LEARNING OBJECTIVES

- Appreciate new concepts in dementia management using disease-specific diagnostic tools and therapies
- Recognize the importance of goal setting for dementia patients and their families
- List three techniques for dealing with agitation in dementia patients
- List three resources to mitigate caregiver burden
Background & New Developments
Dementia Defined

- Decline in cognitive function from baseline
Epidemiology

- Dementia in the US population
  - Over 65: 5-10%
  - Over 85: 30-50%

Dementia is frequently overlooked

- Early symptoms attributed to normal aging
- Physicians don’t detect early changes
Diagnostic criteria

Decline in 2 of the following 5 domains:
1. Memory
2. Language
3. Visuospatial skills
4. Executive function
   * Handling complex tasks
   * Judgment/reasoning

Rule out delirium, psychiatric disorders
Decline from baseline
Results in a decline in function


PowerPoint Notes: There are more specific diagnostic criteria for each type of dementia. New diagnostic criteria have been proposed for AD recently by Dubois et al. Core criteria (supportive history, objective episodic memory impairment) one or more of the following supportive features (med temp lobe atrophy on MRI, abnl CSF biomarkers [low abeta42, high tau, hi phospho-tau], suggestive pattern on PET, proven AD autosomal dominant mutation in immediate family).
Dementia types

- Alzheimer Disease: 60%
- Mixed: 15-20%
- Vascular: 5-10%
- DLB: 5-10%
- Other: 5%
Mild Cognitive Impairment (MCI)

- Subjective complaint
- Objective findings of memory impairment
- Minimal interference with function

MCI types:
- Amnestic, multiple domains

In the US population over 65: 3-19%

PowerPoint Notes: For amnestic form, 10-15% progress to AD per year 1/3 to 1/2 progress to AD eventually 1/3 to 1/2 improve back to baseline (See Gauthier S et al. Mild cognitive impairment. Lancet 2006. 376: 1262-1270.)

Alzheimer Disease

- New diagnostic criteria published in 2011
- Clinical criteria
  - Insidious onset of months to years
  - Progression of cognitive decline
  - Amnestic or nonamnestic symptoms
  - Differential diagnosis of Alzheimer dementia
- Biomarkers
  - Accumulation of amyloid beta
  - Neuronal injury

PowerPoint Notes: RFs:
Established: age, FH, cardiovascular dz
Hypothesized: head trauma, low education, female.
Early onset:
Known mutations, Aut dom inheritance, presents 30-50yo
Later onset:
ApoE epsilon4 allele - present in 15% of population, weak rf for CV dz, strong rf for AD
Incomplete penetrance
AD New Developments

- Disease process seems to start >20 years before onset of symptoms
- A mutation in the gene encoding amyloid precursor protein that prevents cleavage into amyloid-β (Aβ) protects against late-onset AD
- Misfolded tau seems to be transferred from neuron to neuron
- No good news in drug development
  - Monoclonal antibodies to Aβ failed in Phase III trials

Wiener MW, Nature Reviews Neurology 2013
Dementia with Lewy Bodies

**Characteristics**
- Prominent visual hallucinations
- Parkinsonism (gait, balance, rigidity, bradykinesia - rest tremor less common)
- Falls or gait difficulties
- Fluctuations in cognition
- Sensitivity to antipsychotics (extrapyramidal side effects)

**Also**
- REM sleep behavior disorder


PowerPoint Notes:
(Diagnostic criteria same as dementia, plus 2 of the 4 above)
How can I help my patient who is agitated?
Defining agitation

- Aggression
  - Physical
  - Verbal
- Resistance to care
- Delusions
- Hallucinations
- Repetitive vocalizations
- Wandering
Behavioral and Psychiatric Symptoms

- 60-98% of dementia patients

Consequences:
- Increased caregiver stress and unemployment
- Increased risk of NH placement
- Increased health care costs
- More rapid cognitive decline

- 30% of cost of caring for pts with dementia due to BPSD
Workup of agitation

- Differential diagnosis for NEW agitation:
  - Delirium - drugs, infection, CNS process, etc
  - Psychiatric condition
  - Dementia
First, look for a reason

- PHYSICAL
  - Pain, constipation, hunger, thirst

- EMOTIONAL
  - Depression, boredom, fear

- ENVIRONMENTAL
  - Disruption in routine, new caregiver, life stressor, overstimulation, understimulation
Non Pharmacologic Management

* Try to analyze the behavior using A-B-C

A- antecedent
B- behavior
C- consequence
Fix what you can

Also:
- Correct sensory deficits
- Create daily routine with activities
- Create a structured environment
- Ensure adequate sleep and eating
- Provide respite and support to caregivers
- Redirection and distraction
Figure. Screening, Identifying, and Managing Behavioral Symptoms in Patients With Dementia

STEP 1
Are behavioral symptoms occurring?
Screen for behavioral symptoms using standardized tool (e.g., NPI-Q) involve key informant

Yes
No
1. Continue monitoring (follow PCPI schedule)
2. Educate caregiver (see eBox 1)
3. Minimize risk factors for behavioral symptoms (e.g., caregiver distress, patient pain, unmet needs)

STEP 2
What do behavioral symptoms look like?
Describe behavioral symptoms and involve key informant (see eBox 2)

Yes
1. Rule out and treat underlying medical illness
2. Review medications
3. Evaluate and manage pain, nutrition, constipation, hydration, sleep

No
1. Recommend safety strategies
2. Educate caregiver
3. If safety not improved, refer to specialist or admit

STEP 3
What are underlying causes?
Identify potential modifiable triggers of behavioral symptoms (see eBox 3)

Yes
1. Educate caregiver
2. Screen for depression
3. Recommend stress-reduction strategies
4. If distress not improved, refer to specialist

No
1. Rule out and treat underlying medical illness
2. Review medications
3. Evaluate and manage pain, nutrition, constipation, hydration, sleep

STEP 4
What is the treatment plan?
Develop a treatment plan that incorporates family goals; work first on most distressful and unsafe behavioral symptoms

If targeting 1 behavior:
Identify and eliminate modifiable triggers (see Table 1)

If targeting multiple behaviors:
Use generalized approach (e.g., exercise, activities and pleasant events, caregiver education, skills training, environmental simplification, structuring daily routines) (see Table 2)

STEP 5
Are recommendations effective?
Evaluate if plan eliminates or manages behavioral symptoms

Yes
No
1. Problem solve with key informant
2. Revise recommendations
3. Refer to specialists or other team members

1. Determine with key informant reason(s) not implemented or whether implemented appropriately
2. Revise recommendations accordingly
YOU CAN’T FIX CRAZY

BUT YOU CAN SEDATE IT.
Pharmacologic Management

- Antipsychotics
- Acetyl cholinesterase inhibitors
- NMDA antagonists
- Antidepressants
- Anticonvulsants/mood stabilizers

Sink et al, JAMA, 2005; Trinh N 2003
Efficacy of Antipsychotics

* Moderate to low efficacy
* CATIE-AD trial
  * RCT of olanzapine, risperidone, quetiapine
  * 63% discontinued by 12 weeks
  * Olanzapine and risperidone were slightly better than placebo at controlling agitation
  * Did not improve patient quality of life scores
  * Patients on placebo often improved

Adverse Effects of Antipsychotics

- Sedation
- Tardive dyskinesia
- Extrapyramidal symptoms (EPS)
- Weight gain
- Metabolic syndrome
- Prolonged QT
- CVA
- Infection

PowerPoint Notes: Limitations of studies on atypical antipsychotics:
Only AD, VaD (very little on DLB)
Exclude pts with significant medical comorbidities
Short term: 6-18 wks
High withdrawal rates (including placebo) 20-42%
(see Carson S. A systematic review of the efficacy and safety of atypical antipsychotics in patients with psychological and behavioral symptoms of dementia. JAGS 2006; 54:353-361)
Black Box Warning

- Increased risk of mortality
  - 2.3% vs 3.6%
  - Mortality 1.6 times as high as placebo

Therefore:
- Antipsychotics should not be used for insomnia
- Doses should be low
- Discontinuation should be attempted early and often
Discontinuing Antipsychotics

- Federal regulations recommend discontinuation after 3-6 months
- 110 patients with BPSD responsive to risperidone
  - Risk of relapse was almost double in the patients who stopped risperidone after 4-8 months of treatment (60% vs. 33%)
  - Risk of relapse was also high for patients who continued risperidone (33%)

Devanand DP et al, NEJM 2012
Typical antipsychotics...

- **Haloperidol**
  - High risk of tardive dyskinesia and EPS with long term use (over 50% in elderly)
  - If used, use low dose (0.5 mg), and limit to 1-3 days
  - Less QT prolongation
  - Available in IV and IM (atypical antipsychotics are not)
Atypical Antipsychotics

- Risperidone (Risperdal)
- Quetiapine (Seroquel)
- Olanzapine (Zyprexa)
- Ziprasidone (Geodon)
- Aripiprazole (Abilify)
- Clozapine (Clozaril)
Risperidone (Risperdal)

- Emerging (although small studies) to support use with agitated delirium
- Begin 0.25 mg – 0.5 mg, 1-2 times/day
- Effectiveness at low doses in elderly (max 1-3 mg/day)
- Less concern about metabolic syndrome
- Limited in past by only oral route – new routes soon to be available
Quetiapine (seroquel)

- Start at 25 mg
- Can rapidly increase up
- Sedating, use at night
- Least EPS, TD
- May be less effective

Olanzepine (zyprexa)

- 2.5-5 mg
- Sedation (usually started at night)
- Strongly anticholinergic, so beware of side effects, including worsening cognition
- Routes: PO or rapidly dissolving tablet (Zydis)
- Link with weight gain and diabetes...
Ziprasidone (geodon)

- IV form
- 20-80 mg
- Contraindicated with acute CV disease (nondose dependent QT prolongation)
- Unpredictable pharmacokinetics, so should be used only by experienced providers
Clozapine

- Minimal EPS, so preferred for Parkinson’s patients
- Significant rate of agranulocytosis
- Restricted use
Cholinesterase Inhibitors and Memantine

- Some evidence of MILD benefit for agitation
Antiseizure medications

- Valproic acid
- Carbamazepine
- Gabapentin
- Limited evidence for efficacy (if any)
Hey, I just met you, and you seem crazy, so here's some Haldol, and Ativan, maybe.
Benzodiazepines

- Limited evidence
- Likely unhelpful due to potential for:
  - paradoxical agitation
  - increased risk of falls and hip fracture
  - risk of oversedation
Be nice to nurses; we keep the doctors from accidentally killing you.
How can I help my patient’s caregiver?
Why bother?

- Caregivers are at higher risk for:
  - Medical problems
  - Depression and anxiety
  - Financial problems

- Dementia caregivers are especially challenged due to:
  - Protracted length of time of caregiving
  - Difficult behaviors
  - Lack of appreciation from the patient
  - Need for intensive involvement with the patient
Why bother?

- Supporting the caregiver helps the patient:
  - Less depression
  - Less agitated behavior
How to help?

- Support groups
- Education about the disease and how to be a caregiver
- Adult day care
- Hospice (for patients with advanced stage)
Resources

- [www.alz.org](http://www.alz.org) (Alzheimer Association- education, info on clinical trials, local support groups, Safe Return program, much more)

- [www.alzbrain.org](http://www.alzbrain.org) (State of Alabama Dementia Education and Training Act sponsored education site)

- UAB Alzheimer’s Family Program (205) 934-2178 (one on one counseling, support groups)

- [www.alzca.org](http://www.alzca.org) (Alzheimer’s of Central Alabama - info on clinical trials, adult day care scholarships, WanderGuard, local support groups)
Dementia and Goal Setting
Understand prognosis

* Life expectancy from the time of diagnosis:
  * Alzheimer Disease  5-10 years
  * Vascular Dementia  4 years
  * Dementia with Lewy Bodies  4 years
Comparison of Life Expectancy by Quartiles (Men age 70)

Years of life expectancy

US population
AD
Match drug and condition

- **Drug overuse**
  - No indication for the drug

- **Drug underuse**
  - Could benefit from a drug not currently prescribed

- **Drug misuse**
  - Appropriate indication but could be improved by changing dose, frequency, substituting a better drug

Steinman MA, JAMA 2010
Some preventive health can be eliminated in some cases...

- Colonoscopy
- Cholesterol-lowering agents
- Prostate cancer screening
Commitment to Change