Disclosures

• None
Goals

• To define dementia and delirium
• To describe how to differentiate dementia from delirium
• To review types of dementia and delirium
• To discuss methods to diagnose dementia and delirium
Dementia

Major Neurocognitive Disorder

Evidence of significant 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 or knowledgeable informant

2. A substantial impairment in cognitive performance but neuropsychological testing or clinical assessment

DSM V reference
Dementia

Major Neurocognitive Disorder

• Cognitive deficits interfere with independence of everyday activities
  – Differentiates from Mild Neurocognitive Disorder or Mild Cognitive Impairment (MCI)

• Cognitive deficits do not occur in the context of a delirium
EPIDEMIOLOGY OF DEMENTIA

• 6%–8% of people ≥65 yr have Alzheimer dementia (AD)
  ➢ Prevalence doubles every 5 yr
  ➢ Nearly 45% of those aged 85+ have AD

• Vascular dementia co-occurs with an estimated 15%–20% of AD cases — “mixed dementia”

• Lewy body dementia (LBD) — second most common cause of dementia
Types of Dementia?

• Audience
ALZHEIMER DISEASE

• Onset: gradual

• Cognitive symptoms: memory impairment core feature with difficulty learning new information

• Motor symptoms: rare early, apraxia later

• Progression: gradual, over 8–10 yr on average

• Lab tests: normal

• Imaging: possible global atrophy, small hippocampal volumes

REFERENCE
http://goinggentleintothatgoodnight.com/2013/06/19/the-laypersons-guide-to-alzheimers-disease/
VASCULAR DEMENTIA

- Onset: may be sudden/stepwise
- Cognitive symptoms: depend on anatomy of ischemia, but dysexecutive syndrome common
- Motor symptoms: correlates with ischemia
- Progression: stepwise with further ischemia
- Lab tests: normal
- Imaging: cortical or subcortical changes on MRI

REFERENCE
FRONTOTEMPORAL DEMENTIA

• Onset: gradual, usually age <60

• Cognitive symptoms: executive, language, and behavioral dysfunction, including disinhibition and hyperorality

• Motor symptoms: none; may be associated with ALS in rare cases

• Progression: gradual but faster than AD

• Lab tests: normal

• Imaging: atrophy in frontal and temporal lobes
LEWY BODY DEMENTIA

- Onset: gradual
- Cognitive symptoms: memory, visuospatial, hallucinations, fluctuations
- Motor symptoms: parkinsonism
- Progression: gradual, but usually faster than AD
- Lab tests: normal
- Imaging: possible global atrophy
Key Terms and Dementia

- Early onset
  - Occurring less than 65 years of age
- With behavioral disturbance
  - Agitation, Paranoia, Physical Threatening, Sundowning
### Stage 1: No cognitive impairment

Unimpaired individuals experience no memory problems, and none is evident to a healthcare professional during a medical interview.

### Stage 2: Very mild cognitive decline

Individuals at this stage feel as if they have memory lapses, especially in forgetting familiar words or names or the location of keys, eyeglasses, or other everyday objects. However, these problems are not evident during a medical examination or apparent to friends, family, or coworkers.

### Stage 3: Mild cognitive decline

Early-stage Alzheimer disease can be diagnosed in some, but not all, individuals. Friends, family, or coworkers begin to notice deficiencies. Problems with memory or concentration may be measurable in clinical testing or discernible during a detailed medical interview.

### Stage 4: Moderate cognitive decline (mild or early-stage Alzheimer disease)

At this stage, a careful medical interview detects clear-cut deficiencies. The affected individual may seem subdued and withdrawn, especially in socially or mentally challenging situations.

REFERENCE
## Stage 5: Moderately severe cognitive decline (moderate or mid-stage Alzheimer disease)

Major gaps in memory and deficits in cognitive function emerge. Some assistance with day-to-day activities becomes essential.

## Stage 6: Severe cognitive decline (moderately severe or mid-stage Alzheimer disease)

Memory difficulties continue to worsen, significant personality changes may emerge, and affected individuals need extensive help with customary daily activities.

## Stage 7: Very severe cognitive decline (severe or late-stage Alzheimer disease)

This is the final stage of the disease when individuals lose the ability to respond to their environment, to speak, and ultimately to control movement.
## Functional Assessment Staging (FAST)

<table>
<thead>
<tr>
<th>FAST Stage and Characteristics</th>
<th>Clinical Diagnosis</th>
<th>Duration of stage*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No functional decrement</td>
<td>Normal Adult</td>
<td>50 years</td>
</tr>
<tr>
<td>2. Subjective word difficulties</td>
<td>Normal Aged Adult</td>
<td>15 years</td>
</tr>
<tr>
<td>3. Decreased function in demanding employment settings</td>
<td>Compatible with possible incipient Alzheimer's disease in minority of cases</td>
<td>7 years</td>
</tr>
<tr>
<td>4. Decreased ability to handle complex tasks such as finances or planning dinner for guests</td>
<td>Mild Alzheimer's disease</td>
<td>2 years</td>
</tr>
<tr>
<td>5. Requires assistance in choosing proper clothing</td>
<td>Moderate Alzheimer's disease</td>
<td>18 months</td>
</tr>
<tr>
<td>6. a) difficulty dressing properly</td>
<td>Moderately severe Alzheimer's disease</td>
<td>5 months</td>
</tr>
<tr>
<td>b) requires assistance bathing</td>
<td></td>
<td>5 months</td>
</tr>
<tr>
<td>c) inability to handle mechanics of toileting</td>
<td></td>
<td>5 months</td>
</tr>
<tr>
<td>d) urinary incontinence</td>
<td></td>
<td>4 months</td>
</tr>
<tr>
<td>e) fecal incontinence</td>
<td></td>
<td>10 months</td>
</tr>
<tr>
<td>7. a) ability to speak limited to about six words</td>
<td>Severe Alzheimer's disease</td>
<td>12 months</td>
</tr>
<tr>
<td>b) intelligible vocabulary limited to single word</td>
<td></td>
<td>18 months</td>
</tr>
<tr>
<td>c) ambulatory ability lost</td>
<td></td>
<td>12 months</td>
</tr>
<tr>
<td>d) ability to sit up lost</td>
<td></td>
<td>12 months</td>
</tr>
<tr>
<td>e) ability to smile lost</td>
<td></td>
<td>18 months</td>
</tr>
<tr>
<td>f) ability to hold head up lost</td>
<td>Not applicable</td>
<td></td>
</tr>
</tbody>
</table>

*duration of stage in those entering the stage who progress into the next stage; not all patients progress.
Diagnosing Dementia

• DSM-V
  – History of cognitive decline
  – Not attributed to delirium

• Rule out other causes
  – Depression (pseudodementia)
  – Sensory deprivation (hearing)
  – Sleep apnea
  – Substance abuse/dependence
    • Opiates, Benzodiazepines
    • Can lead to dementia
Diagnosing Dementia in the Office

• Screening tests
  – Depression – Geriatric Depression Scale, PHQ-9
  – Cognition
    • Mini Cog
    • MMSE
    • Montreal Cognitive exam
## Diagnosing Dementia in the Office

<table>
<thead>
<tr>
<th>TEST</th>
<th>Time to Complete</th>
<th>Sensitivity Specificity</th>
<th>Score interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE (copyrighted)</td>
<td>10 minutes</td>
<td>18% for MCI 78% for Dementia 88% specific</td>
<td>&gt; 24 normal</td>
</tr>
<tr>
<td>MOCA (free online, translated to multiple languages, instructions online)</td>
<td>10 minutes (training recommended)</td>
<td>90% for MCI 100% for Dementia 87% specific</td>
<td>&lt; 26 abnormal</td>
</tr>
<tr>
<td>Min-Cog</td>
<td>3 min</td>
<td>Similar to MMSE</td>
<td>See next</td>
</tr>
</tbody>
</table>
Mini-Cog Scoring

- 3 item registration, clock drawing, 3 item recall
- Three Item Recall – 1 point for each word correct
- Clock Draw – 2 points for correct clock
  - Numbers and hand placement; if numbers are not correct, score is zero
- Score 0 to 5 points
  - Passing is ≥ 3
    - All 3 words of recall OR Correct Clock and at least one word correct
Montreal Cognitive Exam

- President Trump scored 30/30!
  - Insert political joke here........
- Preferred test for MCI and dementia
  - Evaluates multiple cognitive domains
    - Executive and visual-spatial (driving – also consider Trails A/B, Maze)
    - Memory
    - Language
    - Attention
  - Multiple forms
    - MOCA blind
    - MOCA basic for low educational level
MOCA

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME:
Education:
Date of birth:
Sex:
DATE:

VISUOSPATIAL / EXECUTIVE

Copy cube
Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

[ ]

NAMING

[ ]

MEMORY
Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

FACE VELVET CHURCH DAISY RED
1st trial
2nd trial

ATTENTION
Read list of digits (1 digit/sec). Subject has to repeat them in the forward order

[ ] 2 1 8 5 4
Subject has to repeat them in the backward order

[ ] 7 4 2

Read list of letters. The subject must tap with his hand at each letter A. No points if > 2 errors


Serial 7 subtraction starting at 100

[ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: 3 pts, 2 or 1 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt

LANGUAGE
Repeat: I only know that John is the one to help today.

The cat always hid under the couch when dogs were in the room.

Fluency / Name maximum number of words in one minute that begin with the letter F

[ ] ______ (N ≥ 11 words)

ABSTRACTION
Similarity between e.g. banana - orange = fruit

[ ] train - bicycle

watch - ruler

DELAYED RECALL
Has to recall words WITH NO CUE

FACE [ ] VELVET [ ] CHURCH [ ] DAISY [ ] RED [ ]

Points for UNCUED recall only

Optional

CATEGORY CUE
Multiple choice cue

ORIENTATION
[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

© Z. Nasreddine MD  www.mocatest.org

Administered by: ________________________________
Normal ≥ 26 / 30

Add 1 point if ≤ 12 yr res.

TOTAL __________/30

Add 1 point if ≤ 12 yr res.
## MOCA Scoring

<table>
<thead>
<tr>
<th>MOCA SCORES</th>
<th>Normal Controls (NC)</th>
<th>Mild Cognitive Impairment (MCI)</th>
<th>Alzheimer’s Disease (AD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of subjects</strong></td>
<td>90</td>
<td>94</td>
<td>93</td>
</tr>
<tr>
<td><strong>MoCA average score</strong></td>
<td>27.4</td>
<td>22.1</td>
<td>16.2</td>
</tr>
<tr>
<td><strong>MoCA standard deviation</strong></td>
<td>2.2</td>
<td>3.1</td>
<td>4.8</td>
</tr>
<tr>
<td><strong>MoCA score range</strong></td>
<td>25.2 – 29.6</td>
<td>19.0 – 25.2</td>
<td>21.0 – 11.4</td>
</tr>
<tr>
<td><strong>Suggested cut-off score</strong></td>
<td>≥26</td>
<td>&lt;26</td>
<td>&lt;26Ψ</td>
</tr>
</tbody>
</table>

Ψ Although the average MoCA score for the AD group is much lower than the MCI group, there is overlap between them. The suggested MoCA cut-off score is thus the same for both. The distinction between AD and MCI is mostly dependent on the presence of associated functional impairment and not on a specific score on the MoCA test.
Dementia Diagnosis
Major Neurocognitive Disorder

• History of cognitive decline
  – Informant history essential
    • Important to get corroborating history
• Testing shows deficits
• Rule out contributing factors
  – Pseudo-dementia
• Cognitive decline is affecting daily life
  – IADLs
  – Change from previous baseline
Treatment

• Try to remove potential offending medications
  – Remove Anticholinergic medications
  – Taper off or reduce to lowest effective dose of
    • Benzodiazepines
    • Opiates
• Specialty referral if complicated history, acute onset
• Cholinesterase inhibitors (Donepezil, etc)
• Choosing Wisely – American Geriatric Society
  – “If the desired effects (including stabilization of cognition) are not perceived within 12 weeks or so, the inhibitors [CHIs] should be discontinued.”
• Memantine
• Vitamin E

REFERENCE
Treatment with ChEIs:

• Provide modest benefits in terms of cognition and function at all stages of dementia

• Do not seem to impact progression to disability and need for institutionalization

• Discontinue anticholinergic medication prior to starting

• Start low and increase after 4-6 weeks.
  – Ex: start Donepezil 5 mg daily (usually at night unless vivid dreams) for 4 weeks and then increase to 10 mg daily

• Common side effects:
  – N/V/D: 10-20%, usually self-limiting and temporary
  – Vivid dreams
  – Less common: dizziness, bradycardia, and syncope

Reference
Treatment with Memantine

• Addition of Memantine demonstrated better cognition and function
  – Difference was smaller than the minimum clinically important difference

• Combination therapy with donepezil and Memantine has NOT been shown to be significantly superior to treatment with donepezil alone
Delirium
Delirium assessment

- An acute state of confusion marked by
  - Sudden Onset
  - Fluctuating Course
  - Inattention
  - At times, abnormal level of consciousness

- Symptoms can also include
  - Sleep disturbances
  - Agitated behaviors
  - Delusions and Visual Hallucinations
Delirium assessment

• Identifiable cause (s)

• Other terms used include organic brain syndrome, metabolic encephelopathy, toxic psychosis, acute mental status change, exogenous psychosis, sundowning
Epidemiology

• **At admission** prevalence 14-24%
• Hospitalization incidence 6 to 56%
• 15-53% geriatric patients post-op
• 65% of patients with baseline dementia will experience delirium in the hospital
• **70-80% older patients in ICU**
• 60% nursing home will have at some time
• 83% of geriatric patients prior to death

Reference
Delirium Outcomes

- **Mortality** rate in hospitalized patients **22-76%**
- One year mortality rate is **35-40%**
- **Prolongs hospital course/Increased cost of care** in hospital
  - $16,000 to $64,000 more per patient w/ delirium
  - Burden est. at $38 to $152 BILLION/year in U.S.
- Increases **likelihood of disposition to nursing home, functional decline** and loss of independence
- Strong association with underlying dementia
- Frequently, **patient may never return to baseline or take months to over a year to do so**
- Delirium is often the sole manifestation of serious underlying disease

Reference
Delirium Subtypes

Hyperactive (three or more) (30%)
- Hypervigilance
- Restlessness
- Fast/loud speech
- Anger/irritability
- Combative
- Impatience
- Uncooperative
- Laughing
- Swearing/singing
- Euphoria
- Wandering
- Easy startling
- Distractibility
- Nightmares
- Persistent thoughts

Hypoactive (four or more) (24%)
- Unawareness
- Lethargy
- Decreased Alertness
- Staring
- Sparse/slow speech
- Apathy
- Decreased Motor Activity

Mixed (46%)
Characteristic waxing and waning
Agitated/Combative ↔ Somnolence/Hypoactive

Delirium versus Dementia

• Delirium
  - Rapid onset
  - Primary defect in attention
  - Fluctuates during the course of a day
  - Visual hallucinations common
  - Often cannot attend to MMSE or clock draw

• Dementia
  - Insidious onset
  - Primary defect in short term memory
  - Attention often normal
  - Does not fluctuate during day
  - Visual hallucinations less common
  - Can attend to MMSE or clock draw, but cannot perform well
Delirium Risk Factors

**Predisposing**
- Age
- Cognitive impairment
  - 25% delirious are demented
  - 40% demented in hospital delirious
- Male gender
- High number of meds
- Malnutrition
- Sensory impairment
- Depression

**Precipitating**
- Severe illness (APACHE >16)
- Hip fracture
- Surgery/Anesthesia
- New Psychoactive medications
- Lines/catheters/restraints
- Metabolic disorders:
  - Azotemia
  - Hypo- or hyperglycemia
  - Hypo- or hypernatremia
- Alcoholism/Withdrawal
- Pain
- **Sleep Deprivation**
- Infection (UTI, etc)
Causes

D  Drugs, Drugs and toxins, too
E  Eyes, ears – sensory deprivation
L  Low O2 states (MI, ARDS, PE, CHF, COPD, stroke, shock)
I  Infection
R  Retention (of urine or stool). Restraints
I  Ictal (post) = seizures
U  Underhydration, Undernutrition
M  Metabolic (hypo/hyper glycemia, calcemia, uremia, liver failure, thyroid disorders)
S  Sleep Deprivation, Sedation(over), Stroke

Always add P for Pain
Drugs

• Accounts for 30% of all cases
• Common culprits
  – Anti-histamines
  – Anti-cholinergics
  – Antibiotics (Fluoroquinolones)
  – Some antidepressants
  – Dopamine agonists
  – Hypoglycemics
  – Benzos
  – Opiates
  – Cardiovascular – Amiodarone, Digoxin
Case - 1

• 80 y/o female patient with hx of
  – mild cognitive impairment,
  – multiple medical comorbidities (CAD, CHF, Sleep apnea, obesity, refractory anemia, depression, Chronic UTIs on suppression
  – long term antidepressant (celexa)
  – started on Zyvox for a presumed UTI with VRE, subsequently fever delirium worsened over several days, with peak temp up to 103.6
Case -2

- 56 year old with hx of paraplegia from SC injury, admitted for cholecystitis
- Home medications included high dose fentanyl patch, Baclofen PO 20 mg TID → increased to 60 mg TID on admission
- Baclofen stopped abruptly after surgery – severe agitation, diaphoresis, confusion
- Baclofen withdrawal
Differential Diagnosis

- CNS pathology—stroke, infection, hemorrhage
- Dementia, particularly Lewy Body
- Other Psychiatric disorders
  - Psychosis
- Depression: **41% of hypoactive delirium misdiagnosed as depression** *Farrell Arch Intern Med 1995*
  - Bipolar disorder
- Aconvulsive status epilepticus
- Akathisia (restlessness from PD, w/drawal)
- **Overall, 32-67% missed or misdiagnosed**
Confusion Assessment Method -- CAM

1. Acute change & fluctuation in mental status and behavior
   
   AND

2. Inattention
   
   AND EITHER

3. Disorganized thinking
   
   OR

4. Altered consciousness (Hyper or Hypo)

CAM -- Video

https://www.youtube.com/watch?v=jJCXnoLHahM
Delirium Workup

- **History**
  - Time course of change/baseline
    - Normal and recent *sleep* patterns
  - Recent events – fall, hospitalizations, *medication changes*, emotional stress, change in environment
  - **Medical History**
    - Cognitive Deficits (ADLs/IADLs), *Past Delirium*
    - Comorbid conditions – risks for acute condition
      - COPD, CAD, hx of infections (UTIs), past Stroke
  - Sensory Deprivation – Vision, Hearing
Physical Exam and Diagnostics

• Vital signs/O2 Sat

• General exam
  – Pulm – look for tachypnea
  – Mental Status
  – Neuro findings

• Diagnostics
  – Labs: CBC, lytes, BUN, Cr, glucose, calcium, LFTs, UA, EKG (consider even for baseline), CXR
  – Drug levels (Digoxin, Theophylline, Anticonvulsants)
If routine labs are not revealing, consider:

- Neuroimaging -- not recommended routinely unless focal neuro exam, recent fall/trauma
- CSF – if indicated
- Tox screen/BAL, thyroid, B12, drug levels, ammonia, cultures, ABG
- EEG - in difficult cases to r/o occult seizures or psych disorders - 17% false neg, 22% false pos – usually unrevealing in delirium
Workup

• Remember, Delirium is MULTIFACTORIAL
  – Even if one potential cause is found (UTI), consider contributing factors
    • Pain
    • Sleep
    • Dehydradation/Undernutrition
    • Hypoxemia
    • Baseline cognitive impairment
    • Good chance to review and eliminate potential contributing long-term medications
      – Tylenol PM
Delirium Prevention

• Identify those at highest risk
• Environmental
• Pharmacological
• Family Education
Neuroleptics (Antipsychotics)

- Considered agents of choice for most cases of delirium
- RCTs in agitation and dementia suggest modest benefit
- Side effects can include extrapyramidal SE’s, hypotension, sedation, akathisia
- Sedation effect before antipsychotic effect
- Haloperidol, droperidol
- Atypicals: Risperidone, Olanzapine, Quetiapine, Zirasidone
- **Black box warning for use in patients with Dementia**
- **All used in Delirium is “off label”**
- **Should use at lowest effective dose, with goal of use less than one week**
Neuroleptics -- continued

• Most studies were only 5-7 days duration
• No difference in outcomes Haloperidol vs Risperidone or Olanzapine
• Haloperidol showed efficacy over Lorazepam
• Avg dose of Haloperidol (1-3mg/day), Risperidone (1-3 mg/day)
• No significant EPS reported in any treatment group
• QTc changes were not measured
Haloperidol

• The most studied of ALL antipsychotics (typical/atypical) in delirium, years of use/data

• Blocks postsynaptic dopaminergic $D_1$ and $D_2$ receptors in the brain $\rightarrow$ strong central antidopaminergic $\rightarrow$ depress the CNS at the subcortical level of the brain, midbrain, and brain stem reticular formation

• Hepatic metabolism, CYP 3A4

• Onset of action: **Oral 2 to 6 hours, IM/IV 20 to 60 minutes**

• Side effects
  
  – EPS/Dystonia/NMS – risk much lower for IM/IV form
  
  – QTc prolongation – may be overstated, overall risk is small, attention if other QT prolonging meds/ >50mg in 24hrs
    
    • From Maldonado, J., Critical Care Clinics 24 (2008) 657-722

  – **Less** anticholinergic than Atypicals
Safe Use of Haloperidol

• Baseline EKG for QTc interval
• Correct K+ or Mg +2 if needed
• If Baseline QTc > 440 ms AND use of other QTc prolonging agents, use with caution
• If Baseline QTc increases by > 25% or > 500 ms, d/c Haldol
• IM preferred over IV use d/t QTc risk
• Try to avoid > 3mg/24 hours (EPS risk)
• Treat EPS with D/C med, IV benadryl
• Monitor for NMS (fever, rigidity)
Atypical neuroleptics

- MOA: Dopamine (D1) and Serotonin (5HT2) Antagonism
  - Olanzapine/Quetiapine also have
    - Antihistamine (H1) = Sedation
    - Antiadrenergic (α1β) = Hypotension
    - Antimuscarini (M1) = Anticholinergic
- Risperidone has the most data, has been shown to reduce agitation in patients with dementia
- Are preferred if patient can take oral medication or if high (>3-4.5mg/day) doses of Haloperidol are required (less EPS risk)
- **All are used “off label” in delirium tx**
- Quetiapine is the preferred agent if any past hx of EPS with antipsychotics/PD/LBD, although has highest risk of hypotension/anticholinergic for atypicals
- No Studies comparing IM Ziprasadone vs IM haloperidol in delirium
Atypical Neuroleptics – Cont’d

• Risperidone: for those with side effects from haloperidol or contraindications
  – Starting dose: 0.5mg HS or BID, Inc 0.5-1 mg/day, max 6 mg/day
  – Peak 1 hour, **Half life 20-30 hours**

• Olanzapine (Zyprexa): Starting dose 2.5mg PO HS or BID, Increase by 5 mg/day, max 20 mg/day
  – Peak 6 hours, **Half Life 21-54 hours**

• Quetiapine (Seroquel) – preferred agent in PD or LBD with agitation, 12.5 mg HS or BID, Increase 12.5-25mg/day
  – Peak 1.5 hours, **Half Life 6 hours**

• Ziprasidone (Geodon) – 10 to 20 mg IM, max 40 mg/day, 10mg IM q 2 hours
Summary

• Dementia is (usually) an insidious, chronically degenerative condition, of which there are many types
  – May be mixed (Alzheimer’s/Vascular)

• Delirium is an acute change in mental status with
  – Sudden Onset, Fluctuating Course, Inattention
  – Usually there are underlying causes
Summary

• Differentiation between Dementia and Delirium needs to be based on HISTORY of previous baseline cognition and change from that baseline (acute or chronic change)

• Use Screening tests for Dementia and CAM for delirium
References

- In presentation
- DSM-5, American Psychiatric Association