and cardiovascular and cerebrovascular events may contribute. In addition, treatment with antipsychotic medications is associated with the metabolic syndrome, weight gain, hyperlipidemia, and diabetes mellitus. Recent evidence supports the effectiveness and relative safety of nonpharmacologic interventions for neuropsychiatric and behavioral symptoms (33), which reinforces the recommendations to use drugs sparingly for these symptoms. However, head-to-head trials of pharmacologic and nonpharmacologic interventions have not been done.

Which drugs should clinicians use to treat sleep problems?

Clinicians should try nonpharmacologic methods before using medications in patients with dementia who have insomnia because of the potential risks associated with sedative-hypnotics in this population. Careful attention should be paid to sleep environment, caffeine consumption, daytime sleeping, afternoon and evening medications, and other elements of basic sleep hygiene. Meta-analyses do not support the efficacy of any pharmacologic

43. Zubenko GS, Zubenko WN, McPherson S, Spoor E, Marin DB, Farlow MR, et al. A collaborative study of the emergence and clinical features of the major depressive syndrome of Alzheimer's disease. Am J Psychiatry. 2003;160:857-66. [PMID: 12727688]
44. Brodaty H. Antidepressant treatment in Alzheimer's disease. Lancet. 2011;378:375-6. [PMID: 21764117] doi:10.1016/S0140-6736(11)61031-3
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Table 3. Cognitive Agents for Alzheimer Disease*

Agent	*Mechanism of Action*	*Dosage*	*Benefits*	*Side Effects*	*Notes*
Donepezil	Acetylcholinesterase inhibition	Begin 5 mg/d; if tolerated, increase to target dose of 10 mg/d after 1 month	Delayed symptom progression in mild, moderate, and advanced Alzheimer disease	Nausea, vomiting, diarrhea, anorexia, syncope	The higher end of the dosing range may be harder for patients to tolerate; dose higher than 10mg not recommended
Galantamine	Acetylcholinesterase inhibition	Start 4 mg twice daily; target dose total 24 mg/d; increase by 4 mg twice daily every 1 month until in target range	Delayed symptom progression in mild, moderate, and advanced Alzheimer disease; improvement in caregiver rated quality of life was observed	Nausea, vomiting, diarrhea, anorexia, syncope	Routine liver function testing is unnecessary; the higher end of the dosing range may be harder for patients to tolerate; begin extended-release (once daily) galantamine at 8 mg/d; increase by 8 mg/d every 1 month to the target dose of 24 mg/d; higher dose not recommended
Rivastigmine	Acetylcholinesterase inhibition	Start 1.5 mg twice daily; target range is 6–12 mg/d; increase by 1.5 mg twice daily every 1 month until in target range	Delayed symptom progression in mild, moderate, and advanced Alzheimer disease	Nausea, vomiting, diarrhea, anorexia, syncope	Higher end of the dose range may be less tolerable tolerate; also available as a transdermal patch
Memantine	NMDA-receptor antagonism	Begin 5 mg/d, increase by 5 mg/d every 1 month until target of 10 mg twice daily	Less functional decline, improved cognition, and reduced demands on caregivers in moderate-to-advanced Alzheimer disease	Dizziness, confusion, headache, constipation	Generic available; branded drug only available in sustained-release form; available in tablets or solution; avoid concomitant use with amantadine

**NMDA = N-methyl-d-aspartic acid.*

intervention. If necessary, 25–50 mg of trazodone can be used with cautious monitoring (49).

What other steps should clinicians take to maximize quality of life?

Clinicians should proactively address issues that have the potential to significantly affect quality of life. Examples include the working order of sensory aids, such as glasses and hearing aids; dental care; noise, lighting, and temperature; sufficient social and cognitive stimuli; cleanliness; pain levels; and constipation.

Advance directives have the potential to benefit all patients. Since full incapacitation is inevitable for every person with progressive dementia who lives long enough to experience the full course of the disease, early advance directives maximize the likelihood that the person's wishes for end-of-life care will be carried out.

When should clinicians consult a neurologist, psychiatrist, or other professional?

Clinicians should consider consulting a geriatric psychiatrist, neurologist, geriatrician, or dementia specialist in patients with atypical features of dementia, such as early onset, early noncognitive neurologic symptoms, rapid progression, early personality changes, or unusual symptom patterns. Consulting a geriatric psychiatrist or dementia specialist should also be considered for evaluation or management of difficult-to-treat neuropsychiatric symptoms, such as depression, psychosis, or behavioral disturbances. These symptoms can create dangerous situations for the patient and others and reduce quality of life. Consulting a specialist should also be considered if patients require physical retraint. Referral to a neuropsychologist may be necessary if it is unclear whether dementia is present and when in-depth documentation of impaired and preserved capacities would benefit the patient.

Treatment of dementia requires a broad clinical approach that ideally includes preventive medicine, psychoeducation, behavioral therapy, safety evaluation, and pharmacotherapy. The clinician should expect to interact with a broad range of professionals, including occupational therapists, social workers, physical therapists, and speech and language pathologists, to provide optimal care.

When should clinicians recommend hospitalization?

During the assessment of cognitive impairment, hospitalization should be considered for patients who cannot be evaluated safely or comprehensively as outpatients because of dangerous behavior, unsafe living conditions, compromised nutrition, neglected medical conditions, or lack of cooperation. In addition to safety issues, hospitalization can facilitate thorough history-taking, neuroimaging, other diagnostic studies, neuropsychological evaluation, safety evaluation by occupational therapists, and future care planning.

Psychiatric hospitalization is sometimes required because of the severity of psychiatric symptoms. For example, hospitalization should be considered for depressed patients who exhibit suicidality, decreased food and fluid intake, delusions, depression, immobility, inability to attend to medical conditions, or need for electroconvulsive therapy. Patients with behavioral disturbances who are dangerous to themselves or who cannot be treated safely or successfully as an outpatient because of wandering, violence, calling out, hyperphagia, or a severely disordered sleep–wake cycle, should also be hospitalized. Patients with psychotic hallucinations and delusions may require hospitalization if they do not respond to outpatient treatment,

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48. Gill SS, Bronskill SE, Normand SL, Anderson GM, Sykora K, Lam K, et al. Antipsychotic drug use and mortality in older adults with dementia. Ann Intern Med. 2007;146:775-86. [PMID: 17548409]
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require the addition of multiple medications, are in distress or having behavioral disturbances, or present a risk to others. Involuntary commitment may be required in any of these situations.

How can clinicians help families decide to move a patient with dementia into a long-term care facility?

As dementia progresses, moving to an environment that can adequately address the progressive needs of the patient with dementia is often necessary, either to an assisted-living facility or to a nursing home (50). Some patients may need to move because of inadequate support at home. Generally, a move into a nursing home is prompted by development of physical and cognitive limitations that cannot be managed at home, such as the need for full assistance with transferring, ambulation, toileting, or feeding. Other patients have to move because of unmanageable psychiatric symptoms or high caregiver burden (51).

Families with ample financial resources may be able to provide many services at home that usually are provided in a facility. Periods of respite care may help families delay placement. Families should be supported and guided through the difficult and painful decision-making process. Families may be advised to proactively investigate facilities in their region so a good decision can be made quickly—for example, because of a sudden change in functional ability after a medical illness or accident.

What caregiver needs should be addressed by the clinician?

Caregiving for a patient with dementia is extremely taxing, both physically and emotionally, and inquiring about caregiver well-being is a critical component of dementia care. Common caregiver symptoms include guilt, anger, grief, fatigue, loneliness, demoralization, and depression. The patient's symptoms and the demands on the caregiver change over time, so the well-being of the caregiver must be assessed at every visit.

Most caregivers benefit from a range of interventions (33) that focus on education about dementia, skills training, and the caregiver's own well-being. Many pamphlets, books, and educational Web sites are available. Patient and caregiver safety must be evaluated at each follow-up visit, and caregivers need to be informed about local respite programs and supported in long-term planning.

Caregivers should also be informed of the potential benefits of psychoeducational and other support groups, which are available in most areas. Several large, well-conducted trials have shown that groups with a focus on problem-solving, communication, management of behavioral disturbances, and emotional support were effective in delaying nursing home placement for up to 1 year, diminishing caregiver and patient depression, and reducing patient agitation and anxiety (52-54).

What are the options for end-of-life care?

Hospice criteria for persons with dementia are specific to dementia. Therapy for pain, neuropsychiatric symptoms, and supportive medical care are paramount. Consider discontinuation of medications that have no short-term benefit, such as cholesterol-lowering agents (55, 56).

52. Teri L, Logsdon RG, Uomoto J, McCurry SM. Behavioral treatment of depression in dementia patients: a controlled clinical trial. J Gerontol B Psychol Sci Soc Sci. 1997;52:P159-66. [PMID: 9224439]
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Treatment... A broad approach that addresses comfort and quality of life, cognitive enhancement, stabilization of psychiatric symptoms, and caregiver well-being needs to be adopted. Patients with AD can be treated with acetylcholinesterase inhibitors, and memantine can be added for patients with moderate-to-severe AD. It is important to identify and treat psychiatric symptoms, such as depression, psychosis, anxiety, and behavioral disturbances with both behavioral and pharmacologic treatment to minimize risk factors for cerebrovascular disease and to treat any other conditions that could reduce cognition. Attending to safety issues, regular monitoring of the caregiver's well-being, and suggesting referral to support groups and other psychoeducational activities are also important.

CLINICAL BOTTOM LINE

In the Clinic Tool Kit

Dementia

ACP Smart Medicine Module

http://smartmedicine.acponline.org/content.aspx?gbosID=164

Access the American College of Physicians Smart Medicine module on dementia.

Patient Information

http://psychiatryonline.org/pdfaccess.ashx?ResourceID=243205&PDFSource=6

American Psychiatric Association practice guideline for the treatment of patients with Alzheimer disease and other types of dementia.

www.alz.org

www.alz.org/care/overview.asp

Information from the Alzheimer's Association

www.caregiver.org

Help for caregivers from the National Caregiver Alliance.

www.nia.nih.gov/Alzheimers/

Alzheimer's Disease Education and Referral Center (ADEAR) (1-800-438-4380)

Clinical Guidelines

www.guideline.gov/summary/summary.aspx?doc_id=3690

2014 guideline from the U.S. Preventive Services Task Force guideline on screening for cognitive decline in older adults.

https://www.aan.com/Guidelines/Home/ByTopic?topicId=15

American Academy of Neurology guidelines on diagnosing Creutzfeldt-Jakob disease, assessing driving risk in patients with dementia, early detection of dementia and mild cognitive impairment, and diagnosis of dementia.

WHAT YOU SHOULD KNOW ABOUT DEMENTIA

What is dementia?

Dementia is a group of symptoms related to impaired memory and thinking skills. People with dementia begin to forget things and can have problems with everyday tasks. There are different types of dementia. Dementia symptoms usually start slowly and get worse over time.

What are the symptoms?

- Forgetting things more and more often
- Trouble with familiar activities, like making a meal or a phone call
- Having trouble finding the right words
- Poor judgment, such as leaving the house with no coat in the winter
- Misplacing things or putting things in unusual places, such as keys in the refrigerator
- Personality changes, such as becoming very confused, suspicious, fearful, or dependent
- Unable to follow instructions, such as taking medications
- Unexplained weight loss
- New onset of depression or anxiety

How is it diagnosed?

There is no one specific test for dementia. If a doctor thinks a patient may have dementia, they will review symptoms and ask about medical history. Some other tests a doctor may perform are:

- Memory test—to check memory and concentration
- Neurologic examination—to check for problems that may indicate a brain disorder. A doctor will test things like speech, reflexes, and coordination.
- Brain scans—like MRI or CT scans.
- Laboratory blood tests—which can rule out problems that may cause symptoms similar to dementia.

How is it treated?

There are treatments that may help to manage different symptoms of dementia. These may help people with dementia think better and slow down the worsening of symptoms. Behavior changes can be treated in ways that promote comfort for the patient. For example, creating a calm environment and making sure people with dementia have enough rest can help to manage behavior symptoms. Medicines also may help these and other symptoms. Talk with a doctor for the best treatment options.

For More Information

www.acponline.org/patients_families/products/health_tips/dem_en.pdf
American College of Physicians

www.alz.org/what-is-dementia.asp
Alzheimer's Association

https://caregiver.org/node/92
Family Caregiver Alliance

www.nlm.nih.gov/medlineplus/dementia.html
Medline Plus

ACP℠
American College of Physicians
Leading Internal Medicine, Improving Lives

Patient Information

CME Questions

MKSAP
MEDICAL KNOWLEDGE Self-Assessment Program

1. A 79-year-old man is evaluated for a 1-year history of forgetfulness and not being able to remember names. He is a retired attorney. He reports no problems with performing activities of daily living, planning his day, or managing his finances. He is frustrated but not depressed and is still able to enjoy life. He has hypertension and hyperlipidemia controlled with hydrochlorothiazide and simvastatin.

   On physical examination, he is afebrile, blood pressure is 140/82 mm Hg, and pulse rate is 78/min. Mini-Mental State Examination score is 25. His lungs are clear. The heart is without murmur. Neurologic, motor, and sensory examinations are normal.

   Which of the following is the most likely diagnosis?

   A. Alzheimer disease
   B. Mild cognitive impairment
   C. Pseudodementia
   D. Vascular dementia

2. A 77-year-old woman is evaluated in the emergency department for a 1-week history of progressive agitation and confusion. She has no history of fever or falling episodes. The patient lives in a nursing home, has advanced dementia, and is dependent on others for all activities of daily living. She can indicate when she needs to void and generally is not incontinent. She can ambulate with a cane but must be accompanied because of a tendency to wander. Although she enjoys being around others and can make simple conversation with family members and nursing home personnel, she does not recognize anyone by name or remember what was said. She has a history of osteoarthritis, hypertension, atrial fibrillation, anxiety, and depression. There have been no recent additions or changes to her medications, which are hydrochlorothiazide, warfarin, amitriptyline, alprazolam, and oxybutynin.

   Physical examination is noncontributory. Results of a complete blood count, comprehensive metabolic profile, and urinalysis are normal. A chest radiograph reveals no evidence of infection or heart failure.

   Which of the following is most appropriate as an initial step in management?

   A. Add donepezil
   B. Add risperidone
   C. Discontinue anticholinergic and sedative medications
   D. Obtain an electroencephalogram

3. A 66-year-old man is evaluated for a 2-month history of odd behavior. He is a retired high school principal and has a 5-year history of Parkinson disease. According to his wife, his lifelong interest in repairing household items has lately escalated out of control. Increasingly, the patient starts new tasks he never completes; stays up all night taking apart appliances and furniture but never fixes or reassembles them, and leaves parts strewn throughout the house. The patient insists that he is making necessary repairs and will soon put everything back together. His Parkinson symptoms remain well controlled with ropinirole and levodopa-carbidopa. His motor function is generally good, and he is able to function independently.

   On physical examination, temperature is 36.7°C (98.1°F), blood pressure is 126/80 mm Hg sitting and standing, pulse rate is 72/min, and respiration rate is 16/min; BMI is 27.

   Which of the following is the most likely cause of this patient's symptoms?

   A. Dementia with Lewy bodies
   B. Dopamine agonist medication
   C. Frontotemporal dementia
   D. Progression of Parkinson disease

4. A 73-year-old woman is evaluated for short-term memory loss. She has trouble remembering names, where she placed certain items such as her keys, and occasionally what she did earlier in the day. She avoids some social situations and has lower self-esteem because of memory problems and decreased social contact, but notes no depression, low energy, or sleep disturbance. She still enjoys playing cards with her husband. She does not need help with eating, dressing, or bathing. Her hypertension is well controlled with hydrochlorothiazide. She has no history of stroke. She is concerned about her condition and wants to know if anything can be done about it.

   On physical examination, temperature is 37.2°C (98.9°F), blood pressure is 135/84 mm Hg, and pulse rate is 72/min. She is conversant with a normal range of affect. Neurologic examination is without focal deficit. The remainder of the physical examination is normal. Mini-Mental State Examination score is 26.

   Which of the following is the most appropriate management of this patient?

   A. Anticholinesterase inhibitor
   B. Cognitive rehabilitation
   C. Positron-emission tomography scan
   D. Reassurance that progression to dementia is unlikely

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