Overview of Dementia & Delirium

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BUMCP Internal Medicine Lecture Series
December 15, 2015
Disclosures

I have no financial conflicts of interest to disclose.

http://www.cliparthut.com/clip-arts/647/monopoly-man-647882.jpg
Objectives

Your handout asks us to cover:

1. Define dementia, describe dx criteria
2. Define MCI, dx criteria, conversion to dementia / year
3. Eval of pt with MCI or dementia
5. Define delirium, describe dx criteria, management with pharm & non-pharm methods.
Review Articles I Will Provide


Our plan today

- Review dementia using a **syndromic** approach
- Identify distinguishing features of dementia syndromes
Four quibbles

A quibble is to Shakespeare what luminous vapours are to the traveller: he follows it at all adventures; it is sure to lead him out of his way and sure to engulf him in the mire.

(Samuel Johnson)

Your assigned reading is pretty good. However….

- Mild cognitive impairment is usually NOT associated with “diminished independence…” (p. 38)

Petersen RC. NEJM 2011; 364: 2227-2234
Albert MS et al. Alzheimer’s & Dementia 2011; 7: 270-279
Your assigned reading is pretty good. However….

- “CSF biomarkers have no role in clinical diagnosis of AD…” (true)…”because of the absence of disease-modifying therapies…” (false) (p. 41)

- The reason not to send CSF is because:
  - Lab standards are still not uniform
  - Performance characteristics of tests (spec, sens, PPV, NPV) in *individuals* not yet precisely known.

McKhann GM et al. Alzheimer’s & Dementia 2011; 7: 263-269
Tso J. Continuum (Minneap Minn) 2013; 19: 475-479
Your assigned reading is pretty good. However....

- The presence of motor & cognitive symptoms within 12 months is a handy mnemonic.
- But NOT sufficient to distinguish dementia with Lewy bodies from Parkinson’s disease dementia (p. 42).

Your assigned reading is pretty good. However….

- Non-contrast CT or MRI are useful.
- If there is no contraindication, use a 21st century imaging test (MRI).*

- When checking B12, also check methylmalonic acid.†


† Stabler SP. *NEJM* 2013; 368: 149-160.
Dementia
Number of People with AD is Increasing

Source: Alzheimer’s Association
Alzheimer's treatment needs intensify role of primary doctors

Experts hope dementia prevention options become as routine as those for other common medical problems.

Victoria Stagg Elliott
AMNEWS STAFF

The incidence of Alzheimer's disease is expected to more than triple in the coming decades. And new treatments and research into prevention will put primary care physicians on the front lines of dealing with the debilitating condition.

Much of the management and treatment of the disease has been largely in the realm of the specialist. But with the emergence in the past few years of modestly effective treatments for Alzheimer's that work primarily in the early stages, primary care physicians are already under increasing pressure to diagnose the disease early.

“The most urgent thing clinically is identifying people who, by the nature of the illness, won't present themselves for care,” said Richard J. Ham, MD, director of the Center on Aging at West Virginia University in Morgantown. “Most people don't get diagnosed until they've had the disease for years.”

Early detection remains extremely challenging. Diagnosis of mild cognitive impairment may indicate the patient eventually may develop full-blown Alzheimer's, but it also may not. Treatment efficacy remains modest if it works at all.

“The issue that the researcher and the clinician face is trying to figure out if somebody, especially over the age of 65 or 70, is experiencing cognitive impairment because of depression, heart disease or medications they take, or are they on the way to dementia,” said Steven DeKosky, MD.

Continued on next page
Dementia in a Single Slide

Movement Disorders

Amnestic Dementias

Linguistic Dementias

Comportmental Dementias

Synucleinopathies

Amyloidopathies

Triplet repeat

HD

PSP

CBGD

Frontal Dementia

Pick's Disease

Semantic Dementia

PPA

PD

DLB

AD

Features of Dementia

- Usually gradual in onset & progression
  - Exception: vascular dementia
- Affects at least 2 cognitive domains
  - Memory *often* but not always involved
- Represents a *decline from a premorbid ability*
- Affects ADLs
- No better explanation

Galasko D. Continuum (Minneap Minn) 2013; 19: 397-410
Elements of Diagnosis in Any Cognitive Complaint
Diagnosis =
Tests of major cognitive domains
  +
Tempo of evolution of symptoms
  +
Associated neurologic signs
  +
Context (other diseases, etc.)
Diagnosis =

+ Tests of major cognitive domains
  Frontal, perisylvian, visuospatial, praxis, mood, \( \Psi \)

+ Tempo of evolution of symptoms
  Gradually progressive, stepwise, fluctuating, chronic, subacute, acute, or combination

+ Associated neurological signs
  Focal signs, parkinsonism, neuropathy, myopathy

+ Context (e.g., other diseases)
  Vascular disease elsewhere, infectious diseases, liver disease, lung disease
Cognitive domains

Tempo of evolution

Associated neuro signs

Context
Key Syndromes
Primary Amnestic Syndromes

- Alzheimer’s Disease
- Mild Cognitive Impairment
Auguste D., ca. 1902

Alois Alzheimer, ca. 1907

Maurer K et al. Lancet 1997; 349: 1546-1549
Key Concept

Significant declines in cognitive function do not represent normal aging.

Multiple refs. E.G., Brain & Cog 2006;60:146.
Adapted from Petersen, 2002

Impaired memory, normal ADLs

Impaired memory, impaired ADLs

Function

Mild Cognitive Impairment*

Probable AD**

Definite AD†

Age
Alzheimer’s Disease

- **DOMAINS**
  - Memory invariably involved
  - Apraxia, amnesia, aphasia, agnosia, neglect
- **TEMPO**
  - Gradually progressive
- **ASSOCIATED FINDINGS**
  - Paratonia
- **CONTEXT**
  - Usually otherwise healthy

*Neurology* 1984;34:939.  
*DSM IV 1994*
Key Concepts of AD

- Age is the single greatest risk factor
- Acetylcholine is the main transmitter affected
  - Glutamate, NE, 5-HT, & others are affected
- Apo-E status increases risk
- Role of insulin-like growth factors unclear
- Aβ-42 is increased in brain but low in CSF
- Tau is increased in CSF
- PET CT and β-amyloid CT may soon be approved for general use

Do not send these labs
The 3 FDA-approved cholinesterase inhibitors are equal in efficacy for AD.

- EXCEPTION: Exelon appears better for Parkinson’s disease dementia.

- TIP: avoid oral Exelon, favor Exelon patch.
  - Oral has more diarrhea, nausea.

Begin with cholinesterase inhibitor therapy, add memantine for mid- to late-stage disease once cholinesterase inhibitor dose is stable.
Treatment of AD

- Cholinesterase inhibitors slow decline even in late stage AD.
- “Lack of efficacy” in late stage disease is not a reason to d/c.
- Possible reasons to d/c in late stage dz:
  - Side effects (nausea, diarrhea)
  - Ethical: what are we prolonging?
- Additional possible benefit in late stage dz: psychiatric sx (depression, anxiety, agitation)

Future Treatment of AD

- Immunotherapy is in phase 3 clinical trials*[^1], †[^1]
- Genetic tx of Apo-E is in phase 1-2 trials ‡[^2]
- Pre-symptomatic detection is a focus of intense work§[^3]
- Prevention is the target of a $100 M clinical trial £, ¥[^4]
- See www.banneralz.org/ for more info

[^1]: Agadjanyan MG et al. *Alz & Dem* 2015; 11: 1246-1259
[^5]: Tariot PN et al. *Alz & Dem* 2014; 10(4): supplement P247
Mild Cognitive Impairment (MCI)
Mild Cognitive Impairment (MCI) Amnestic Type: Clinical Definition

- **DOMAIN**
  - Memory *only*
  - Memory impairment corroborated by friends/family
  - Intact ADLs

- **TEMPO**
  - Gradual onset, variable decline
  - Conversion to AD: ~ 16 – 20% per year

- **ASSOCIATED FINDINGS**
  - Otherwise normal

- **CONTEXT**
  - Otherwise healthy

Mild Cognitive Impairment (MCI) Amnestic Type: Research Definition

- Subjective memory impairment corroborated by other informants
- Performance on objective memory tests > 1.5 SD below norms for age & education
- Intact ADLs
- Otherwise normal cognitive function

Albert MS et al. *Alz & Dem* 2011; 7: 270-279
Amnestic MCI: Key Points

- Increased risk of AD
  - Conversion rate to AD 16-20% per year
  - 1-2 % per year for healthy elderly
- Is all MCI just early AD?
  - Maybe yes, maybe no
  - Seems safe to assume that not all MCI is the same
  - Some MCI patients appear stable over many years

Petersen R. *NEJM* 2011; 364: 2227-2234
Amnestic MCI: Treatment

- Optimal tx not known
- “Vitamin E & Donepezil for Treatment of MCI”*
  - Vitamin E showed no benefit
  - Aricept slowed progression to AD only during the first 12 months of therapy
- Many questions remain
  - Are all subjects with MCI the same?
  - Is 3 years sufficient follow up?
  - Subgroup analyses suggest higher benefit for some subjects – there seem to be subtypes of MCI (likely true pre-AD MCI derives most benefit)
- Should we still use donepezil in MCI????

Other Dementias

M. C. Escher, “The Magic Mirror”
Lithograph, 1946
Other Dementias

- Vascular
- Parkinson’s plus
  - Dementia with Lewy bodies
  - PSP
  - CBD
- Frontal
- NPH
Multi-infarct dementia

- No formal diagnostic criteria
- DOMAINS
  - Multiple domains (and may look like AD)
- TEMPO
  - Gradual; step-wise hx not always clear
- ASSOCIATED FINDINGS
  - Supported by MRI findings
  - Often multiple abnormalities on elemental exam
  - Hachinski ischemic index score (?)
- CONTEXT
  - Vascular risk factors
  - Treatment of modifiable risk factors

\(^1\)See Chui et al., *Arch Neurol* 2000;57:191-196
Parkinson’s Plus Syndromes

- Dementia with Lewy bodies (DLB)
- Progressive supranuclear palsy (PSP)
- Corticobasal degeneration (CBD)
- Multiple system atrophy (MSA)
Parkinson’s Plus Syndromes

- Common to all syndromes:
  - **DOMAINS**
    - All associated with apraxia, amnesia, bradyphrenia.
  - **TEMPO**
    - Gradual
    - Progression often atypical for PD (rapid, fluctuating, etc.).
  - **ASSOCIATED FINDINGS**
    - Parkinsonism w/o sustained improvement on Sinemet.
  - **CONTEXT**
    - Cognitive & motor impairments evolve within 12 months of each other.
    - No better explanation (e.g., multi-infarct).

Lopez et al., *Neurology* 1999;53:1292-1299
Parkinson’s Plus Syndromes

- Common to all syndromes:
  - Cholinergic deficit → cholinesterase inhibitor therapy is appropriate
  - Unknown if memantine may benefit
  - Trial of carbidopa / levodopa may or may not be of benefit, and benefit may not be sustained
  - Antipsychotic medications may be needed for aggression, hallucinations
    - Quetiapine usually least offensive


Lopez et al., *Neurol* 1999;53:1292-1299
Parkinson’s Plus Syndromes

- Dementia with Lewy Bodies (DLB; DLBD)
  - DOMAINS
    - Amnesia with motor findings
  - TEMPO
    - Gradual, *fluctuating cognition* (dramatic)
  - ASSOCIATED FINDINGS
    - *Parkinsonism*
    - *Visual hallucinations*
  - CONTEXT
    - Sensitivity to neuroleptics
    - Hallucinations other than visual
    - Early falls
    - Depression
    - REM sleep behavior disorder

McKeith et al., *Neurology* 2000;54:1050-1058
Lopez et al., *Arch Neurol* 2002;59:43-46
Parkinson’s Plus Syndromes

- Progressive Supranuclear Palsy (PSP)
  - DOMAINS
    - Apraxia, amnesia
  - TEMPO
    - Gradual
  - ASSOCIATED FINDINGS
    - Supranuclear vertical gaze palsy
    - Early postural instability
    - Axial rigidity
  - CONTEXT
    - Otherwise healthy

Litvan et al., Neurol 1996;47:1-9
Parkinson’s Plus Syndromes

- Corticobasal(ganglionic) Degeneration CB(G)D
  - DOMAINS
    - Alien limb/“useless arm” = severe, *asymmetric* apraxia & rigidity
    - Cortical sensory loss
  - TEMPO
    - Gradual
  - ASSOCIATED FINDINGS
    - Stimulus-sensitive myoclonus
    - Frontal release signs
  - CONTEXT
    - Otherwise healthy

Riley & Lang, *Adv Neurol* 2000;82:29-34
Frontal Dementias
Frontal & Frontotemporal Dementias

- Frontal dementia (behavioral variant)
- Semantic dementia
- Primary progressive aphasia (PPA)
Frontal/Frontotemporal Dementia

- **DOMAINS**
  - Early personality change OR (AND?)
  - Early language impairment
  - [Apraxia, executive dysfunction, vigilance errors, perseveration/impersistence, concrete thought, anosognosia]

- **TEMPO**
  - Gradual onset, decline of variable rapidity

- **ASSOCIATED FINDINGS**
  - Frontal release signs

- **CONTEXT**
  - Often younger (~ 50’s)

Warren JD & MN Rossor *BMJ* 2013; 347:f4827. doi 10.1136/bmj.f4827

Working Group on Frontotemporal Dementia and Pick’s Disease, *Arch Neurol* 2001
NPH

- **DOMAINS**
  - Difficulty walking
  - Urinary incontinence
  - Memory problems *but no cortical signs* (aphasia, apraxia, agnosia)

- **TEMPO**
  - Gradual onset, decline of variable rapidity

- **ASSOCIATED FINDINGS**
  - “Magnetic gait”

- **CONTEXT**
  - Prior SAH or CNS dz more consistent with NPH

• Single LP in each of 3 patients.
• One patient later found to have obstructive 3\textsuperscript{rd} ventricular lesion
Tips on NPH


- **HISTORY**
  - Pts with dementia > 2 years are less likely to respond to surgery.
  - If gait disorder began before or concurrently with dementia, improvement with surgery is more likely.

- **TESTING**
  - Evans index & callosal angle helpful.
  - Large volume LP: 30-50 cc.
  - Poor sensitivity (~25%) but good positive predictive value.
  - Look for improvement of gait immediately after LP.
Evan’s index

- Ratio of maximum width of frontal horns to maximum transverse inner diameter of the skull
- Frequently used by neurosurgeons
- High sensitivity, low specificity (large in both atrophy and hydrocephalus)
- No direct correlation between Evans Index and response to shunting

Courtesy Bruce L. Miller, MD  “Dementia Update” February 16, 2012
Hydrocephalus: Callosal Angle

- Measured on coronal images at the level of the posterior commissure
- Coronal images should be perpendicular to AC-PC line
Delirium

R. Magritte, “God’s Salon”  
Oil on canvas, 1948
Key Points

1. Delirium is an *acute, fluctuating* alteration in mental status characterized by altered level of *consciousness*, fluctuating *attention*, and globally clouded *cognition*.

2. Risk increases with age, presence of dementia, polypharmacy, severity of illness, and metabolic derangement.

3. Delirium increases *risk of death*.

4. Delirium increases is costly and increases length of hospital stay.

5. The best treatment for delirium is *prevention*, and directed interventions can prevent delirium.

6. Other treatments exist, but prevention is key.
Key Points

- Delirium is most commonly a *medical* condition
  - You don’t have to be a neurologist or psychiatrist to diagnose or manage it.
  - You *do* have to be a meticulous internist.
Epidemiology

- 20-50% older patients (esp. postoperatively)
- 70-90% of patients in ICU
- 80% of patients at end of life
- Community prevalence: < 1-2%

- Mortality 25-75% (comparable to MI or sepsis)
- One-year mortality: 35-40%

- Up to 20% of 12.5 M patients > 65 years
- Cost ≈ $2,500/pt ($6.9 billion) per year

DHHS 2004 CMS Statistics (pub. #03445)
Inouye, Clin Geriatr Med 199;14:745-764
Definitions

- Synonyms:
  - Acute confusional state (psychiatry)
  - Encephalopathy (neurology)

- Delirium is a syndrome not a diagnosis
  - It has an underlying cause
  - Dementia is not the cause (but can contribute)
  - Your job is to find & correct the cause
Clinical Features

- Acute
  - May occur gradually (hours to a few days)
  - Not weeks or months
  - Reliable informants often needed

- Fluctuating
  - Symptoms wax and wane over 24 hours
  - Often worse at night (“sundowning”)
  - Commonly with lucid intervals

Compiled from Inouye 2006; Lipowski, 1990; Maldonado, 2008
Clinical Features

- Perceptual disturbances are common
  - Illusions or hallucinations in \( \approx 30\% \) of pts

- Psychomotor disturbances
  - Hyperactive, hypoactive, or both

- Altered sleep-wake cycle
### Risk Factors

**Table 2. Predisposing Factors for Delirium.**

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of 65 years or older</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td></td>
</tr>
<tr>
<td>Cognitive status</td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td></td>
</tr>
<tr>
<td>History of delirium</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Functional status</td>
<td></td>
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<tr>
<td>Functional dependence</td>
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<tr>
<td>Immobility</td>
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<tr>
<td>Low level of activity</td>
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<tr>
<td>History of falls</td>
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<tr>
<td>Sensory impairment</td>
<td></td>
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<tr>
<td>Visual impairment</td>
<td></td>
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<tr>
<td>Hearing impairment</td>
<td></td>
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<tr>
<td>Decreased oral intake</td>
<td></td>
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<tr>
<td>Dehydration</td>
<td></td>
</tr>
<tr>
<td>Malnutrition</td>
<td></td>
</tr>
</tbody>
</table>

**Drugs**

- Treatment with multiple psychoactive drugs
- Treatment with many drugs
- Alcohol abuse

**Coexisting medical conditions**

- Severe illness
- Multiple coexisting conditions
- Chronic renal or hepatic disease
- History of stroke
- Neurologic disease
- Metabolic derangements
- Fracture or trauma
- Terminal illness
- Infection with human immunodeficiency virus

# Precipitating Factors

## Table 3. Precipitating Factors or Insults That Can Contribute to Delirium.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Primary neurologic diseases</th>
<th>Intercurrent illnesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedative hypnotics</td>
<td>Stroke, particularly nondominant hemispheric</td>
<td>Infections</td>
</tr>
<tr>
<td>Narcotics</td>
<td>Intracranial bleeding</td>
<td>Iatrogenic complications</td>
</tr>
<tr>
<td>Anticholinergic drugs</td>
<td>Meningitis or encephalitis</td>
<td>Severe acute illness</td>
</tr>
<tr>
<td>Treatment with multiple</td>
<td></td>
<td>Hypoxia</td>
</tr>
<tr>
<td>drugs</td>
<td></td>
<td>Shock</td>
</tr>
<tr>
<td>Alcohol or drug withdrawal</td>
<td></td>
<td>Fever or hypothermia</td>
</tr>
</tbody>
</table>

- **Anemia**
- **Dehydration**
- **Poor nutritional status**
- **Low serum albumin level**
- **Metabolic derangements** (e.g., electrolyte, glucose, acid-base)
- **Surgery**
  - Orthopedic surgery
  - Cardiac surgery
  - Prolonged cardiopulmonary bypass
  - Noncardiac surgery
- **Environmental**
  - Admission to an intensive care unit
  - Use of physical restraints
  - **Use of bladder catheter**
  - Use of multiple procedures
  - Pain
  - Emotional stress
  - Prolonged sleep deprivation

Treatment

1. PREVENTION
2. PREVENTION
3. PREVENTION
A MULTICOMPONENT INTERVENTION TO PREVENT DELIRIUM IN HOSPITALIZED OLDER PATIENTS

SHARON K. INOuye, M.D., M.P.H., SIDNEY T. Bogardus, Jr., M.D., PETER A. CHARPENTIER, M.P.H., LINDA LEO-SUMMERS, M.P.H., DENISE ACAMPORA, M.P.H., THEODORE R. Holford, Ph.D., AND LEO M. COONEY, JR., M.D.
Preventing Delirium

1. Orientation & therapeutic activities
2. Early mobilization
3. Minimize psychoactive drugs
   a. Orientating stimuli
   b. Normal sleep-wake cycles
4. Adaptive equipment
   a. Glasses, hearing aids
5. Early intervention for volume depletion
Preventing Delirium*

- In addition to the above…
  6. Optimize oxygen delivery to brain
  7. Monitor fluid & electrolyte balance
  8. Pain management
  9. *Attend to bowel & bladder function*

Treating Delirium

- Acute stabilization
  - Airway
  - Hydration/volume status
  - Close nursing supervision (ICU?)
  - Positioning (prevent decubiti)
  - DVT prophylaxis
Treating Delirium

- Environmental cues
  - Calendars, clocks, familiar home objects
  - Reorienting by staff
- Limit staff & room changes
- Allow for uninterrupted sleep at night
  - Coordinate VS measures, meds, etc.
- Low noise, low light at night
- Up and about during the day
Pharmacologic Treatments
Table 4. Pharmacologic Treatment of Delirium.

<table>
<thead>
<tr>
<th>Class and Drug</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotic</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Haloperidol</td>
<td>0.5–1.0 mg twice daily orally, with additional doses every 4 hr as needed (peak effect, 4–6 hr)</td>
<td>Extrapyramidal symptoms, especially if dose is &gt;3 mg per day</td>
<td>Usually agent of choice</td>
</tr>
<tr>
<td></td>
<td>0.5–1.0 mg intramuscularly; observe after 30–60 min and repeat if needed (peak effect, 20–40 min)</td>
<td>Prolonged corrected QT interval on electrocardiogram</td>
<td>Effectiveness demonstrated in randomized, controlled trials&lt;sup&gt;20,37&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Avoid in patients with withdrawal syndrome, hepatic insufficiency, neuroleptic malignant syndrome</td>
<td>Avoid intravenous use because of short duration of action</td>
</tr>
<tr>
<td>Atypical antipsychotic</td>
<td></td>
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</tr>
<tr>
<td>Risperidone</td>
<td>0.5 mg twice daily</td>
<td>Extrapyramidal effects equivalent to or slightly less than those with haloperidol</td>
<td>Tested only in small uncontrolled studies</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>2.5–5.0 mg once daily</td>
<td>Prolonged corrected QT interval on electrocardiogram</td>
<td>Associated with increased mortality rate among older patients with dementia</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25 mg twice daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td></td>
<td>Paradoxical excitation, respiratory depression, oversedation</td>
<td>Second-line agent</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5–1.0 mg orally, with additional doses every 4 hr as needed*</td>
<td></td>
<td>Associated with prolongation and worsening of delirium symptoms demonstrated in clinical trial&lt;sup&gt;37&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reserve for use in patients undergoing sedative and alcohol withdrawal, those with Parkinson's disease, and those with neuroleptic malignant syndrome</td>
</tr>
<tr>
<td>Antidepressant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>25–150 mg orally at bedtime</td>
<td>Oversedation</td>
<td>Tested only in uncontrolled studies</td>
</tr>
</tbody>
</table>

* Intravenous use of lorazepam should be reserved for emergencies.
Magritte, *Time Transfixed*, Oil on canvas, 1938
Extra slides (not covered)
Key Concepts of AD

- Depression is common & treatable
  - Depression may be an early sign (???)
- Parkinsonism can appear in advanced stages
- Cholinesterase inhibitors are first-line
  - May benefit even in late stages
- NMDA antagonists studied only in late stage dz
Normal Errors of Memory
THE SEVEN SINS OF MEMORY
{ How the Mind Forgets and Remembers }
DANIEL L. SCHACTER
Chair of Harvard University's Department of Psychology

“A GRIPPING AND THOUGHT-PROVOKING EXPLORATION.” — STEVEN PINKER
Normal Memory Errors

- Omissions
  - Transience
  - Absent-mindedness
  - Blocking

- Commission
  - Misattribution
  - Suggestibility
  - Bias
  - Persistence
Normal Memory Errors

- Omissions: common patient complaints
  - Transience: normal loss of detailed memory over time
    - Recall problem
    - Ebbinghaus, 1885
  - Absent-mindedness: attentional disruption
    - Encoding problem
  - Blocking: inability to access known information
    - Retrieval problem
Parkinson’s Plus Syndromes

- **Multiple System Atrophy (MSA; Shy-Drager)**
  - **DOMAINS**
    - Apraxia, amnesia, anomia
  - **TEMPO**
    - Gradual but rapidly progressive
  - **ASSOCIATED FINDINGS**
    - Orthostasis & urinary incontinence
    - Parkinsonism
    - Cerebellar dysfunction (ataxic dysarthria, limb ataxia, sustained gaze-evoked nystagmus)
    - Corticospinal dysfunction
  - **CONTEXT**
    - Otherwise healthy
    - (OPCA/SND: Probably pathologic diagnoses, subset of MSA.)
Multiple System Atrophy: Features*

I. Autonomic dysfunction
   Orthostatic hypotension, urinary dysfunction

II. Parkinsonism

III. Cerebellar dysfunction

IV. Corticospinal tract dysfunction

* simplified
Multiple System Atrophy: Diagnosis

- Possible MSA*
  - Features from 3 categories of I-IV
- Probable MSA
  - Autonomic failure or urinary dysfunction AND
  - DOPA-unresponsive parkinsonism OR cerebellar dysfunction
- Definite MSA
  - Pathologic confirmation

* simplified

Research in AD

- AD begins earlier in Latinos than Anglos (Arch Neurol 2005;62:774)
- Survival in AD depends on age at dx (Arch Neurol 2005;62:779)
- Atypical antipsychotics may increase risk of MI & stroke (Am J Ger Psych 2006;14:191)
- CSF levels of tau and Aβ-42 may predict conversion from MCI to AD (Lancet Neurol 2006;5:228)
- Impaired odor detection may predict AD (Ann Neurol 2005;58:155)
- Immune tx with myelin oligodendroglial glycoprotein reduced Aβ-42 deposits in mice (J Clin Invest 2005;115:2423)
More on Clinical Features of Delirium

- Global cognitive impairment
  - Implies *not* focal, such as aphasia, apraxia, or spatial neglect
    - Though memory, language, praxis, and spatial reasoning commonly affected….why?
  - Reduced clarity of awareness of environment
  - Disorganized thinking, rambling flow of ideas

- Attentional dyscontrol
  - Attentional systems profoundly affected (why?)
  - Difficulty focusing, sustaining, & shifting attention
  - Difficulty maintaining thread of conversation
Treating Delirium

- Diligent search for underlying causes
  - **Infection** (pneumonia, bladder, sepsis)
  - GI: bowel obstruction, perforated ulcer or diverticulum, hyperammonemia, pancreatitis
  - **Pulmonary**: PE, hypoxemia, pleural effusion
  - **CV**: MI, CHF, hyper-/hypotension, dehydration
  - **Renal**: electrolytes, uremia, ARF
  - **Skin**: decubiti (infection)
  - **Sensory deprivation**: glasses, hearing aids
  - **Neurologic**: stroke, meningitis, encephalitis, occult seizure
  - **Iatrogenic**: drugs, polypharmacy, narcotics, untreated pain
  - **Substance use/withdrawal**: ETOH, benzos, narcotics
Pathogenesis of delirium

- Not well understood
- Implicates multi-nodal, polysynaptic pathways
- Imaging & electrophysiology supports widespread neocortical dysfunction
- May be the only presenting symptom of life-threatening illness (MI, infection, impending respiratory failure).
  - Do your very best workup ever.
Pathogenesis of delirium

- Likely multifactorial
  - Evidence of cholinergic dysfunction*
  - Possible role of dopamine & other neurotransmitters†
  - Cytokines, TNF-α, and interferon may contribute‡
  - Chronic stress → hypercortisolemia → hippocampal serotonin£

† Cole Am J Geriatr Psychiatry 2004;12:7-21
‡ Broadhurst & Wilson, Br J Psychiatry 2001;179:288-289.