

Memory loss - when is it Alzheimer's?



By Chris MacKnight, MD, MSc, FRCPC; and Kenneth Rockwood, MD, FRCPC

In this article:

1. How to assess a patient with suspected Alzheimer's disease.
2. The different stages of Alzheimer's disease.
3. How to deal with a patient with Alzheimer's disease.
4. When is it not Alzheimer's disease?
5. When to refer patients.

Case

Mrs. Smith is 83-years-old and was brought in by her daughter to assess her memory. She is taking acetylsalicylic acid (because of a possible TIA a few years back) and hydrochlorothiazide for her hypertension. She had a partial colectomy two years ago for a perforated diverticulum, and bounced back quickly after the operation.

Mrs. Smith isn't very happy. She recognizes her memory impairment and finds it frustrating, yet she says she is no worse than anyone else her age. Her daughter, however, describes a slow steady memory decline over the past twelve to eighteen months. Examples include forgetting appointments, mixing up the grandchildren and their birthdays, and losing things in the home. Mrs. Smith has even accused her daughter of taking things from the house. She frequently asks the same question, and calls her daughter several times a day with the same question.

Is it Alzheimer's?

Mrs. Smith's situation is not unusual. Memory complaints are common with aging. Dementia occurs in 8% of Canadians over 65 and in 35% of those over 85.¹ Patients and their families may not recognize the presence, or importance, of memory problems.^{2,3,4} Unfortunately, about 65% of Canadians with dementia are undiagnosed and this lack of recognition delays access to effective therapy and appropriate planning for the future. Keeping a supply of the Alzheimer Society's "10 Warning Signs" in the office is a good way to promote awareness among patients and their families. The Patient Information sheet at the end of the article provides these "10 Warning Signs."⁵

Dementia is a syndrome of cognitive impairment resulting in functional loss. The most common cause is Alzheimer's disease, with vascular dementia and mixed Alzheimer's/vascular disease coming in second and third.¹ Alzheimer's disease can be diagnosed when dementia is present, with a characteristic course of insidious onset and slow progression, with no evidence of other causes. The criteria for dementia are shown in Table 1.

We describe one approach to the diagnosis of dementia in primary care.⁶



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How to assess the patient

The main goal in patient assessment is largely to determine if the problem is Alzheimer's disease. To do this, primary-care physicians should assess memory and functional impairment. These assessments almost always require interviewing someone who knows the patient well. If there are atypical features in the history or physical examination suggesting a diagnosis other than Alzheimer's disease, a specialist referral is appropriate. Finally, searching for and addressing potentially reversible causes of cognitive impairment, though rarely successful, must not be neglected.

Achieving these goals can be a lot to accomplish in primary care. We recommend spreading the evaluation and management

Is it Alzheimer's?

Practice Point

Steps to assessing your patient:

First visit: Take a history and any laboratory tests.

Second visit: Take a collateral history; speak to a family member.

Third visit: Conduct a physical examination.

Fourth visit: Discuss a management plan.

planning over several visits. Most cases of Alzheimer's disease can and should be managed in primary care, without consulting a specialist.

How to Assess Memory

For Mrs. Smith, the history of memory impairment is very convincing, and characteristic of Alzheimer's disease. There is no reported fluctuation or step-wise pattern that would raise suspi-



cions of other disorders. The daughter's history is supported by Mrs. Smith's brief cognitive test and poor results in the Mini-Mental State Examination (MMSE).⁷

Mr. Jones, also 83, comes in because he is concerned with his memory, after his older brother was recently diagnosed with Alzheimer's disease. He thinks his memory has been poor for a while, but neither he nor his wife can precisely describe the timeline of the decline. They are not sure if it is worsening, but are sure that if it is, the process is very slow. They describe misplacing his keys, having trouble with names (though he often wakes at 3 a.m. when the name comes back), and some-

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† Randomized, double-blind, placebo-controlled study of 2,458 postmenopausal women with at least one vertebral fracture. All patients received 1 g/d calcium and, if baseline levels were low, 500 IU/d vitamin D.

†† Three-year clinical study (VERT-MN) in 1,226 postmenopausal women (18.1% vs 29%; $p < 0.001$). All patients received 1 g/d calcium and, if baseline levels were low, 500 IU/d vitamin D.

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Is it Alzheimer's?

Table 1

Criteria for Dementia

- Memory impairment
- Some other cognitive impairment (*i.e.* language, executive function, apraxia, agnosia.)
- Functional loss resulting from the cognitive impairment.
- Not present exclusively during an episode of delirium.
- The clinical picture cannot be completely explained by depression.

times mixing up the grandchildren. He laughs about an episode last year, when he dropped his wife off at the mall, told her he would pick her up in an hour, went home, and forgot all about her. When he heard her voice on the telephone, the memory came back.

These memory symptoms are not as serious as Mrs. Smith's. Although Mr. Jones is a bit forgetful, he is still able to learn and retain new information; he just has trouble retrieving it when he needs it. His story is more consistent with a mild, age-related memory impairment.

How to Assess Functional Loss

Mrs. Smith denies she has reduced any activities. Her daughter disagrees. Her mother no longer keeps the home as clean and now needs help. She stopped bringing the whole family over for Sunday dinner a year ago, after a few cooking disasters. Mrs. Smith is no longer able to keep the accounting books for her church. Although she used to be a rapid knitter, she has been working on the same pair of mittens for six months. This history of functional decline is very convincing.

Mr. Jones and his wife, on the other hand, cannot think of anything that he has given up. They still spend their winters in Florida, and have no difficulty with the drive. He continues to do his taxes and does his sons' returns as well. He has recently bought a computer (to e-mail his grandson at university) and had no problem learning to use it and has become quite adept at surfing the Net. Not only does Mr. Jones not have any convincing history of functional

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loss, but his history demonstrates an ability to acquire new, complex skills, something that is expected to be difficult for most people with dementia.

Obtaining Collateral Information

These examples demonstrate the importance of obtaining collateral history. Without her daughter's input, the very articulate Mrs. Smith might never have been suspected of having a memory deficit. Mr. Jones, on the other hand, is somewhat concerned with his memory, yet his history, as verified by his wife, is reassuring.

Not all families feel comfortable discussing deficits in front of the affected person. With the patient's permission, it is usually a good idea to have at least a few private moments with a family member, to ensure that everything is being reported accurately.



Sounds like Alzheimer's?

Mr. Leblanc, 82, presents with hallucinations. Over the past six months, he has experienced recurrent hallucinations, mostly of small, deformed people. He finds these images quite distressing. He and his wife describe some memory deficit (though he scores 26/30 on the MMSE). Over the past year he has given up his woodworking hobby, and can no longer handle the family finances.

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Is it Alzheimer's?

This patient displays stage incongruence, in that he has a symptom associated with moderate or severe dementia (hallucinations) early in the course, when the rest of his symptoms best fit in the mild dementia category. He does not have Alzheimer's disease, but Lewy body disease, a dementia characterized by early hallucinations and sometimes parkinsonism.⁸ It is important to recognize that most of these patients will have severe, irreversible side effects if given an antipsychotic. Atypical antipsychotics are sometimes safe if used cautiously.

The idea of stage incongruence is immensely helpful in the diagnosis and management of dementia. Alzheimer's disease has a characteristic progression through recognizable stages (see Table 2); when symptoms occur at the wrong time, stage incongruence is present, meaning that either the diagnosis is not Alzheimer's disease, or that a second disorder, such as delirium, is present.

Other atypical features which should prompt referral to a specialist include young age at onset (< 60; few of these will have Alzheimer's disease), rapid progression (from very well to significantly impaired over several months), and the triad of dementia, urinary incontinence and gait disturbance, which indicates the possibility of normal pressure hydrocephalus, which is sometimes reversible. Prominent non-memory symptoms early in the course, such as an aphasia with only mild memory impairment, should also prompt a referral.

Conducting the Physical Examination

A physical examination is necessary to pick up clues that the problem is not Alzheimer's disease. Any unexplained neurologic finding in mild dementia is not compatible with Alzheimer's disease. Late in the disease, mild parkinsonism is typical, though other findings are not. The neurologic examination should concentrate on evaluation of tone (rigidity), symmetry of strength, the presence of a tremor or other involuntary movement, and an examination of gait. Asymmetric reflexes or a positive Babinski response can indicate stroke. Ataxia or clumsiness could indicate cerebellar involvement. Finally, myoclonus, the sudden jerk of a muscle to cause a movement across a joint, may be a sign of Creutzfeldt-Jakob disease.

Is it Alzheimer's?

Table 2

Typical Stages of Alzheimer's Disease

Mild

Forgetful about recent events.

Difficulty with complex tasks, such as driving, hobbies, finances.

Low mood and suspicion.

Normal physical examination.

Moderate

Difficulty cooking, handling money.

Unable to maintain the home.

Difficulty managing medications.

Little recall for recent events.

Agitation, aggression.

Severe

Difficulty dressing, grooming.

Difficulty swallowing.

Fecal incontinence.

Gait disturbance.

Hallucinations and delusions.

No longer recognizes family and has little recall of past life.

Restricted vocabulary.

Often neurologic abnormalities, such as mild rigidity and mild parkinsonian gait.

NB: Other symptoms occur as well; not all symptoms are present in all subjects.

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ASA use: 32%

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Is It Delirium, Not Dementia?

Delirium is an acute confusional state that can usually be distinguished from dementia. The rapid onset of delirium (hours or days) sets it apart from most causes of dementia. Poor attention (easily distracted, difficulty maintaining one's train of thought) are more prominent in delirium than the memory complaints which are characteristic of dementia. The physical examination or simple laboratory tests almost always reveal the underlying cause, typically an infection, adverse drug reaction, or metabolic derangement. With treatment, most people recover fully, though the episode of delirium is an indicator that they are at increased risk for dementia in the future.⁹



Two situations are sometimes difficult to sort out. The first is when the history of the onset and duration is lacking (such as in a patient who lives alone). In that case it is best to proceed as if the problem is delirium, while obtaining what information you can from friends, family and neighbors. Often after several rounds of history-taking, proof that the impairment has been long-standing and only slowly progressive becomes available.

The other situation is the sudden change in a person with established dementia — is it progression of the underlying disease or a delirium? In general, new symptoms in Alzheimer's disease (such as hallucinations or agitation) develop gradually. A sudden, dramatic change is a sign that a new disorder may be present, and a careful evaluation is necessary, as the patient may not be able to give an accurate history. The idea of stage congruence can also be helpful here, in that the presence of symptoms not expected at a particular stage of dementia argue strongly for the presence of a new disorder.

Is It Depression, Not Dementia?

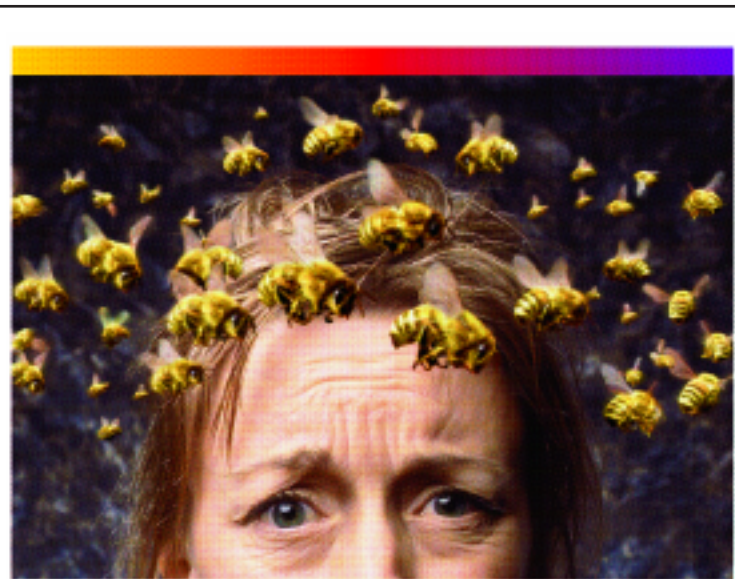
Depression can sometimes present with prominent symptoms of memory and concentration loss. It can be difficult to distinguish from dementia, because many of the associated symptoms (apathy, appetite loss, hypo- or hypersomnia) can all be present in early dementia as well. If there is a suggestion of low mood and other classic symptoms of depression, such as early-morning awakening or anhedonia, it is reasonable to treat with an adequate dose of an antidepressant before giving a firm diagnosis of dementia. In younger people, mood and memory symptoms often resolve completely; in older adults, mood symptoms often improve, but the memory complaints do not. So-called “depressive pseudodementia” is rare, and more often the mood symptoms are part of the presentation of the dementia.¹⁰

Reversible Causes of Dementia

Less than 10% of cases of dementia seen in a memory clinic have a potentially reversible cause of cognitive impairment, and less than half of these actually do reverse with treatment.¹¹ The most common reversible cause is the adverse effect of a medication, typically anticholinergics (*i.e.*, amitriptyline or dimenhydrinate) or sedatives (*i.e.*, diazepam or lorazepam).¹² Every effort should be made to stop such medications before giving a firm diagnosis of dementia.

Putting it all together

The evaluation of memory complaints involves a careful history of the memory problem, its onset and associated functional loss. This assessment must involve a reliable informant. Further evaluation (the physical examination, consideration of delirium,



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Is it Alzheimer's?

depression and potentially reversible causes) is aimed at distinguishing Alzheimer's disease from other dementias. Most patients require only a basic laboratory evaluation and do not need neuroimaging. For more details, consult the Conclusions from the Canadian Consensus Conference on Dementia. (See Suggested Readings below.)

Distinguishing normal, age-associated memory complaints from something more sinister involves determining the quality of the memory loss, but more importantly any associated functional loss. With early recognition of dementia comes an opportunity for early intervention and, perhaps, some period of preservation of independence. 

References

1. Canadian Study of Health and Aging Working Group: Canadian Study of Health and Aging: Study methods and prevalence of dementia. *CMAJ* 1994; 150:899-913.
2. Sibley A, MacKnight C, Rockwood K, et al: The effect of the living situation on the severity of dementia at diagnosis. *Dement Geriatr Cogn Disord* 2002; 13:40-5.
3. Callahan CM, Hendrie HC, Tierney WM: Documentation and evaluation of cognitive impairment in elderly primary care patients. *Ann Intern Med* 1995; 122:422-9.
4. Sternberg SA, Wolfson C, Baumgarten M: Undetected dementia in community-dwelling older people: The Canadian Study of Health and Aging. *J Am Geriatr Soc* 2000; 48:1430-4.
5. 10 Warning Signs. <http://www.alzheimer.ca/english/disease/warningsigns.htm>
6. Rockwood K, MacKnight C: *Understanding Dementia: A Primer of Diagnosis and Management*. Pottersfield Press: Halifax, Nova Scotia, 2001.
7. 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.
8. Rojas-Fernandez C, MacKnight C: Dementia with Lewy Bodies: A review and pharmacotherapeutic implications. *Pharmacotherapy* 1999; 19:795-803.
9. Rockwood K, Cosway S, Carver D, et al: The risk of dementia and death after delirium. *Age Aging* 1999; 28:551-6.
10. Clarfield AM: The reversible dementias: Do they reverse? *Ann Intern Med* 1988; 109:476-86.
11. Larson EB, Reifler BV, Featherstone HJ, et al: Dementia in elderly outpatients: A prospective study. *Ann Intern Med* 1984; 100:417-23.
12. Visser PJ, Verhey FR, Ponds RW et al: Distinction between preclinical Alzheimer's disease and depression. *J Am Geriatr Soc* 2000; 48:479-84.

Suggested Readings

1. Patterson CJS, Gauthier S, Bergman H, et al: The recognition, assessment and management of dementing disorders: Conclusions from the Canadian Consensus Conference on Dementia. *CMAJ* 1999; 160 (suppl 12):S1-S15.
2. Freter S, Bergman H, Gold S, et al: Prevalence of potentially reversible dementias and actual reversibility in a memory clinic cohort. *CMAJ* 1998; 159:657-62.