

# Early Diagnosis of Dementia

KAREN S. SANTACRUZ, M.D., and DANIEL SWAGERTY, M.D., M.P.H.  
University of Kansas Medical Center, Kansas City, Kansas

Until recently, the most significant issue facing a family physician regarding the diagnosis and treatment of dementia was ruling out delirium and potentially treatable etiologies. However, as more treatment options become available, it will become increasingly important to diagnose dementia early. Dementia may be suspected if memory deficits are exhibited during the medical history and physical examination. Information from the patient's family members, friends and caregivers may also point to signs of dementia. Distinguishing among age-related cognitive decline, mild cognitive impairment and Alzheimer's disease may be difficult and requires evaluation of cognitive and functional status. Careful medical evaluation to exclude treatable causes of cognitive impairment is important. Patients with early dementia may benefit from formal neuropsychologic testing to aid in medical and social decision-making. Follow-up by the patient's family physician is appropriate in most patients. However, a subspecialist may be helpful in the diagnosis and management of patients with dementia with an unusual presentation or following an atypical course. (*Am Fam Physician* 2001; 63:703-13,717-8.)

📄 A patient information handout on dementia, provided by an AAFP staff patient education writer, is presented on page 717.

See editorial  
on page 620.

The prevalence of dementia is expected to increase dramatically in future years as life expectancy continues to increase and the baby-boomer population ages. The cumulative incidence of Alzheimer's disease has been estimated to be as high as 4.7 percent by age 70, 18.2 percent by age 80 and 49.6 percent by age 90.<sup>1</sup> Pro-

posed risk factors for dementia include a family history of dementia, previous head injury, lower educational level and female sex.<sup>2</sup> Alzheimer's disease is the most common cause of dementia; many of the remaining cases of dementia are caused by vascular disease and Lewy body disease. Vascular disease and Lewy body disease often occur in combination with Alzheimer's disease.<sup>3,4</sup>

TABLE 1

## Signs and Symptoms That May Indicate the Need for Evaluation for Dementia

### Cognitive changes

New forgetfulness, more trouble understanding spoken and written communication, difficulty finding words, not knowing common facts such as the name of the current U.S. president, disorientation

### Psychiatric symptoms

Withdrawal or apathy, depression, suspiciousness, anxiety, insomnia, fearfulness, paranoia, abnormal beliefs, hallucinations

### Personality changes

Inappropriate friendliness, blunting and disinterest, social withdrawal, excessive flirtatiousness, easy frustration, explosive spells

### Problem behaviors

Wandering, agitation, noisiness, restlessness, being out of bed at night

### Changes in day-to-day functioning

Difficulty driving, getting lost, forgetting recipes when cooking, neglecting self-care, neglecting household chores, difficulty handling money, making mistakes at work, trouble with shopping

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test for apraxia is to ask the patient to pantomime the use of a common object such as a hammer or a toothbrush. Agnosia can be evaluated by first asking the patient to close

his or her eyes and then placing an object, such as a key or a coin, in the patient's hand and asking the patient to identify it without looking at it. Inability to recognize a com-

### Mini-Mental State Examination

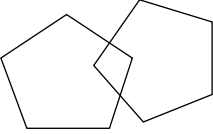
Maximum score	Score	
		<b>Orientation</b>
5	_____	What is the (year) (season) (date) (day) (month)?
5	_____	Where are we: (state) (county) (town or city) (hospital) (floor)?
		<b>Registration</b>
3	_____	Name three common objects (e.g., "apple," "table," "penny"): Take one second to say each. Then ask the patient to repeat all three after you have said them. Give one point for each correct answer. Then repeat them until he or she learns all three. Count trials and record. Trials: _____
		<b>Attention and calculation</b>
5	_____	Spell "world" backwards. The score is the number of letters in correct order. (D__L__R__O__W__)
		<b>Recall</b>
3	_____	Ask for the three objects repeated above. Give one point for each correct answer. (Note: recall cannot be tested if all three objects were not remembered during registration.)
		<b>Language</b>
2	_____	Name a "pencil" and "watch." Repeat the following: "No ifs, ands or buts."
1	_____	Follow a three-stage command:
3	_____	"Take a paper in your right hand, fold it in half and put it on the floor." Read and obey the following:
1	_____	Close your eyes.
1	_____	Write a sentence.
1	_____	Copy the following design.
		
		Total score: _____

FIGURE 1. The Mini-Mental State Examination, a useful tool for assessing cognitive function and documenting subsequent decline. Scores of 24 or higher are generally considered normal; see Table 4 for education and age norms.

Adapted with permission from 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;12:196-8, and Cockrell JR, Folstein MF. Mini-mental state examination (MMSE). *Psychopharm Bull* 1988;24(4):689-92.

mon object despite normal sensory function signifies agnosia.

Asking the patient to perform a series of simple tasks is a way to evaluate executive functioning. For example, the patient can be asked to put a piece of paper in his or her right hand, fold it in half and put it on the floor. This task would be difficult for a patient with impairment in the ability to plan, initiate, sequence and monitor complex behavior. Asking the patient to perform serial subtraction of 7s (backward from 100 to 65), to spell the word “world” backward and to produce verbal word lists, such as names of animals or items in a grocery store, are other ways to test executive functioning and abstract thinking.

Although the Mini-Mental State Examination (MMSE) is not diagnostic of dementia and does not distinguish well between various confusional states,<sup>8</sup> it is useful for assessing cognitive function and documenting subsequent decline (*Figure 1*). Because judgment and insight are not tested by the MMSE, many clinicians ask additional questions to assess these aspects of cognition. Judgment and insight can be assessed, for example, by asking the patient, “What would you do if you were in a crowded building and smelled smoke?”

When conversational skills are well preserved, an early decline in memory may be difficult to detect, especially during a short, focused office visit. The MMSE can detect cognitive impairment by evaluating orientation, attention, recall, language and ability to follow commands. A score higher than 23 is generally considered normal, although performance varies with the patient’s age and education (*Table 4*).<sup>9</sup>

### Differential Diagnosis

*Figure 2* summarizes an approach to the early diagnosis of dementia. If dementia is suspected, a medication review and assessment for chronic disease processes are warranted. If no improvement occurs after appropriate measures are taken to eliminate

*Serial Mini-Mental State examinations (or other cognitive testing) can help document changes over time.*

unnecessary medications and optimize treatment of chronic diseases, physical examination and laboratory tests are recommended to rule out specific treatable causes of dementia. Hearing or vision deficits, hypothyroidism, vitamin B<sub>12</sub> deficiency and depression are among the disorders that can cause symptoms of dementia. Such disorders are relatively easy to detect and should be excluded by appropriate laboratory tests, physical examination and psychologic tests. Electrocardiography and chest radiography can sometimes be useful to rule out treatable systemic diseases, although

**TABLE 4**  
**Median Scores on Mini-Mental State Examination by Age and Educational Level**

Age (years)	Educational level			
	4th grade	8th grade	High school	College
18 to 24	22	27	29	29
25 to 29	25	27	29	29
30 to 34	25	26	29	29
35 to 39	23	26	28	29
40 to 44	23	27	28	29
45 to 49	23	26	28	29
50 to 54	23	27	28	29
55 to 59	23	26	28	29
60 to 64	23	26	28	29
65 to 69	22	26	28	29
70 to 74	22	25	27	28
75 to 79	21	25	27	28
80 to 84	20	25	25	27
>84	19	23	26	27

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## Diagnostic Work-Up of Dementia

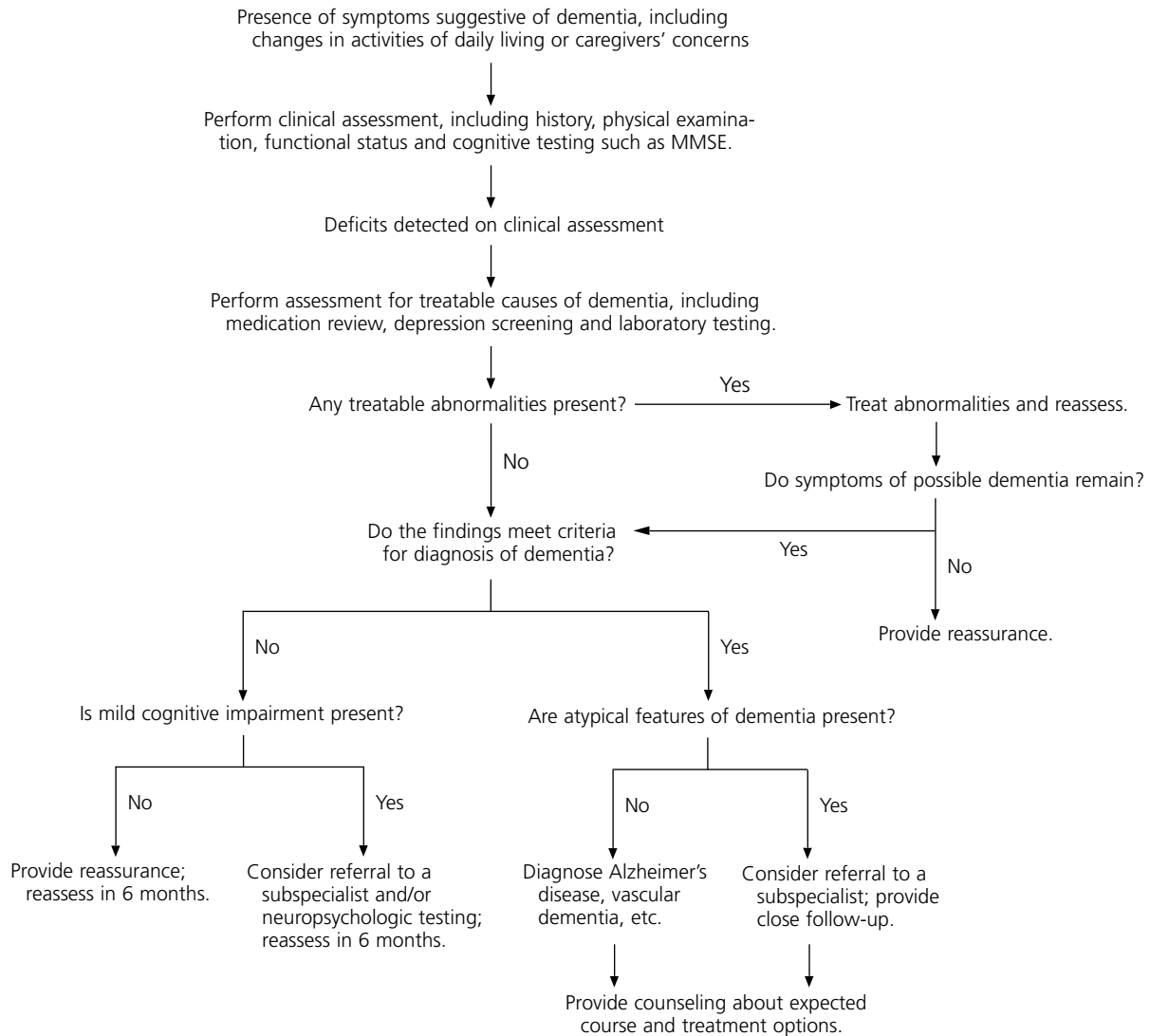


FIGURE 2. An approach to the early diagnosis of dementia. (MMSE = Mini-Mental State Examination)

their necessity should be guided by the history and physical examination.

Table 5 lists laboratory tests to consider in the evaluation of dementia. Tests recommended for the diagnostic work-up of dementia include a complete blood cell count (to exclude anemia and infection), urinalysis (to exclude infection), serum electrolyte, glucose and calcium levels, blood urea nitrogen, serum creatinine level and liver function tests (to investigate metabolic disease).<sup>10</sup> Syphilis serology, erythrocyte sedimentation rate, serum folate level, human immunodeficiency

virus (HIV) status, urine check for heavy metals and toxicology screening may be indicated in a minority of cases (Table 6).<sup>5</sup>

Lumbar puncture is usually not necessary except when the onset of dementia occurs before 55 years of age or when a specific condition such as infection, syphilis or vasculitis is suspected.<sup>10</sup> However, in at least one prospective study it was found that cerebrospinal fluid analysis for the 42 amino acid form of  $\beta$ -amyloid may be suggestive of Alzheimer's dementia, although not diagnostic.<sup>11</sup> Further studies into the existence of bio-

markers for the diagnosis of early Alzheimer's disease are ongoing.

The utility of computed tomography or magnetic resonance imaging to rule out vascular disease, tumor, subdural hematoma or normal-pressure hydrocephalus remains controversial. Radiologic imaging of the central nervous system is probably not necessary in patients presenting with dementia, unless localizing neurologic signs or symptoms are noted. Clearly, it is important to search for a reversible cause of dementia. However, in one meta-analysis it was revealed that fewer than 11 percent of patients with cognitive decline had partially or fully reversible disease.<sup>12</sup>

## Diagnosis

### DEMENTIA

DSM-IV criteria for the diagnosis of dementia require the presence of multiple cognitive deficits in addition to memory impairment<sup>6</sup> (Table 1). Early in the disease, memory impairment may be the only clinical finding, and this single finding would not meet the diagnostic

TABLE 5  
Laboratory Tests for Evaluation of Dementia

Urinalysis and microscopy	Erythrocyte sedimentation rate*
Complete blood cell count	Serologic tests for syphilis (or similar)
Serum electrolyte levels, including magnesium	Chest radiography*
Serum chemistry panel, including liver function tests	Electrocardiography*
Thyroid function tests	Toxicology screening*
Serum vitamin B <sub>12</sub>	Urine toxicology
	Serum toxicology (alcohol, salicylates, other)

\*—To be considered, not universally needed.

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criteria for dementia. In order to fulfill DSM-IV criteria, cognitive impairment must be of the degree that social or occupational function is reduced, with the functional impairment representing a decrease in the patient's normal ability.

TABLE 6  
Additional Tests to Consider in the Diagnostic Work-Up of Dementia

Test	Indication
Electroencephalography	Possible seizures; Creutzfeldt-Jakob disease
Lumbar puncture	Onset of dementia within the preceding six months; dementia rapidly progressive
Heavy metal screen	History of potential exposure
Human immunodeficiency virus	History of potential exposure
Lyme disease titer	History of exposure and compatible clinical picture
Ceruloplasmin, arylsulfatase, electrophoresis	Wilson's disease, metachromatic leukodystrophy, multiple myeloma
Slit lamp examination	History and examination suggest Wilson's disease
Apolipoprotein E	Need to increase likelihood that diagnosis of Alzheimer's disease is correct
Genetic testing for Alzheimer genes, other dementia genes	Family history is strong, and confirmation is clinically necessary

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*Referral to a subspecialist may be warranted when the presentation or clinical course is atypical of dementia.*

#### **AGE-RELATED COGNITIVE DECLINE AND MILD COGNITIVE DISORDER**

Age-related cognitive decline is characterized by memory loss without other cognitive problems (the DSM-IV criteria are described in *Table 2*). If memory deficit is present but the other diagnostic criteria for dementia are not, a diagnosis other than dementia should be considered.<sup>6</sup> A disorder similar to age-related cognitive decline is described as “mild cognitive disorder” in the World Health Organization ICD-10 classification (*International Statistical Classification of Diseases, 10th rev.*).<sup>13</sup>

The diagnosis of mild cognitive disorder can be made if the cognitive decline is temporally related to cerebral or systemic disease. Otherwise, the diagnosis of age-related cognitive decline should be considered. According to the DSM-IV, age-related cognitive decline represents cognitive changes that are within normal limits given the person’s age. Age-associated cognitive decline is characterized by a decline in only one of the five broad neuropsychologic domains associated with dementia: memory and learning; attention and concentration; thinking; language; and visuospatial functioning.<sup>14</sup> According to the International Psychogeriatric Association,<sup>14</sup> additional criteria should be met to make a diagnosis of age-related cognitive decline. These criteria include the report of cognitive decline from a reliable source, a gradual onset of at least six months’ duration and a score of more than one standard deviation below the norm on standardized neuropsychologic testing such as the MMSE.

#### **MILD COGNITIVE IMPAIRMENT**

The diagnosis of mild cognitive impairment is difficult and controversial. The term “mild cognitive impairment” has been coined

to describe a condition that may or may not eventually lead to dementia.<sup>13</sup> One study showed that patients with mild cognitive impairment had a more rapid decline in cognitive function than control patients, but a less rapid decline than patients with mild Alzheimer’s disease.<sup>15</sup>

The definitions of and the distinctions between mild cognitive disorder, age-associated cognitive decline and mild cognitive impairment are controversial. Referral for more extensive neuropsychologic testing, with follow-up intervals of six to nine months, is warranted in patients with mild or borderline cognitive deficits.<sup>16</sup>

#### **Referral**

The decision to refer the patient with recently diagnosed dementia to a subspecialist is influenced by both practical and medical considerations. Many family physicians choose to follow their patients with dementia even when clinical features are atypical or suggestive of less common etiologies for the dementia.

However, a neurologist or psychiatrist can sometimes assist in the diagnosis and care of patients with less common dementias, including Pick’s disease, dementia of frontal lobe type, dementia with Lewy bodies, progressive supranuclear palsy, multiple-systems atrophy and normal-pressure hydrocephalus. Consensus criteria have been established for the diagnoses of dementia with Lewy bodies and vascular, or multi-infarct, dementia (*Table 7*).<sup>17,19</sup> Symptoms that may be helpful in identifying the less common causes of dementia include significant personality changes, extrapyramidal signs, rapid progression, gaze palsy, parasympathetic abnormalities, cerebellar signs, early urinary incontinence and gait abnormalities. Other reasons for referral to a neurologist or psychiatrist include rapidly progressive dementia, dementia in a young patient or the presence of psychiatric comorbidities or severe behavior disturbances.

In a nonresearch setting, neuropsychologic testing is not considered necessary if the diag-

**TABLE 7**  
**Features of Multi-Infarct Dementia and Dementia with Lewy Bodies**

**Multi-infarct dementia**

*The characteristic features include stepwise deterioration and patchy distribution of deficits, focal neurologic signs and evidence of vascular disease as indicated by history, physical examination and laboratory testing.*

MODIFIED HACHINSKI ISCHEMIA SCORE:	POINTS
Abrupt onset . . . . .	2
Stepwise progression . . . . .	1
Fluctuating course . . . . .	2
Nocturnal confusion . . . . .	1
Relative preservation of personality . . . . .	2
Depression . . . . .	1
Somatic complaints . . . . .	1
Emotional incontinence . . . . .	1
History of hypertension . . . . .	1
History of stroke . . . . .	2
Focal neurologic signs . . . . .	2
Focal neurologic symptoms . . . . .	2

SCORING: *Dementia is not likely to be due to vascular causes if the total score is 4 or less; dementia is likely to be due to vascular causes if the total score is 7 or more.*

**Dementia with Lewy bodies**

*The central feature is progressive cognitive decline with resultant functional impairment. Persistent memory impairment may occur with disease progression. Deficits on tests of attention, frontal-subcortical skills and visuospatial ability may be prominent.*

ESSENTIAL FEATURES FOR DIAGNOSIS:

- Two of the following core features are essential for a diagnosis of probable dementia with Lewy bodies; one is essential for possible dementia with Lewy bodies.
- Fluctuating cognition and pronounced variations in attention and alertness
  - Recurrent visual hallucinations that are typically well formed and detailed
  - Spontaneous motor features of parkinsonism

FEATURES SUPPORTIVE OF THE DIAGNOSIS:

- Repeated falls
- Syncope
- Transient loss of consciousness
- Neuroleptic sensitivity
- Systematized delusions
- Hallucinations

SCORING: A diagnosis of dementia with Lewy bodies is less likely in the presence of the following:

- Stroke disease, evident as focal neurologic signs or on brain imaging
- Evidence of any physical illness or other brain disorder sufficient to account for the clinical picture

*Modified Hachinski ischemia score adapted with permission from Rosen WG, Terry RD, Field PA, et al. Pathological verification of ischemic score in differentiation of dementias. Ann Neurol 1980;7:486-8. Criteria for dementia with Lewy bodies adapted with permission from McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology 1996;47:1113-24.*

nosis of dementia can be made using standard criteria. In general, neuropsychologic testing is indicated when patients with abnormal findings on the mental state examination show normal physical functioning and when the index of suspicion is clinically high but screening tests are normal.<sup>16</sup> Neuropsychologic tests evaluate a wide variety of intellectual domains, including the level of arousal, attention and orientation, recent and remote memory, language, praxis, visuospatial function, calculations and judgment. Although there are published norms for most of the commonly used standardized tests, the tests are not always definitive. Serial examination may be necessary. Neuropsychologic tests may also be useful in determining competency for legal purposes, in distinguishing dementia from depression and in helping the patient make important decisions regarding jobs and finances.

### Management and Treatment

Early diagnosis and intervention allow the patient to compensate for the disability, minimize disease-related and medication complications, improve quality of life and optimize the use of resources. While new experimental cholinergic drugs for the treatment of Alzheimer's disease are introduced periodically, tacrine (Cognex) and donepezil (Aricept) are the only cholinesterase inhibitors currently

labeled for the symptomatic treatment of Alzheimer's disease. Acetylcholinesterase inhibitors act by delaying neurotransmitter degradation, thereby enhancing cortical cholinergic activity.

Clinical trials in patients with mild to moderate dementia suggest that symptomatic improvement is possible.<sup>20,21</sup> Cholinergic side effects, such as nausea, vomiting and diarrhea, are usually transient but may be intolerable to some patients. Monitoring of serum transaminase levels is recommended with use of tacrine because of potential hepatotoxicity. Experimental treatment options, some with potentially fewer side effects than those associated with currently available agents, may soon be available for the treatment of Alzheimer's disease.

The primary management strategy for progressive dementia is to preserve function and independence, and to maintain quality of life for as long as possible. Frequent (every three to six months) clinic visits may be indicated to achieve these goals by maximizing the patient's general health and interacting with caregivers to optimize the patient's social environment. Nonpharmacologic interventions, including measures to ensure safety at home and long-term decisions regarding finances, a living will and nursing home placement, are often important considerations.

The management of vascular dementia consists of controlling risk factors such as hypertension and smoking. The use of anticoagulants is indicated in many of these patients. Because of its safety, aspirin is the most commonly used agent. Use of warfarin (Coumadin) may also be considered in a limited number of patients, such as those without a significant risk of falling but with a definite history of stroke.

The treatment of dementia with Lewy bodies has not been well studied. However, it is important to note that parkinsonian features in these patients rarely respond to dopaminergic drugs, and that adverse responses to neuroleptic agents may occur.<sup>22</sup>

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### The Authors

KAREN S. SANTACRUZ, M.D., is an assistant professor in the departments of pathology and neurology at the University of Kansas School of Medicine, Kansas City. She completed a residency at the University of California, Irvine, Medical Center, where she trained in anatomic pathology and neuropathology. She developed an interest in dementia through her interaction with the Alzheimer's Disease Research Center at the University of California, Irvine.

DANIEL SWAGERTY, M.D., M.P.H., is an assistant professor in the departments of family medicine and internal medicine in the University of Kansas School of Medicine. He is also associate director of the Center on Aging at the University of Kansas. Dr. Swagerty completed medical school, a family practice residency and a geriatric medicine fellowship at the University of Kansas School of Medicine. He also completed a master's degree in public health at the University of Kansas School of Medicine.

*Address correspondence to Karen S. SantaCruz, M.D., Department of Pathology, University of Kansas School of Medicine, 3901 Rainbow Blvd., Kansas City, KS 66160-7410. Reprints are not available from the authors.*

## Final Comment

Physicians and patients can obtain information about potential experimental treatment options and ongoing clinical trials at the Alzheimer's Disease Education and Referral (ADEAR) Center Web site ([www.alzheimers.org](http://www.alzheimers.org)) or through an Alzheimer's disease information specialist at ADEAR (800-438-4380). The ADEAR Center is a service of the National Institute on Aging (NIA).

Although no method of curing or arresting Alzheimer's disease is currently available, early diagnosis is important for several reasons. The most compelling reason is that early diagnosis allows the patient and family to plan for the future and identify outside sources of assistance. Moreover, as potentially useful and proven treatments become available, early diagnosis of dementia will become increasingly important. Although screening all elderly patients for dementia is not warranted,<sup>23</sup> being alert for cognitive and functional decline is a prudent way of recognizing dementia in its early stage.

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