Acute and Chronic Cognitive Impairment

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Disclosure Statement

Dr. Robbins has nothing to disclose.
Learning Objectives

1. Review delirium.
2. Describe differential diagnosis of dementia.
3. Discuss evaluation of cognitive impairment.
Case Discussion

A 79-yo woman with mild dementia is 2 days post-op for an elective right total hip arthroplasty. The nurses note that she was trying to get out of bed and screamed at them when they put her back to bed. When you see her, she is somnolent but arousable. You ask her where she is, but she just picks at the sheets and speaks nonsensically.
1. The appropriate next step is:

A. Order a chest x-ray.
B. Order a CT head with contrast.
C. Order EEG.
D. Do no further testing; this is predictable progression of dementia.
E. Review her outpatient medications.
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Diagnostic Criteria for Delirium

- Acute disturbance of cognition (inattention: can’t focus, shift, or sustain attention)
- KEY: Rapid onset (hours to days), fluctuation
- Tactile or visual delusions common (auditory hallucinations rare)
Causes of Delirium

D  Drugs (toxicity and withdrawal)
E  Electrolyte disturbance
L  Lack of drugs, liver disease
I  Infection
R  Reduced sensory input
I  Intracranial
U  Urinary retention/fecal impaction
M  Myocardial/metabolic/pulmonary
Risk Factors for Delirium

• Use of restraints
• Four or more medicines in 24 hours
• Use of indwelling urinary catheter
• History of dementia, stroke, or Parkinson’s disease
Is Neuroimaging Always Needed?

Neuroimaging unnecessary if:

• Clinical evaluation discloses an obvious treatable medical illness or problem.
• No evidence of trauma or new focal neurologic signs.
• Patient is arousable and able to follow simple commands.
### The Yale Delirium Prevention Program

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Intervention</th>
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<tbody>
<tr>
<td>Cognitive impairment</td>
<td>Reality orientation</td>
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<tr>
<td></td>
<td>Therapeutic activities</td>
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<tr>
<td>Sleep deprivation</td>
<td>Non-pharmacologic sleep protocol</td>
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<tr>
<td>Immobilization</td>
<td>Early mobilization</td>
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<tr>
<td>Vision impairment</td>
<td>Vision aids</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>Amplifying devices</td>
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<tr>
<td>Dehydration</td>
<td>Early recognition and volume repletion</td>
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</table>
Impact of Delirium Prevention

- Reduced number of delirium episodes
- Reduced total days of delirium
- Did not reduce severity of delirium or risk of recurrence
2. Normal aging may be associated with which of the following?

A. Short-term memory loss
B. Difficulty with calculations
C. Word-finding difficulties
D. Difficulty remembering names
E. Reduction in vocabulary
2. Normal aging may be associated with which of the following?

A. Short-term memory loss  
B. Difficulty with calculations  
C. Word-finding difficulties  
D. Difficulty remembering names  
E. Reduction in vocabulary

- A: 21%  
- B: 7%  
- C: 16%  
- D: 53%  
- E: 3%
“Normal” Aging Changes in Cognition

- Slowing in rate at which information can be received and processed
- Reduction in “explicit memory” (eg., the ability to recall a specific name, number, or location on demand)
Case Discussion

76-yo woman is brought to see you by her daughter, who is concerned about her failing memory. Six months ago, the daughter took over management of her mother’s checkbook after she failed to pay bills. Her mother seems unable to knit, something she enjoyed for years. She has difficulty finding the right words to complete a thought.
3. What is your diagnosis?

A. This patient has dementia.
B. This patient is depressed.
C. This patient is delirious.
D. This patient has mild cognitive impairment.
3. What is your diagnosis?

- A. This patient has dementia. (47%)
- B. This patient is depressed. (10%)
- C. This patient is delirious. (0%)
- D. This patient has mild cognitive impairment. (42%)
Criteria for Dementia

- Acquired impairment of short- and long-term memory and at least 1 of the following: abstract thinking, judgment, language, praxis, visual recognition, constructional abilities, or personality
- Severe enough to interfere with daily function
- Gradual decline and progression (ie, absence of delirium)
Dementia; Prevalence & Cost

• Subsample (856 persons) of Health and Retirement Study 3-4 hr in-home cognitive assessment for dementia
• Dementia prevalence @ 15% for age > 70
• Annual cost @ $50,000 per demented person
• Projected cost 2040 @ $379 to $511 billion/yr
Cases of Alzheimer’s Disease by Age per 100,000
4. The hallmarks of Alzheimer’s disease are:

A. Memory loss, personality change, delusions
B. Memory loss, ataxia, mood changes
C. Memory loss, aphasia, apraxia, agnosia, executive dysfunction
D. Memory loss, depression, abulia
E. Memory loss, acalculia, spasticity
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Criteria for Alzheimer’s Disease

- Memory loss plus 1 or more: aphasia, apraxia, agnosia, executive dysfunction
- Usually few motor signs apparent early
- Subtle behavioral and personality changes early
Screening Questions for Alzheimer’s Dementia

- Aphasia: can’t come up with words, substitutes words, new words
- Apraxia: has difficulty using utensils, tools
- Agnosia: doesn’t recognize familiar people; gets lost in familiar surroundings
- Executive dysfunction: can’t manage checkbook, use computer
Features Inconsistent with Alzheimer’s Disease

• Sudden onset
• Focal neurological findings
• Seizures, early marked change in personality/behavior
• Gait disorder early in disease course
Distribution of Neurofibrillary Tangles and Amyloid Plaques

RED: heaviest
BLUE: lightest

Case Discussion

76-yo ex-college professor complains that his memory just isn’t as good as it was. Daughter confirms that he has more difficulty remembering discussions that took place earlier in the day. He’s still paying bills and doing the crossword puzzles. His mental status screening test shows minimal impairment.
5. What is your diagnosis?

A. This patient has dementia.
B. This patient is depressed.
C. This patient is delirious.
D. This patient has minor neurocognitive disorder
E. This patient is normal for his age.
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41%
Mild Cognitive Impairment or “Minor Neurocognitive Disorder”

- Complaint of memory impairment
- Objective memory loss (adjusted for age and education)
- Preserved general cognitive function
- Intact activities of daily living
- High risk of developing dementia (5%-10% annually) but 40%-70% do not progress
Difficulty with Concentration: Depression vs Dementia

- Patient comes in alone complaining about memory = depression.
- Patient brought in by loved one who complains about patient’s memory = dementia.
“Pseudodementia” (Dementia Syndrome of Depression)

• Some depressed elderly patients will have objective evidence of impaired cognition that improves with Rx.

• Clues include inconsistent performance on mental status testing, “I don’t know” instead of near miss.
When Depression Mimics Dementia

• 23/57 hospitalized depressed elderly appeared demented (“pseudodementia”); 34/57 did not have signs of dementia.

• Among “pseudodemented,” signs of dementia resolved with Rx of depression.

• At 3 yrs: 10/23 “pseudodemented” had signs of dementia in absence of depression (vs 4/34 who were not “pseudodemented”).
When Dementia Mimics Depression: Abulia

- Diffuse frontal lobe disease (e.g., vascular dementia) associated with apathy, lack of motivation, flat affect.
- Dementia and primitive reflexes usually present (e.g., grasp reflex, palmomental response).
- Abulic patient may seem to enjoy activities if others initiate them.
Case Discussion

An 80-yo man has slowly progressive memory loss and word finding difficulties. Family took over his finances 2 months ago. His physical exam is unremarkable. No focal findings on neurological exam.
6. The next step mostly likely to result in improvement in his function?

A. MRI of brain
B. CBC, metabolic panel, TSH, B12
C. EEG
D. PET scan
E. Medication review
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A. MRI of brain  
B. CBC, metabolic panel, TSH, B12  
C. EEG  
D. PET scan  

E. Medication review
# Potentially Reversible Dementias

<table>
<thead>
<tr>
<th>Cause</th>
<th>Count</th>
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<tbody>
<tr>
<td>Drugs</td>
<td>16</td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>7</td>
</tr>
<tr>
<td>Hyperparathyroid</td>
<td>3</td>
</tr>
<tr>
<td>B12 Deficiency</td>
<td>2</td>
</tr>
<tr>
<td>Subdural Hematoma</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31</strong> (10%)</td>
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</table>

Screening for Dementia

• > 50% of persons with dementia have not received a diagnosis of dementia.

• Practical screening tools improve detection (eg, MMSE).
Mental Status Screening Tests

- Mini-Mental Status Exam (MMSE): 12-item, 30-point tool administered in 10-15 minutes
- St Louis Univ Mental Status (SLUMS) 30-point; includes cutoffs for education/MCI
  [http://medschool.slu.edu/agingsuccessfully/pdfsurveys/slumsexam_05.pdf](http://medschool.slu.edu/agingsuccessfully/pdfsurveys/slumsexam_05.pdf) ($1.99 iPhone app)
- Mini-cog: Draw clock face and 3-word recall
- MOCA: [www.mocatest.org](http://www.mocatest.org)
Should We Screen for Dementia?

• Under current Medicare Pay for Performance: “Whether or not patient (> 65 yo) was screened for cognitive impairment using a standardized tool”

• Affordable Care Act will require clinicians to assess for cognitive impairment as part of annual wellness visit. [www.healthcare.gov/law/full/index.html](http://www.healthcare.gov/law/full/index.html)
Potential Benefits of Screening

• Clarify advance directives while patient still competent.
• Begin discussion about alternatives to driving, housing alternatives.
• Prevent financial victimization or self-neglect; remove firearms.
• Participate in research.
“Average” Dementia Evaluation

- History, PE, mental status testing, comprehensive neuropsychological testing
- CBC, SMA 6, TSH, VDRL, B12, folate, calcium, U/A
- Genetic testing
- Brain imaging (CT or MRI)
“Reversible” Dementia

- 1970s: Reversible dementia said to be 5%-10% of all dementia.
- Early studies flawed; often done in hospital setting (confounded by delirium) and no follow-up to document reversibility.
- Outpatient studies with follow-up suggest 1% or less are reversible.
“Structural neuroimaging with either a noncontrast CT or MR scan in the initial evaluation of patients with dementia is appropriate. (Guideline)” … “Screening for depression, B12 deficiency, and hypothyroidism should be performed. (Guideline)”
Incidence and Causes of Dementia

- Record review of 560 consecutive patients newly diagnosed with dementia
- No cases of reversible dementia due to NPH, subdural hematoma, B12 deficiency, hypothyroidism, or neurosyphilis
- Conclusion: “None of the patients with dementia reverted to normal with treatment of the putative reversible cause.”

Case Discussion

An 80-yo woman has short-term memory loss consistent with Alzheimer’s dementia. She scores 20/30 on the MMSE. Her family asks about starting donepezil (eg, Aricept).
7. What should you tell them?

A. It will reverse her dementia.
B. It will delay nursing home placement.
C. It will increase her life expectancy.
D. It may have modest effects on scales measuring cognition and function.
E. It will have major side effects and should be avoided.
7. What should you tell them?

A. It will reverse her dementia.
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D. It may have modest effects on scales measuring cognition and function.
E. It will have major side effects and should be avoided.
Summary of Cholinesterase Inhibitor Trials in AD

- Nearly 9000 patients in 22 RCT, range 3 to 12 months of donepezil (eg, Aricept), rivastigmine (eg, Exelon), or galantamine (eg, Razadyne)
- Modest positive benefit in cognitive, behavioral, ADL, and global scales; few side effects; modest side effects (GI)
- Rare evidence of dose response
- Clinical outcomes (caregiver burden, nursing home placement, etc) not measured
Memantine

- NICE (National Institute of Health and Clinical Excellence) update 2011 based on 6 studies since 2004 (6-mo studies).
- Behavioral, ADL, and global scales modestly better in moderate/severe dementia.
- Clinical outcomes (eg, caregiver burden) not measured.
- ADR: Falls and agitation.
- Conclusion: Use in moderate dementia if intolerant of CIs or severe dementia.
Medical Foods

- Caprylidene (Axona) is a medium-chain triglyceride derived from coconut or palm oil.
- Theory: Alternative fuel for brain of AD patients (poor uptake of glucose).
- Small, short-term, manufacturer-sponsored trials show “benefit.”
- Approximately $90 per month.
Lifestyle and Dementia

• Bronx Aging Study: Education and cognitive leisure activities “protective” against development of AD (N Engl J Med. 2003;348:2508-2516)

• 15 minutes aerobic exercise 3x/week reduces likelihood of dementia (Ann Intern Med. 2006;144(2):73-80)
Lifestyle and Dementia

Australian study of 170 participants with MCI: In randomized, controlled, 24-week trial of home-based physical activity intervention (70,000 steps/week) vs “usual care” showed modest improvement in cognition

(JAMA. 2008;300:1027-1037)
Does the Diagnosis of a Specific Type of Dementia Matter?
Diagnosis and Treatment of Dementia: The Dismal Failure of Medical Science

- No direct evidence linking screening and improved decision making. (USPSTF. Ann Intern Med. 2013;159:601-612)

- No current intervention will prevent or delay the onset of dementia. (http://consensus.nih.gov/2010/docs/alz/AIM_alz.pdf)

- Treatment for dementia (cholinesterase inhibitors and NMDA receptor antagonist) is minimally effective. (Ann Intern Med. 2008;148:370-378)
The Dementia Epidemic: Any Good News?

• “Cognitive function and ageing study” suggests that dementia prevalence declined between early 1990s compared to 2008-2011 (8.3% vs 6.5%, age > 65).

• Linked to better education and reduction of ASCVD/CVA.

• Obesity, diabetes, and inactivity threaten to reverse this trend.
Case Discussion

80 yo with 12 mos of becoming more sedentary, slowed movement, unsteady gait, 2 falls, no injury. Stepwise progression of deficits. Uses walker. Speech diminished in volume, less distinct. Can’t manage finances. No change in mood or personality. Diabetic, smoker, hypertensive. Flat affect. Muscle tone increased, right grip weak, asymmetric reflexes, no tremor. 23/30 on MMSE (deficits in memory and calculations).
8. The most likely diagnosis is?

A. Alzheimer’s disease
B. Pick’s disease
C. Huntington’s disease
D. Parkinson’s disease
E. Vascular dementia
8. The most likely diagnosis is?

- A. Alzheimer’s disease (8%)
- B. Pick’s disease (2%)
- C. Huntington’s disease (1%)
- D. Parkinson’s disease (1%)
- E. Vascular dementia (88%)
Vascular Dementia

- Subcortical or mixed dementia
- Stepwise progression, prior strokes, focal neuro symptoms/signs
- Preserved personality but “emotional incontinence” or apathy common
- Definitive diagnosis difficult
Case Discussion

A 69-yo man has developed rigidity, a short-stepped gait, and masked facies. He also has become more forgetful (MMSE = 19). His family thinks he sees things that aren’t real.
9. The most likely diagnosis is?

A. Pick’s disease
B. Alzheimer’s disease
C. Diffuse Lewy body dementia
D. Progressive supranuclear palsy
E. Parkinson’s disease and depression
9. The most likely diagnosis is?

A. Pick’s disease
B. Alzheimer’s disease
C. Diffuse Lewy body dementia
D. Progressive supranuclear palsy
E. Parkinson’s disease and depression
Diffuse Lewy Body Dementia

Dementia, parkinsonism, and visual hallucinations (may develop severe EPS if prescribed neuroleptics)
Case Discussion

A 64-yo man is brought in by his family after exposing himself in public. He has been urinating in the kitchen sink and refuses to bathe. His MMSE is 26/30. He has some wording finding difficulties.
10. The most likely diagnosis is:

A. Alzheimer’s disease
B. Frontotemporal dementia
C. Diffuse Lewy body dementia
D. Vascular dementia
E. Creutzfeldt-Jakob disease
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A. Alzheimer’s disease
B. Frontotemporal dementia
C. Diffuse Lewy body dementia
D. Vascular dementia
E. Creutzfeldt-Jakob disease

Correct answer: B.
Frontotemporal Dementia

- Pick’s disease and non-specific degeneration of frontal lobes; corticobasal dementia, progressive supranuclear palsy ("Parkinson plus" syndromes)
- Behavioral problems early (disinhibition and/or profound apathy) plus aphasia
- Memory and visuospatial problems later
Case Discussion

A 76-yo man has increasing difficulty walking. He complains that his feet seem stuck together. He has mild memory loss. He has urge urinary incontinence.
11. You order the following test:

A. TSH
B. CT scan
C. Carotid ultrasound
D. EEG
E. Cystoscopy
11. You order the following test:

A. TSH
B. CT scan
C. Carotid ultrasound
D. EEG
E. Cystoscopy
Normal Pressure Hydrocephalus

- Clinical triad of dementia, ataxia, urinary incontinence (wacky, wobbly, and wet)
- Frequency of NPH and response to shunt surgery controversial
- Ataxia most responsive; dementia probably least responsive
Case Discussion

An 84-yo woman has developed rapidly progressive dementia over 4 months. She has a low-grade fever, is very rigid, and has myoclonic jerks when startled. EEG shows triphasic sharp wave complexes.
12. This pattern is consistent with which diagnosis?

A. Creutzfeldt-Jakob Disease
B. Subdural hematoma
C. Cerebral vasculitis
D. HIV dementia
E. Herpes encephalitis
12. This pattern is consistent with which diagnosis?

A. Creutzfeldt-Jakob Disease
B. Subdural hematoma
C. Cerebral vasculitis
D. HIV dementia
E. Herpes encephalitis

65% ✓ A. Creutzfeldt-Jakob Disease
1% B. Subdural hematoma
17% C. Cerebral vasculitis
0% D. HIV dementia
17% E. Herpes encephalitis
Creutzfeldt-Jakob Disease

- Rapidly progressive dementia over several months with myoclonus
- Frequently have periodic synchronous bi- or triphasic sharp wave complexes on EEG
- Tend to be younger patients
- Transmissible (viral-like “prions”)
- Rare (1 per million in US)
- “Variant” CJD = mad cow disease
Case Discussion

An 81-yo patient with advanced dementia is hoarding food at her assisted living facility and repeatedly leaving her room wearing only her underwear. She makes sexually inappropriate comments to visitors. The administrator asks you to “do something” to control these behaviors.
13. You should:

A. Begin donepezil 10 mg at bedtime.
B. Begin haloperidol 0.5 mg bid.
C. Begin olanzapine (eg, Zyprexa) 2.5 mg hs.
D. Begin valproate 250 mg tid.
E. Offer to help the staff find ways to manage the behaviors non-pharmacologically.
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Which Behaviors “Responsive” to Medication?

• RESPONSIVE: Agitation, depression, delusions, hallucinations, aggression
• REFRACTORY: Wandering, hoarding/hiding objects, repetitive questioning, apathy, social inappropriateness
• Behavioral approach to refractory Sx
Do Cholinesterase Inhibitors Treat Neuropsychiatric Symptoms?

- 272 pts in 12-week trial of donepezil (Aricept) for treatment of agitation in Alzheimer’s disease (avg MMSE 8/30)
- Donepezil no more effective than placebo
“Popular Drugs for Dementia Tied to Deaths”
NY TIMES 4/12/05

- FDA reviewed all atypical antipsychotics in dementia.
- 17 placebo-controlled studies, 5106 elderly subjects with dementia, average duration of Rx 10 weeks.
- Deaths: 4.5% (Rx) vs 2.6% (placebo).
Risk of Death in Elderly Users of Conventional vs Atypical Antipsychotics

Retrospective evaluation of Medicare data suggests that death rate in nursing home residents on typical antipsychotics is the same, if not greater than, the atypical antipsychotics.

CATIE-D Results

• Randomized trial comparing olanzapine, quetiapine, risperidone, and placebo for agitation/aggression in demented patients

• “Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer disease.”

New Treatments for Dementia: Are They Worth Remembering?

- 5 FDA-approved medications for Rx of dementia; no evidence yet of clinically significant alteration in disease course.
- Stop the amitriptyline (et al).
- Read while you exercise.
- "Searching for a breakthrough, settling for less."
Answers

1. E
2. D
3. A
4. C
5. D
6. E
7. D
8. E
9. C
10. B
11. B
12. A
13. E
Supplementary Slides
Caregiver/Practitioner Resources

• Alzheimer’s Association 1-800-272-3900 or www.alz.org

• Government funded clinical trials in AD can be found at http://clinicaltrials.gov
Additional Reading

- Le Couteur DG et al. Political drive to screen for pre-dementia; not evidence based and ignores the harms of diagnosis. BMJ. 2013;347:f5125.
Additional Reading