Differentiating the D's
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Learning Objectives
1. Diagnose and treat geriatric depression
2. Define delirium
3. Describe differential diagnosis of dementia
4. Discuss evaluation of cognitive impairment
5. Review prevention & treatment of dementia

Case Discussion
• Mr Bluesome is an 80-yo Caucasian male in general good health c/o vague abdominal pain, fatigue, and dyspnea that is intermittent and unrelated to exertion. His appetite is “OK” and weight is stable. His sleeping is fine but “restless” during the day. His wife died 1 year ago with colon cancer. Exam unremarkable except for moderate DJD. Extensive work-up by 2 other physicians was negative.

1. What is your next step?
   A. Order pulmonary function test with lung volumes
   B. Order cardiac ultrasound
   C. Prescribe buspirone for daytime anxiety
   D. Order upper endoscopy
   E. Screen for depression

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Overview of Late-Life Depression
• Depression is not a normal part of aging; independent, community-dwelling elderly have lower prevalence of depression
• Depression more common among elderly in medical settings (30% of CVA, cancer, or MI)
• 80% of late-life depression treated by PCP

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Overview of Late-Life Depression

- Gender gap narrow with advancing age
- Signs of depression often precede medical illness (Alzheimer’s, CVA, MI, etc)
- Increases health care costs, including polypharmacy, office and ER visits, length of inpatient stay
- Increased ethanol use and drug abuse
- Increased mortality 4-fold or more for many illnesses (MI, cancer, CVA, etc)

DSM-IV Diagnostic Criteria for Depression

- Diagnostic criteria include depressed mood plus 4 or more of the following symptoms >2 weeks (SIG: E CAPS):
  - Impaired Sleep, lack of interest, Guilt, low Energy, c/o difficulty Concentrating, poor Appetite, Psychomotor retardation, Suicidal

Early vs Late-Life Depression

- Anxiety more common in elderly
- Multiple somatic complaints common
- Vegetative signs less reliable (eg, poor appetite, sleep disturbance, lack of energy)

Anhedonia
(No Pleasure, Lack of Interest)

- Single most reliable sign of depression
- Ask specifically about activities over last 24-48 hours and enjoyment, if any, of each
- Distinguish things they can no longer perform from those they can perform but no longer enjoy

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 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 (grasp reflex, palmo mental response, rooting, snout, glabellar)
- Abulic patient may seem to enjoy activities if others initiate them

Suicidality

- Elderly 13% of population, 24% of completed suicides
- Elderly men at greatest risk; >85 yo, 1/2000 commit suicide annually
- Often first episode of depression
- Most had seen a physician within 1 month of suicide

Case Discussion

- Mr Bluesome admits that he’s felt worthless for the last several weeks and has not enjoyed any of his usual activities (walking the dog, reading the newspaper, playing golf). He often lacks the energy to get out of bed in the morning. He worries that his children visit only out of obligation because he was a poor father to them. He has trouble concentrating when he has to pay bills or work on the computer.

Case Discussion (cont.)

- You specifically ask about suicidality; he says he’s felt as if life isn’t worth living at times but feels his religious beliefs prohibit him from taking his own life. He contracts for safety.

2. What should you do?

A. Admit to inpatient mental health unit for ECT
B. Begin amitriptyline 25 mg bedtime
C. Begin risperidone 1 mg daily
D. Begin trazodone 50 mg bedtime
E. Begin citalopram 10 mg daily and refer for psychotherapy

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Management Principles

• Multidisciplinary, multimodal approach may be more cost-effective
• Exercise can improve both major and minor depression
• Key: write prescription for patient to re-engage in activities previously enjoyable even if initially not pleasurable

Principles of Medication Management

• Cochrane review (26 randomized trials) showed little difference in efficacy between medications for Rx of geriatric depression
• Start lower (generally half the dose of younger patients) but may need to go to same therapeutic range to achieve efficacy
• Phone contact within 2 weeks re: tolerance
• Visit within 4-6 weeks to discuss response, dose increase

Drug Treatment of Geriatric Depression

• SSRIs are preferred initially (better tolerated, not more effective)
• Side effects include anorexia, nausea; rarely, tremor or hyponatremia
• SNRIs (serotonin-norepinephrine reuptake inhibitors) such as sustained release venlafaxine (eg, Effexor) or duloxetine (Cymbalta) more expensive, not clearly more effective

Other Agents

• Bupropion (eg, Wellbutrin) ‘activating’ and may be useful; caution: lowers seizure threshold
• Mirtazapine (eg, Remeron); allegedly more sedating, weight gain
• Trazodone (eg, formerly Desyrel) less effective; may be useful when insomnia is prominent (begin 50 mg at bedtime)

Duration of Treatment

• 6 to 12 months after remission for first episode of depression (relapse rate higher in elderly)
• Data on risks/benefits of treatment longer than 2 years lacking for patients >65 yo

Electroconvulsive Therapy

• ECT is still a consideration for severe, medication refractory depression in elderly (especially with psychosis)
• Response usually becomes apparent after 3 to 5 treatments (6-12 total)
• Unilateral lead placement may reduce cognitive loss but not as effective

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Take-Home Points

• Late-life depression is common and morbid; screening for it routinely is worthwhile.
• Both drug treatment and nondrug management can be helpful.
• Antidepressant drugs are equally effective; side effect profiles vary and drive selection.
• Successful drug treatment requires close follow-up, reassurance, and willingness to increase dose to therapeutic level.

Case Discussion

• A 79-yr 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.

3. The most likely cause of her confusion is:
   A. Depression
   B. Advanced dementia
   C. Delirium
   D. Early dementia
   E. Mild cognitive impairment

DSM-IV Diagnostic Criteria For Delirium

• \textit{Acute} disturbance of cognition (\textit{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
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
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>Nonpharmacologic sleep protocol</td>
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<td>Immobility</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>
</tr>
</tbody>
</table>

4. 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

“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.

5. What is your diagnosis?

- A. This patient has dementia.
- B. This patient is depressed.
- C. This patient is delirious.
- D. This patient had mild cognitive impairment.

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5. What is your diagnosis?

- A. This patient has dementia. 29%
- B. This patient is depressed. 1%
- C. This patient is delirious. 0%
- D. This patient had mild cognitive impairment. 36%

Epidemiology of Dementia

- Prevalence of dementia in community: 3% to 10% >65 yo, 30% to 50% >85 yo
- Incidence of dementia approx 3% among elderly >75 yo
- Fourth leading cause of mortality >80 yo
- 75% of AD patients admitted to nursing homes for an average of 3 yrs

Cost of Dementia

- >5.0 million elderly with dementia
- Formal and informal costs (includes value of unpaid caregivers) = approximately $150 billion annually
- Delay onset by 5 years = 50% decline in prevalence

(DSM-IV 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)

DSM-IV Criteria for Dementia

- 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

6. 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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**DSM-IV 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

**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.

7. 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.
E. This patient is normal for his age.
“Mild Cognitive Impairment”

- 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 (16% annually)

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.

8: 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

‘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

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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.”


Potentially Reversible Dementias

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<tr>
<th>DRUGS</th>
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<tbody>
<tr>
<td>HYPOHYROID</td>
<td>7</td>
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<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>TOTAL</td>
<td>31 (10%)</td>
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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).

9: 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

Summary of Cholinesterase Inhibitor Trials in Alz Disease

- 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

- 3 RCTs in 1066 subjects, 12-28 weeks (moderate to severe in 1 study)
- Cognitive scale benefit similar to ChEI in 2 studies of mild/mod dementia
- Behavioral, ADL, and global scales modestly better in mod/severe dementia
- Caregiver burden not measured
- ADR: No different than placebo

Diagnosis and Treatment of Dementia: the Dismal Failure of Medical Science

- No direct evidence linking screening and improved health outcomes (USPSTF. Ann Intern Med. 2003;138:927-937.)
- No current intervention will prevent or delay the onset of dementia (consensus.nih.gov/2010)
- Treatment for dementia (cholinesterase inhibitors and NMDA receptor antagonist) is minimally effective Ann Intern Med. 2008;148:370-378.

Case Discussion


10. The most likely diagnosis is?

A. Alzheimer’s disease
B. Pick’s disease
C. Huntington’s disease
D. Parkinson’s disease
E. Vascular dementia

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-yr 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.

11. 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-yr 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.

12. The most likely diagnosis is:

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

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12. The most likely diagnosis is:

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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-yr man has increasing difficulty walking. He complains that his feet seem stuck together. He has mild memory loss. He has urge urinary incontinence.

13. 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-yr woman has developed rapidly progressive dementia over 4 months. She has a low-grade fever, is very rigid, and has myoclonic jerks when startled.

14: Which test is most likely to confirm your diagnosis?
- A. An EEG
- B. Head CT
- C. Brain MRI
- D. EMG/nerve conduction
- E. Lumbar puncture

Creutzfeldt-Jakob Disease

• Rapidly progressive dementia over several months with myoclonus and periodic EEG bursts; younger patients
• Transmissible (viral-like “prions”)
• Rare (1 per million in U.S.)
• “Variant” CJD = mad cow disease

Case Discussion

• An 81-yr 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.

15: You should
- A. Begin sertraline 50 mg daily
- 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 nonpharmacologically
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CATIE-D Results
• 421 pts with psychosis, agitation or aggression; mean time to discontinuation of assigned drug 8 weeks - olanzapine (eg, Zyprexa), risperidone (eg, Risperdal) or quetiapine (Seroquel)
• ‘Adverse effects offset advantages in the efficacy of atypical antipsychotic drugs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer disease’
  Schneider L et al, NEJM 355:1525: 10/12/06

Answers
1. E
2. E
3. C
4. D
5. A
6. C
7. D
8. E
9. D
10. E
11. C
12. B
13. B
14. A
15. E

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