Comprehensive Assessment and Diagnosis of Dementia

Rebecca Logsdon, PhD
UW School of Nursing-Psychosocial & Community Health
Northwest Research Group on Aging and Alzheimer’s Disease Research Center

Soo Borson, MD
UW School of Medicine - Psychiatry & Behavioral Sciences
Geriatric and Family Services Clinic and Alzheimer’s Disease Research Center
Assessing Older Adults

- Presenting Problems
- History
- Medical Status
- Cognition
- Day to Day Functioning
- Support
  - Family, Friends
  - Church, Community Groups
  - Social Service Agencies
- Evidence of Abuse or Neglect
Abuse & Neglect

n=154, Baylor Medical Center Geriatrics Clinic

Depression  Dementia

47 referred for abuse/neglect: 62%  51%
97 referred for other reasons: 12%  30%
Diagnosis of Dementia

Multiple cognitive deficits

Memory Impairment

One or more of the following disturbances:

- language disturbance
- visual spatial problems
- lack of awareness of problems
- poor judgement, reasoning
Prevalence of Dementia

In 1998:
- 4-5 million people had mild to moderate dementia
- 1.5 million had severe dementia

By 2040:
- 14 million people will have dementia

In Nursing Homes:
- 60% of residents have dementia
Causes of Dementia

More than 70 conditions can cause dementia

- 65% Alzheimer's Disease
- 33% Other Irreversible Conditions
  - Micro-vascular disease, Pick's disease, Parkinson's disease,
  - Alcohol or drug abuse,
  - HIV/AIDS, Huntington's disease
- 2% to 3% Reversible Conditions
  - Brain tumor
  - Severe depression
Diagnosis of Alzheimer's Disease

Dementia
Gradual onset, continuing decline
Cognitive deficits are not due to:
- other central nervous system conditions
- systemic conditions known to cause dementia
- substance induced conditions
Diagnosis of Alzheimer's Disease

There is no single test for AD

Medical evaluation rules out other causes
  - tests include blood tests, neurological exam, CT or MRI scan, detailed cognitive testing, interview with family

With thorough assessment, clinical diagnosis is 70-90% accurate

The definitive diagnosis is made at autopsy, by examining changes in brain tissue
Diagnosis of Vascular Dementia

Focal neurological signs and symptoms or laboratory evidence of cerebrovascular disease
- History of CVA
- Severe hypertension
- More abrupt onset and/or stepwise progression

Deficits don’t occur exclusively during the course of a delirium
Pure AD

AD with severe cerebral amyloid angiopathy

Mild AD with vascular involvement

AD with vascular lesions

AD with CVD

VaD with AD changes

VaD with small-vessel disease

Pure VaD

Agüero-Torres & Winblad, 2000
Disease vs Illness: How Strokes Affect Expression of AD

102 college-educated nuns, aged 76-100, autopsied after cognitive diagnosis

Snowdon et al. JAMA 1997; 277: 813-817.
Clues: Vascular Dementia

- Cognitive syndrome
  - Poor executive function, impaired attention/memory

- Neurological and other signs
  - Focal, lateralized, gait impairment, severe urinary urgency

- Course
  - Abrupt, fluctuating/stepwise, progressive, can be stable for long periods
Cerebrovascular Risk Factors and Disease: Key Issues in AD

- Cardiovascular instability
  - Dehydration, hypotension
  - Hypertension
- Heart disease
  - Coronary artery disease
  - Arrhythmias, esp. atrial fibrillation
  - Congestive heart failure
- Hypercholesterolemia
- Hyperhomocysteinemia [folate, B12, B6]
- Diabetes
- Stroke
Types of Vascular Dementia

Cortical

- Cortico-subcortical occipito-temporal infarct

Subcortical White Matter

- White matter lesions predominate

Strategic

- Thalamic infarct

Subcortical Lacunar

- Lacunar infarcts predominate

Images courtesy of Timo Erkinjuntti.
Non-AD Degenerative Brain Diseases

- Frontotemporal dementias
- Parkinson’s dementia
- Dementia with Lewy bodies
- Hippocampal sclerosis

- Creutzfeldt-Jakob disease
- Huntington’s disease
- Progressive supranuclear palsy
- Corticobasal degeneration
- Striatonigral degeneration

Diabetic and microvascular dementias may have a neurodegenerative component.
70% of treated dementia patients are treated first – if at all – by a primary care physician (family physician or internist).
Alzheimer’s Disease: Underdiagnosed, Undertreated

Prevalence: 4,520,000
Diagnosed: < 50%
Treated: 20%
Treated with AChEIs: 12%

* Any psychotropic drug including anti-dementia drugs.

Early Misdiagnosis

AD patient initially diagnosed with AD

First Diagnosis Given

- Non-AD dementia: 35%
- Depression: 14%
- Stroke: 14%
- Normal aging: 9%
- No diagnosis: 7%
- Other: 21%

Source: Consumer Health Sciences, LLC. Alzheimer's Caregiver Project. 1999.
Recognition of Dementia in Primary Care

Borson et al (submitted)
Primary Care Barriers To Dementia Diagnosis and Treatment

- Symptom recognition
- Knowledge of diagnostic and assessment procedures
- Attitudes
- Unable to “hear” family concerns
- Practice limitations

Boise et al, 1999
Improving Diagnosis

- Screening
- Collateral information
- Strategic workup
Screening Would Improve Detection

![Graph showing the percentage of correct responses for different CDR stages with Mini-Cog and Physician methods.]

- **Mini-Cog**
- **Physician**

**CDR Stage**
- **0**
- **0.5**
- **1**
- **2**
- **3**

**Sample Size**
- **Norm**
- **MCI**
- **Mild**
- **Mod**
- **Severe**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Norm</th>
<th>MCI</th>
<th>Mild</th>
<th>Mod</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>189</td>
<td>94</td>
<td>83</td>
<td>74</td>
<td>27</td>
</tr>
</tbody>
</table>

*** p < .001

Borson et al, submitted
Improving Diagnosis

- Screening
- Collateral information
- Strategic workup
Family: 4 F's

• Forgetting
  - Conversations, intended activities, planned occasions?
  - Medications?
  - Directions?

• Functioning
  - IADLs (e.g. mail, meals, taxes, bills, care of possessions and surroundings)
  - Initiative (e.g. hobbies, interests, people)?

• Feeling
  - Mood, behavior, or personality change?

• Further symptoms?
Improving Diagnosis

- Screening
- Collateral information
- Strategic workup
Strategic Workup

- General screen - weight loss, dehydration, acute and chronic disease signs, chronic disease control
- Neurologic screen - vascular, Parkinson, frontal signs; gait and balance; neuropathy
- Laboratory screen - mainly for associated or secondary problems
- Brain imaging (structural screen) - surgical and vascular lesions
Dementia: Early Stages

• Daily Living Skills
  - ability to follow complex instructions
  - ability to manage finances, bill paying, work
  - memory limitations
  - communication difficulties-word finding

• Safety Issues
  ✓ Driving
  ✓ Availability of firearms
  ✓ Use of power tools (chain saw, woodworking tools, lawnmower)
Communication: Early Stage

- Allow sufficient time for unhurried interactions
- Double-check instructions to make sure the person understands them
- Try using written instructions
- Avoid challenging the person, or do so in a non-threatening way
- Attend to the needs of the family, be aware of differences of opinion among significant others
Information About Resources: Early Stage

- Legal and financial planning
  - State Bar Association or local contacts
- Educational materials: National Alzheimer’s Association
  - 1-800-272-3900 or www.alz.org
- Research programs
  - 1-206-764-2069 or www.uwadrc.org or www.clinicaltrials.gov
- Caregiver/patient support groups: Local Alzheimer’s Assoc.
  - 1-800-848-7097 or www.alzwa.org
Dementia: Middle Stages

- Daily Living Skills
  - household chores, laundry, shopping, cleaning
  - ability to use the telephone
  - ability to take medications
  - ability to follow simple instructions

- Safety Issues
  - Wandering, getting lost
  - Home safety, hot water temp, kitchen appliances
  - Ability to stay home alone, need for supervision
Communication: Middle & Late Stages

- Use a soothing voice
- Speak slowly and clearly (not loudly)
- Maintain eye contact and a pleasant facial expression
- Use non-threatening body language
- Do one task at a time
- Reduce distracting background noises
Information About Resources: Middle Stages

- Case management
  - Aging & Disability Services; www.aasa.dshs.wa.gov
- In-home assistance, chore services
  - Aging & Disability Services, church groups, agencies, family members, www.seniorservices.org
- Adult Activity Centers
  - Senior Centers, www.adultday.org
- Respite services
  - Aging & Disability Services, National respite locator, www.respitelocator.org
Dementia: Late Stages

- Daily Living Skills
  - assistance with dressing, bathing, toileting
  - need to provide simple, structured, meaningful activity
  - providing adequate nutrition
  - maintaining mobility

- Safety Issues
  ✓ Home safety, knives, cleaning supplies, etc
  ✓ Eating nonfood items
Information About Resources: Later Stages

- Management of agitation, wandering, personal care
  - Alzheimer’s Association: 1-800-848-7097 or www.alzwa.org

- Move to residential care facility (Assisted living, Adult Family Home, Nursing Home)
  - Aging and Disability Services: www.aasa.dshs.wa.gov

- How to work with facility staff
  - Alzheimer’s Association: 1-800-848-7097 or www.alzwa.org
  - Long Term Care Ombudsman: www.ltcop.org

- Hospice/end of life care
  - Department of Health: www.doh.gov
  - Alzheimer’s Association: 1-800-848-7097 or www.alz.org
Integrating Medical and Psychosocial Treatments for Dementia

Soo Borson MD
UW School of Medicine - Psychiatry & Behavioral Sciences
Geriatric and Family Services Clinic and
Alzheimer’s Disease Research Center

Rebecca Logsdon PhD
UW School of Nursing-Psychosocial & Community Health
Northwest Research Group on Aging and
Alzheimer’s Disease Research Center
Treatment of Dementia: Cognitive Symptoms

- Environmental Support
- Pharmacologic Treatment
- Medical Management
- Community Resources
Treatment of Dementia: Cognitive Symptoms

Environmental support

- Reduce clutter/simplify
- Visual cues and reminders
- Phone calls, notes, photographs
- Familiar routine, household tools
- Safety modifications (wandering safeguards, remove firearms, power tools, dangerous items)
Dementia Management

- Basic medical treatment of dementia
- Risk reduction
  - Comorbidities
  - Dementia-problem focused care
- Resources
  - Life care planning
Treatment of Dementia: Cognitive Symptoms

Pharmacotherapy for Mild to Moderate AD

Cholinesterase Inhibitors:

- Donepezil (Aricept®)
- Rivastigmine (Exelon®)
- Galantamine (Reminyl®)

- Temporarily delay clinical progression, preserve function.
- Delay or help control some behavioral symptoms.
- Do not prevent progression of brain pathology.
- Few controlled trials comparing two drugs with each other.
- AChEIs can be used in moderate and severe AD too.
Does Earlier Treatment Yield Better Outcomes?

- Evidence from clinical trials of AChEIs
  - Early and sustained cognitive improvement
  - Reduced current and future behavioral symptoms
  - Better function, less caregiving time
  - Delayed nursing home placement

- Most findings confirmed in naturalistic studies
## Improvement in Cognition:
**6-month pivotal trial of donepezil**

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Change in ADAS-cog (LOCF*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 7</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.8%</td>
</tr>
<tr>
<td>Donepezil 5 mg/day</td>
<td>15.4%</td>
</tr>
<tr>
<td>Donepezil 10 mg/day</td>
<td>25.2%</td>
</tr>
</tbody>
</table>

* Last observation carried forward.
† Includes patients who did not improve or decline.

Rogers et al, 1998
## Comparative Efficacy: Meta-Analysis of AChE Clinical Trials

<table>
<thead>
<tr>
<th>Drug/ Dose</th>
<th>Number of Subjects</th>
<th>Relative treatment effect, Drug vs Placebo $\Delta$ ADAS-Cog (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donepezil</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 mg</td>
<td>N = 2188</td>
<td>-2.22</td>
</tr>
<tr>
<td>10 mg</td>
<td>N = 1759</td>
<td>-3.00</td>
</tr>
<tr>
<td><strong>Galantamine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-18 mg</td>
<td>N = 1263</td>
<td>-2.77</td>
</tr>
<tr>
<td>24 mg</td>
<td>N = 2837</td>
<td>-3.19</td>
</tr>
<tr>
<td>32 mg</td>
<td>N = 1960</td>
<td>-2.66</td>
</tr>
<tr>
<td><strong>Rivastigmine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-12 mg</td>
<td>N = 1424</td>
<td>-3.17</td>
</tr>
</tbody>
</table>

Ritchie et al. 2004
AD Stage and Clinical Efficacy

N = 1475, combined rivastigmine RCTs

- mild, MMSE >22
- moderate, MMSE 16-21
- moderately severe, MMSE <16

Mean change in ADAS-Cog scores (ITT-LOCF)

- improvement
- worsening

P=0.018 *
P< 0.001 *

rivastigmine 6-12 mg/day

placebo

* pairwise comparisons, ANOVA

Kurz et al. 2004
Impact on Behavior
2 donepezil RCTs

• **Mild to moderate AD (MMSE 19 [10-26])**
  - N = 286, 1 year outpatient RCT; >80% completed
  - Donepezil-treated patients declined half as fast on global rating of behavior, cognition and function

• **Moderate to severe AD (MMSE 12 [5-17])**
  - N = 290, 6 month NH RCT; >80% completed
  - Donepezil treatment associated with sustained behavioral improvement
  - Depression/dysphoria, anxiety and apathy were most responsive symptoms

Winblad et al. 2001; Feldman et al. 2001
Improvement in Everyday Function

6 month RCT of galantamine

![Bar chart showing improvement in everyday function.](image)

**p < 0.05.  
**p < 0.01.  
*p = 0.06.**

Disability in Alzheimer's Disease cluster

Blesa et al, 2000
Impact on Caregiver Time

N = 325, 2 RCTs of galantamine

Kaufer, Borson, Sadik 2005 (in press)
AChEI Therapy and Time to Nursing Home

Cumulative % New Users Placed Over 2 Year Followup

Total N = 5562
Either vs neither, P < 0.001

The Real World: Donepezil vs. Rivastigmine Refills

A retrospective analysis: duration of index therapy (months)

Data on file (Pfizer); Broderick WC et al. 2003
Treatment of Dementia: Cognitive Symptoms

Pharmacotherapy for Moderate to Severe AD

N-methyl D-aspartate agonist—Glutamate Regulation:

Memantine (Namenda®)

- Preserve ADL function a little longer (about 7 months).
- Safe in combination with cholinesterase inhibitor.
- Can be used in mild to moderate AD too - clinical data pending.
Memantine + Donepezil in Moderate to Severe AD

- Does adding memantine help AD patients stably treated with donepezil?
- Randomized, double-blind, placebo-controlled, parallel group study
- 24-week double-blind treatment
- Multiple outcomes (cognition, behavior, function, caregiver activity, costs, NHP)

Farlow et al. Neurology. 2003;60(suppl 1):A412
Cognition: Severe Impairment Battery

- **Memantine**
- **Placebo**

Mean Change from Baseline

- N=12
- N=11
- N=10
- N=96
- N=12

End Point

- 0
- 4
- 12
- 28

*p=0.002 ITT-OC analysis; †p<0.001 LOCF analysis

Keys To Medical Management of Dementia (1): Comorbid Conditions

- All: can the patient follow doctor’s recommendations?
- Cardiovascular disease
  - Evaluate total treatment package
- Respiratory disease; sleep apnea
  - Evaluate capacity for self-management
- Diabetes
  - Medication adherence
  - Closer monitoring of metabolic control
- Irritable bowel
  - Avoid anticholinergics
# Living Alone With Dementia

N=139, 18 month follow up - 22% had harm events

<table>
<thead>
<tr>
<th>Failure to... (n)</th>
<th>Harm (n)</th>
<th>Emergency Help (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eat/ drink (9)</strong></td>
<td>Dehydration (5); infection (2); delirium (1); hip fracture (1)</td>
<td>Ambulance/ ED (8); police (1)</td>
</tr>
<tr>
<td><strong>Report medical problem (5)</strong></td>
<td>Delirium (1); infection (1); late effect of neglected injury (1)</td>
<td>Ambulance/ ED (4); urgent MD home visit (1)</td>
</tr>
<tr>
<td><strong>Use assistive devices (5)</strong></td>
<td>Contusion (2); bone fracture (1); skin laceration (2)</td>
<td>Ambulance/ ED (5)</td>
</tr>
<tr>
<td><strong>Maintain hygiene (4)</strong></td>
<td>Infection (4)</td>
<td>Urgent MD home visit (4)</td>
</tr>
<tr>
<td><strong>Use meds properly (4)</strong></td>
<td>Delirium (1); cardiac complications (1); edema (1)</td>
<td>Ambulance/ ED (2); police (1)</td>
</tr>
<tr>
<td><strong>Recognize environment (2)</strong></td>
<td>Struck another (1); psychosis with COPD exacerbation (1)</td>
<td>Ambulance/ ED (2)</td>
</tr>
<tr>
<td><strong>Turn off stove (1)</strong></td>
<td>Smoke damage</td>
<td>Fire and ambulance</td>
</tr>
<tr>
<td><strong>Protect resources (1)</strong></td>
<td>Financial fraud</td>
<td>Police</td>
</tr>
</tbody>
</table>

Tierney et al, JAGS 2004; 52: 1435-1441
Keys to Medical Management of Dementia (2): Associated Conditions

- Incontinence
  - Avoid anticholinergics
  - Address intentional dehydration
  - Non-pharmacologic treatment

- Complications of impaired self-maintenance
  - Dehydration, hypotension, obstipation
  - Subnutrition
  - Fall risk

- Drug-dementia interactions
Conclusions

• Dementias are chronic conditions
• Total disease medical management approaches are required
• Components include
  - Practice-based screening
  - Early diagnosis
  - Optimal individualized treatment
  - Anticipate future bad events to prevent them
Treatment of Dementia: Cognitive Symptoms

Experimental Pharmacologic Research:

**NSAIDS** (controversial; interrupted due to safety concerns)

**HRT** (combination estrogen and progesterone studies discontinued in 2002 when WHI found it doubled risk of dementia; in 2004 estrogen alone discontinued because it was not protective against dementia)

**Vitamin E** may slow progression by about 7 months; current research evaluating use in MCI shows no real benefit

**Ginkgo Biloba** may improve some symptoms of AD; current research on safety and efficacy does not support better efficacy

**Statins** do not reduce prevalence or delay onset of dementia
Treatment of Dementia: Cognitive Symptoms

Community Support

- Early stage support groups
- Adult activity centers
- Case management
- Chore services
- Respite
- Medication assistance
- Transportation
Behavior Problems in Dementia

- Occur in 70-90% of individuals at some point
- Increase as disease progresses from mild to severe stages
- Primary source of stress & burden to family caregivers
- Common cause of institutionalization
- May be difficult to treat, and require combination behavioral and pharmacologic intervention
Choosing our Battles: When should we intervene?

- Distressing or frightening to the individual.
- Creates an unsafe situation for the individual or those around him/her.
- Causes significant distress to the caregiver or prevents necessary care.
Memory Behaviors: RMBPC

n = 201

- Frequency (%)
- Caregiver Reaction

Questions: 90%
Recent Events: 85%
Losing Things: 82%
Forgetting Day: 73%
Concentration: 68%
Past Events: 59%
Hiding things: 34%

Severity:
- Severe
- Mod
- Mild
Depressive Behaviors: RMBPC

n=201

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Frequency</th>
<th>Caregiver Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxious</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Sad</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Hopeless</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Burden</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Lonely</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Crying</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Failure</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Suicidal</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Severe, Moderate, Mild
Disruptive Behaviors: RMBPC

n=210

- **Arguing**: Severe 43, Mild 23
- **Waking**: Severe 21, Mild 20
- **Verbal Aggression**: Severe 20, Mild 15
- **Embarrassing**: Severe 15, Mild 10
- **Dangerous**: Severe 10, Mild 6
- **Talking Loudly**: Severe 6, Mild 5
- **Threats to Hurt**: Severe 5, Mild 5
- **Destroying Property**: Severe 5, Mild 5

Legend:
- **Frequency**
- **Caregiver Reaction**
Treatment of Dementia: Behavioral Symptoms

- Caregiver support
- Activity-based approach
- Problem solving & caregiver training
- Pharmacologic interventions
Who Cares for Alzheimer's Disease Patients?

- Wives: 43%
- Daughters: 27%
- Husbands: 23%
- Sons: 7%
Time Spent Caregiving
(Hours per Week)

- Primary Caregiver
- Paid Help
- Family & Friends

Not Employed
Employed

0  20  40  60  80  100  120

120
100
80
60
40
20
0
Caregiver Depression & Burden

- Helplessness
- Grief
- Self-Doubt
- Anger
- Guilt
- Anxiety
- Sleep Disturbance
- Alcohol Abuse
Caregivers Hold the Keys to Success

- Energy, desire, ability to do things differently
- Willingness to ask for and accept help from others
- Flexibility in thinking and problem solving
- Sense of humor
- Patient, but able to be firm
- Belief that things can change
- Good prior relationship with patient
Activity Based Approach: Using Pleasant Activities

- What did the person enjoy in the past?
- What does he/she enjoy now?
- How can tasks be modified to accommodate current abilities?
- Who is available to help with these activities?
Pleasant Events and Dementia

**Early-Mid Stages**
- Reading magazines, newspaper.
- Going on outings (to the park, a picnic, etc.).
- Playing music, singing.
- Recalling and discussing past events.
- Exercising (walking, dancing, etc.).
- Gardening.

**Mid-Late Stages**
- Being read to (newspaper/book).
- Being outside.
- Going for a ride in the car.
- Listening to music.
- Watching favorite videos.
- Getting a hand or shoulder massage.
- Watching birds, squirrels.
A-B-C Approach to Problem Solving

Problem Behaviors Occur in Three Parts

- **Antecedent** = A triggering event.
- **Behavior** = The behavior itself.
- **Consequence** = The response to the behavior.
A-B-C Approach

- Describe behavior in observable terms
- Identify antecedents & consequences
- Develop a reasonable plan to try for a week
- Identify who will carry out the plan
- Evaluate success
- Revise, try another plan or go on to the next problem
Treatment of Agitation in Alzheimer’s Disease: A Randomized Placebo Controlled Clinical Trial


And members of the Alzheimer’s Disease Cooperative Study

Neurology, 2000, 55, 1271-1278

Funded by the National Institute of Aging (AG-010483)
## Treatment of Agitation in Dementia: ADCS-2CGIC Outcome

<table>
<thead>
<tr>
<th></th>
<th>BMT (N=41)</th>
<th>Haloperidol (N=34)</th>
<th>Trazodone (N=37)</th>
<th>Placebo (N=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Improved</td>
<td>32</td>
<td>32</td>
<td>41</td>
<td>31</td>
</tr>
<tr>
<td>% No Change</td>
<td>20</td>
<td>21</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>% Worse</td>
<td>49</td>
<td>47</td>
<td>46</td>
<td>42</td>
</tr>
</tbody>
</table>

(Intent to treat analysis; no significant differences)
When Agitated Behavior Is Severe ...

- Cholinesterase inhibitors are not enough
- Atypical antipsychotics are first-line agents
- Other agents if antipsychotics fail or as adjunct therapy
Olanzapine for Agitation/Aggression

Nursing Home Study (N=206)

- Placebo
- OLZ 5 mg
- OLZ 10 mg
- OLZ 15 mg

Agitation, aggression and psychosis improved at 5-10 mg

Placebo vs Olanzapine 5 mg: p = 0.006; vs 10 mg: p<0.001; vs 15 mg: p=0.24
Street JS et al. Arch Gen Psychiatry. 2000;57:968-976; OLZ = olanzapine
Olanzapine Side Effects

- Extrapyramidal symptom rate similar to placebo
- Somnolence in 25-39% vs. 6% placebo (p<0.001); dose related
- Gait impairment in 14-19% vs. 2% placebo (p<0.05)
- Gait impairment linked to somnolence and may increase falls risk

Street JS et al. 2000; Rubenstein. 2000
Risperidone: Pooled Data
12-Week Phase III Trials

- INT-24, AUS-5, USA-63, 1,150 elderly nursing home/institutionalized patients
  - 722 risperidone vs. 428 placebo
  - Median age ~82; ~80% at least 75 years old
  - Mixed diagnoses: AD ~69%, AD + VaD ~11%, VaD ~20%
  - Behavioral symptoms for average of 3 years at entry into study

Janssen Pharmaceutica (Data on file)
BEHAVE-AD Psychosis
Subscore (Observed)

Baseline  Week 4  Week 8  Week 12 Endpoint

Placebo  Risperidone

*p=0.001; #p=0.002; †p=0.003; Janssen Pharmaceutica (Data on file)
Cohen-Mansfield Agitation Inventory Total Score (Observed)

Baseline  Week 4  Week 8  Week 12  Endpoint

Risperidone

Placebo

*\(p<0.001;\) Janssen Pharmaceutica (Data on file)
Clinical Global Improvement
Risperidone vs. Placebo

Risperidone (N=718)
Placebo (N=427)

Overall p<0.001; Janssen Pharmaceutica (Data on file)
Tardive Dyskinesia: 
Risperidone vs. Haloperidol

Onset Over 9-Month Follow-Up

- Risperidone (N=61)
- Haloperidol (N=61)

Mean age 66 yr, matched for duration of exposure and median dose (1 mg/day)

Peto-Prentice p=0.045; Jeste D 1999
Atypical Antipsychotics and Incidence of Tardive Dyskinesia

- **Risperidone**
  - N=255 demented patients free of dyskinesia
  - 1-year open-label extension after placebo-controlled trial
  - Mean age 82.5 years, mixed diagnoses
  - Mean modal dose of risperidone = 0.96 mg/day, mean total duration of use = 273 days
  - Incident TD in 2.6%*

*Jeste DV 2000*
Other Atypical Antipsychotics

- Quetiapine
- Ziprasidone
- Aripiprazole
- Clozapine
FDA “Black Box” Warning

- Applies to all atypical antipsychotics
- Pooled data on > 5000 older adults with dementia in placebo-controlled clinical trials
- Death rate doubled over 10 weeks in active vs placebo treatment groups (> 4% vs > 2%)
- Note that ‘typical’ antipsychotics also associated with excess deaths
Other Psychotropic Classes May Help in Geriatric Agitation and Aggression

- **Mood-stabilizing anticonvulsants**
  - Divalproex, carbamazepine, gabapentin

- **Serotonin modulators**
  - Trazodone, citalopram

- **β-adrenergic blockers**
  - Propranolol, pindolol

- **Antiandrogens (especially sexual aggression)**
  - Estrogen, progestogens, leuproliide
Treating Agitation or Psychosis in Dementia

Summary of AAN Evidence-Based Recommendations

• Use antipsychotic agents to treat agitation or psychosis when environmental intervention fails (Practice Standard)

• Atypical agents may be better tolerated than traditional neuroleptics (Practice Guideline)

Adapted from: Doody RS et al. 2001
Treating Agitation or Psychosis in Dementia (Cont.)

Summary of AAN Evidence-Based Recommendations

• Agitation associated with other neurobehavioral syndromes may require different treatments
  - For depression, selected tricyclics, MAO-B inhibitors (Deprenyl) and SSRI should be considered
  - Side-effect profiles guide choice

Adapted from: Doody RS al. 2001
Think About Causes of Behavioral Symptoms in Dementia

• Agitation may have physical causes (discomfort, medication, sensory deprivation, acute illness)

• Agitation may have emotional causes (loneliness, boredom, forgetting that loved ones have visited, feelings of neglect)
Internet Resources for Updating Dementia Information

UW Alzheimer’s Disease Research Center
  www.uwadrc.org
Alzheimer’s Association
  www.alz.org
Alzheimer’s Disease Education and Referral Center
  www.alzhiemers.org
NIH Clinical Trials database
  www.clinicaltrials.gov