Dementia

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Dementias are acquired neurodegenerative disorders involving a syndrome of cognitive impairment accompanied with social and functional decline. The most common dementia is Alzheimer's Disease and in 2010 it was estimated that 500,000 Canadians have Alzheimer's Disease or a related dementia.

Major Areas of Cognitive Decline
Amnesia (memory disturbance)
Apraxia (inability to perform complex motor activities)
Aphasia (speech disturbance)
Agnosia (failure to recognize or identify objects despite normal sensory function)

DSM-V Criteria

Mild Neurocognitive Disorder
A. Evidence of *modest* cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on:
    1. Concern of the individual, an informant, or healthcare professional that there has been a mild decline in cognitive function; AND
    2. A *modest* impairment in cognitive performance by neuropsychological testing or clinical assessment.
B. The cognitive deficits do *not* interfere with capacity for independence in everyday activities.
C. The cognitive deficits do not occur exclusively in the context of delirium.
D. The cognitive deficits are not better explained by another mental disorder.
   Specify whether due to a particular cause. (ex. Alzheimer's disease, Vascular disease etc.)

Major Neurocognitive Disorder
A. Evidence of *significant* cognitive decline from a previous level of performance in one or more cognitive domains based on:
    1. Concern of the individual, an informant, or healthcare professional that there has been a *significant* decline in cognitive function; AND
    2. A *substantial* impairment in cognitive performance by neuropsychological testing or clinical assessment.
B. The cognitive deficits interfere with capacity for independence in everyday activities.
C. The cognitive deficits do not occur exclusively in the context of delirium.
D. The cognitive deficits are not better explained by another mental disorder.
   Specify whether due to a particular cause. (ex. Alzheimer's disease, Vascular disease etc.)

Major or Mild Neurocognitive Disorder Due to Alzheimer's Disease
A. The criteria are met for major or mild neurocognitive disorder.
B. There is insidious onset and gradual progression of impairment in one or more cognitive domains. Major neurocognitive disorder requires at least two domains impaired.
C. Criteria are met for either Probable Alzheimer's Disease or Possible Alzheimer's Disease.
   For major neurocognitive disorder
   Probable Alzheimer's disease is diagnosed if either of the following is present; otherwise possible Alzheimer's disease should be diagnosed
    1. Evidence of a causative Alzheimer's disease genetic mutation from family history or genetic testing.
    2. All there for the following are present:

a. Clear evidence of decline in memory and learning and at least one other cognitive domain.
b. Steadily progressive, gradual decline in cognition, without extended plateaus.
c. No evidence of mixed etiology.

For mild neurocognitive disorder:
Probable Alzheimer's disease is diagnosed if evidence of a causative Alzheimer's disease genetic mutation from family history or genetic testing.

Possible Alzheimer's disease is diagnosed if no evidence of a causative Alzheimer's disease genetic mutation from family history or genetic testing, and all of the following are present

1. Clear evidence of decline in memory and learning
2. Steadily progressive, gradual decline in cognition, without extended plateaus.
3. No evidence of mixed etiology

D. The cognitive deficits are not better explained by another mental or physical disorder.

The following tables are taken from a review series about the diagnosis and treatment of dementia from the Canadian Medical Association Journal. These articles from 2008 are evidence-based guidelines that were created using a systemic review of current literature. These articles have also been included in this folder.

Box 1: Recommendations for the diagnosis of dementia* (part 1 of 2)

Brief cognitive tests

- A range of brief cognitive tests, including the Montréal Cognitive Assessment,[2] the DemTect,[3] the 7-Minute Screen,[4] the General Practitioner Assessment of Cognition[5] and the Behavioural Neurology Assessment Short Form,[6] may be more accurate than the Mini-Mental State Examination in discriminating between dementia and the normal state. There is insufficient evidence to recommend one test over the others [grade B recommendation, level 2 evidence; new recommendation].
- Brief cognitive tests have not been developed to differentiate between dementia subtypes and should not be used for this purpose [grade D recommendation, level 2 evidence; new recommendation].

Clinical diagnosis

- The diagnosis of dementia remains clinical. There is good evidence to retain the diagnostic criteria currently in use[7] [grade A recommendation, level 2 evidence; new recommendation].
- The sensitivity of clinical diagnosis for possible or probable Alzheimer disease based on the NINCDS–ADRDA criteria† remains high. The specificity is lower. The continued use of the NINCDS–ADRDA criteria is recommended [grade A recommendation, level 1 evidence; new recommendation].
- "Mild" Alzheimer disease can be diagnosed with a high degree of specificity, when the presenting clinical picture is one of memory impairment [grade B recommendation, level 1 evidence; new recommendation].

Laboratory investigations

- For all patients who have a clinical presentation consistent with Alzheimer disease with typical cognitive symptoms or presentation, only a basic set of laboratory tests should be ordered to rule out causes of chronic metabolic encephalopathy producing chronic confusion and memory loss [grade B recommendation, level 3 evidence; recommendation unchanged].
  - Complete blood count (to rule out anemia)
  - Thyroid stimulating hormone (to rule out hypothyroidism)
  - Serum electrolytes (to rule out hyponatremia)
  - Serum calcium (to rule out hypercalcemia)
  - Serum fasting glucose (to rule out hyperglycemia)
- The serum vitamin B_{12} level should be determined in all older adults suspected of having dementia or cognitive decline [grade B recommendation, level 2 evidence; new recommendation].
- Older adults found to have a low vitamin B_{12} level should be given vitamin B_{12} (either orally or parenterally) because of potential improvement of cognitive function and the deleterious effects of low vitamin B_{12} levels on multiple organ systems, besides the effects on cognition [grade B recommendation, level 2 evidence; new recommendation].
- Determination of serum folic acid or red blood cell folate levels in older adults in Canada is optional and may be reserved for patients with celiac disease, inadequate diet or other condition that prevents them from ingesting grain products [grade E recommendation, level 2 evidence; new recommendation].
- There is currently insufficient evidence to support the need for the determination of serum homocysteine levels in older adults with suspected dementia or cognitive decline [grade C recommendation, level 3 evidence; new recommendation].
- There is currently insufficient evidence that treatment of elevated serum homocysteine levels affects cognition [grade C recommendation, level 3 evidence; new recommendation].

continued

Box 1: Recommendations for the diagnosis of dementia* (part 2 of 2)

- Genetic testing, including screening for the apolipoprotein E gene, is not recommended for the purpose of diagnosing Alzheimer disease because the positive and negative predictive values are low [grade E recommendation, level 2 evidence; new recommendation].

Neuroimaging with computed tomography and magnetic resonance imaging

- Cranial computed tomography scanning is recommended if one or more of the following criteria are present [grade B recommendation, level 3 evidence; recommendation unchanged]:
  - Age < 60 years
  - Rapid (e.g., over 1–2 months) unexplained decline in cognition or function
  - Short duration of dementia (< 2 years)
  - Recent and significant head trauma
  - Unexplained neurologic symptoms (e.g., new onset of severe headache or seizures)
  - History of cancer (especially types that metastasize to the brain)
  - Use of anticoagulants or history of bleeding disorder
  - History of urinary incontinence and gait disorder early in the course of dementia (as may be found in normal pressure hydrocephalus)
  - Any new localizing sign (e.g., hemiparesis or a Babinski reflex)
  - Unusual or atypical cognitive symptoms or presentation (e.g., progressive aphasia)
  - Gait disturbance
- There is fair evidence to support the use of structural neuroimaging with computed tomography or magnetic resonance imaging to rule in concomitant cerebrovascular disease that can affect patient management [grade B recommendation, level 2 evidence; new recommendation].

Neuropsychological testing

- The diagnosis and differential diagnosis of dementia is currently a clinically integrative one. Neuropsychological testing alone cannot be used for this purpose and should be used selectively in clinical settings [grade B recommendation, level 2 evidence; new recommendation].
- Neuropsychological testing may aid in:
  - addressing the distinction between normal aging, mild cognitive impairment or cognitive impairment without dementia, and early dementia [grade B recommendation, level 2 evidence; new recommendation];
  - addressing the risk of progression from mild cognitive impairment or cognitive impairment without dementia to dementia or Alzheimer disease [grade B recommendation, level 2 evidence; new recommendation]; and
  - determining the differential diagnosis of dementia and other syndromes of cognitive impairment [grade B recommendation, level 2 evidence; new recommendation].

*Based on recommendations from the Third Canadian Consensus Conference on Diagnosis and Treatment of Dementia, held in March 2006.
†The criteria of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) are provided in Box 4.

Table 1: Medications approved for the treatment of symptoms of Alzheimer disease in Canada*

Drug	Starting dose	Titration	Contraindications, warnings and precautions	Most common adverse effects†
Cholinesterase inhibitors				
Donepezil	5 mg once daily	• If well tolerated, increase dose to 10 mg once daily after at least 4–6 weeks • Maximum dose is 10 mg/d	• Contraindicated in patients with known hypersensitivity to drug or piperidine derivatives, and those with conduction abnormalities (except right bundle-branch block) or unexplained syncope • Use with caution in patients at risk of ulcers (monitor for gastrointestinal bleeding), those with a history of seizures, asthma or chronic obstructive pulmonary disease, and older patients with low body weight • Use may exaggerate the effects of succinylcholine-type muscle relaxants	• Nausea: 11% • Diarrhea: 10% • Headache: 10% • Insomnia: 9% • Pain: 9%
Galantamine (extended release)	8 mg once daily in the morning, preferably with food	• After 4 weeks, increase dose to 16 mg once daily (initial maintenance dose) • If initial maintenance dose is well tolerated, consider increasing to 24 mg once daily after at least 4 weeks • Maximum dose is 24 mg/d	• Contraindicated in patients with known hypersensitivity to drug, those with conduction abnormalities (except right bundle-branch block) or unexplained syncope, and those with severe hepatic or renal impairment • Monitor body weight if weight loss is of concern (more common among women and patients with low body weight) • Use with caution in patients at risk of ulcers (monitor for gastrointestinal bleeding) and those with a history of seizures, asthma or chronic obstructive pulmonary disease • Use will likely exaggerate the effects of succinylcholine-type muscle relaxants	• Nausea: 17% • Dizziness: 10% • Headache: 8% • Injury: 8% • Vomiting: 7%
Rivastigmine (oral)	1.5 mg twice daily (in the morning and at night), with food	• If well tolerated, increase dose to 3 mg twice daily after at least 2 weeks‡ • If well tolerated, increase dose to 4.5 mg twice daily and then to 6 mg twice daily, after at least 2 weeks each time • If treatment is interrupted for more than several days, reinitiate starting dose and titrate as above • Maximum dose is 6 mg twice daily	• Contraindicated in patients with known hypersensitivity to drug, those with conduction abnormalities (except right bundle-branch block) or unexplained syncope, and those with severe hepatic impairment • Monitor body weight if weight loss is of concern (more common among women) • Use with caution in patients at risk of ulcers (monitor for gastrointestinal bleeding), those with renal impairment (monitor closely), and those with a history of seizures, asthma or chronic obstructive pulmonary disease • Use will likely exaggerate the effects of succinylcholine-type muscle relaxants	• Nausea: 37% • Vomiting: 23% • Dizziness: 19% • Diarrhea: 16% • Headache: 15%
***N*-methyl-D-aspartate (NMDA) receptor antagonist**				
Memantine	5 mg once daily, in the morning	• If well tolerated, increase in weekly increments of 5 mg to maintenance dose of 10 mg twice daily	• Contraindicated in patients with known hypersensitivity to drug and those with severe renal impairment • Use with caution in patients with cardiovascular disease or a history of seizures • Conditions that raise urinary pH (e.g., renal tubular acidosis, urinary tract infection with *Proteus* bacteria) can reduce elimination of the drug in urine • Monitor patients ophthalmi c condition periodically • Do not combine with related drugs such as amantadine, ketamine and dextromethorphan	• Dizziness: 7% • Constipation: 6% • Confusion: 6% • Headache: 6% • Hypertension: 3%

*The information in this table was derived from the product monographs of the medications, as approved by the Therapeutic Products Directorate, Health Canada.[62]
†The 5 most common adverse events reported in controlled clinical trials for which the frequency was higher in the treatment group than in the placebo group.
‡Most specialists in dementia care suggest increasing the dose of rivastigmine only every 4 weeks.

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