Management of the Acutely Agitated Long Term Care Patient
“Graying” of the Population

US Population Over Age 65

 Millions of Persons

Year

1900 1920 1940 1960 1980 1990 2010 2030
Defining Dementia

- Clinical state characterized by loss of function in multiple cognitive domains.
- Decline must represent a decline from a previously higher level of functioning.
- Diagnosis of dementia should NOT be made if the cognitive deficits occur exclusively during the course of a delirium.
- Alzheimer disease most prevalent.

The prevalence of dementia increases with age so that 10% of those older than 65 years suffer from dementia. This increases dramatically to 47% in those older than 85 years. It has been suggested that dementia will be the epidemic of the 21st century.

References
Clinical Disease Progression

Years From Diagnosis

MMSE Score

Mild

Moderate

Severe

Clinical Disease Progression

Cognitive Symptoms

Diagnosis

Loss of Functional Independence

Behavioral Problems

Nursing Home Placement

Death

Reprinted from Clinical Diagnosis and Management of Alzheimer’s Disease, H Feldman and S Gracon; Alzheimer’s Disease: symptomatic drugs under development, pages 239-259, copyright 1996, with permission from Elsevier.
<table>
<thead>
<tr>
<th>Stage 1</th>
<th>No objective or subjective functional deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 2</td>
<td>Subjective functional deficit</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Objective functional deficit and interference with complex social tasks</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Deficient performance of complex ADL</td>
</tr>
<tr>
<td>Stage 5</td>
<td>Deficient performance of basic ADL</td>
</tr>
<tr>
<td>Stage 6</td>
<td>Decreased ability to dress, bathe, and toilet independently</td>
</tr>
<tr>
<td>Stage 7</td>
<td>Loss of speech, locomotion, and consciousness</td>
</tr>
</tbody>
</table>

What Is “Agitation”?

- Any inappropriate verbal, vocal or motor activity that is not an obvious expression of need.
- It is not a diagnostic term but rather a syndromal term (group of symptoms) that describes the clustering of behaviors.
- Agitation can result from a variety of underlying general medical, or neuro-psychiatric or psychosocial conditions.

Adapted from: Mansfield C et al. (Various references)
Phenomenology of Agitation and Aggression

• Physically nonaggressive
  – Pacing
  – Restlessness
  – Inappropriate robing/disrobing
  – Inappropriate handling of objects (executive dysfunction)

• Physically aggressive
  – Hitting
  – Kicking
  – Biting
  – Scratching
  – Pushing
  – Spitting
  – Pinching


Phenomenology of Agitation and Aggression

• Verbally nonaggressive
  – Complaining
  – Attention seeking
  – Repeated questions/phrases
  – Screaming

• Verbally aggressive
  – Threats
  – Obscenities
  – Accusations
  – Name calling


Possible Etiologies
Agitation “Pie” Chart

- Caregiver related
- Idiopathic
- Manifestation of a medical disorder
- Confusion
- Medication side effects
- Psychiatric comorbidity
- Environment related
Medical Causes

- Recent onset of illness/surgery
- Recent change in medication/polypharmacy
- Sleep disturbances: primary, secondary
- Chronic/acute pain
- Cardiovascular disease
- Visual impairment
- Poor nutrition
- Respiratory infection
- Urinary tract infection
Management of Acute Episodic Agitation in the Absence of Psychosis or Mood Disturbance

Nonpharmacologic Management

- Evaluate: Reassurance/Redirection alone
- Evaluate: Environmental Triggers Adjustment
- Set-up routines that are patient-specific
- Remove offending pharmacologic agents (such as adjunct anticholinergics, benzodiazepines, etc.)
- Ensure support and patient specific education for the caregiver and/or staff
General Principles of Management of Agitation (cont’d)

- For acute episodic non-persistent agitation that occurs in the absence of mood or psychotic disturbances
  - The *first line approach* requires assessment and a trial of non-pharmacologic management

- For the patient with agitation and concurrent psychosis and/or mood disturbance, the general principles support combining pharmacologic and non-pharmacologic interventions
What Are the Most Common Psychiatric Disorders in the Elderly?

<table>
<thead>
<tr>
<th></th>
<th>Outpatient Care</th>
<th>Long-Term Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia</td>
<td>10% &gt; age 65</td>
<td>Dementia</td>
</tr>
<tr>
<td></td>
<td>45% &gt; age 85</td>
<td>50-70%</td>
</tr>
<tr>
<td>Depression</td>
<td>4-5%</td>
<td>Affective disorders</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>1-5%</td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>Psychosis</td>
<td>0.1-4%</td>
<td>MR/DD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-5%</td>
</tr>
</tbody>
</table>
Prevalence of Symptoms of Psychosis and Agitation in Dementia

Cache County Study of Memory in Aging (CCSMA)

- First US population study of behavioral disturbances in dementia
- Evaluated the prevalence and severity of mental and behavioral disturbances in the elderly
- 5092 individuals were screened
- Participants with dementia (n=329) were compared to control group without dementia (n=673)

# Prevalence of Symptoms of Psychosis and Agitation in Dementia

<table>
<thead>
<tr>
<th>NPI Item</th>
<th>Dementia (n=329) %</th>
<th>No Dementia (n=673) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apathy</td>
<td>27.4</td>
<td>3.1</td>
</tr>
<tr>
<td>Depression</td>
<td>23.7</td>
<td>7.0</td>
</tr>
<tr>
<td>Agitation/aggression</td>
<td>23.7</td>
<td>2.8</td>
</tr>
<tr>
<td>Irritability</td>
<td>20.4</td>
<td>4.5</td>
</tr>
<tr>
<td>Delusions</td>
<td>18.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Anxiety</td>
<td>17.0</td>
<td>5.6</td>
</tr>
<tr>
<td>Aberrant motor behavior</td>
<td>14.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>13.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>9.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Elation</td>
<td>0.9</td>
<td>0.3</td>
</tr>
</tbody>
</table>

New Admissions to Nursing Homes

454 new admissions were followed for 1 month

- 79 patients (17%) had behavioral problems that required intervention
- Most frequent diagnoses were dementia complicated by delusions, depression, and/or delirium

Behavioral Problems in Nursing Home Residents

- Restlessness 38%
- Passive aggression 38%
- Active aggression 26%
- Verbal aggression 26%
- Wandering 24%

Psychobehavioral Metaphors

- Identify most salient symptom cluster
- Is there a pattern analogous to a drug-responsive syndrome?
- Use as a rational guide to therapy

**Behavioral Clusters Matched to Potentially Relevant Medication Classes**

- **Disturbed affect/mood**
  - Anticonvulsants
  - Antidepressants
  - Atypical Antipsychotics

- **Anxiety**
  - Antidepressants
  - Anxiolytics-avoid
  - Anticonvulsants
  - Atypical Antipsychotics?

- **Psychosis**
  - Atypical antipsychotics
  - High-potency typical antipsychotics-avoid

- **Agitation/aggression**
  - Anticonvulsants
  - Antidepressants
  - Anxiolytics-avoid
  - Atypical Antipsychotics
  - Cholinergic agents?

References:
- Tariot P. *J Clin Psychiatry*. 1999;60(suppl 8):11-20
- Shapira NA et al. ACNP 2002
General Principles of Geriatric Pharmacotherapy (cont’d)

- Know the cautions, warnings and physician liability in the medicine’s current FDA approved package insert
- With risk for tolerability or safety problems “start low, increase slowly, but obtain meaningful efficacy”
- Different conditions often necessitate different dosages to obtain efficacy
- Tolerability and safety profiles are also often different depending on age, body mass, gender, ethnicity, culture of origin and diagnosis
Pharmacological Approach

• There is no US FDA-approved treatment for agitation associated with dementia

• Dementia with agitation is not viewed as a disease

• Proper documentation and diagnosis leads to better choice of class of medications and increases probability of success
Atypical Antipsychotics and the News

- Multicenter Trial of Atypicals in Dementia patients (first non Industry Sponsored) reported in the 10/12/06 issue of USAToday
- Placebo vs Risperidone, Olanzapine and Quetiapine showed no significant clinical difference in 421 randomized patients with DAT for 8 weeks
- Side effects included worsening confusion, sleepiness, tremors and muscle stiffness
- Conclusion: these drugs should be given to patients who are carefully monitored for improvements and adverse events, they are the last line of therapy & they should be used only in the short term

- New England Journal of Medicine, Lon Schneider et. al., 10/06
# ADA Consensus on Antipsychotic Drugs and Obesity and Diabetes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weight Gain</th>
<th>Diabetes Risk</th>
<th>Dyslipidemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Risperidone</td>
<td>++</td>
<td>D</td>
<td>D</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>++</td>
<td>D</td>
<td>D</td>
</tr>
<tr>
<td>Aripiprazole*</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ziprasidone*</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Newer drugs with limited long-term data.

+=increased effect; -=no effect; D=discrepant results.

## Risk of Cerebrovascular Adverse Events in Elderly Patients With Dementia

<table>
<thead>
<tr>
<th></th>
<th>Number of Trials</th>
<th>CVAEs</th>
<th>Numbers Needed to Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Active Drug</td>
<td>Placebo</td>
</tr>
<tr>
<td>Risperidone¹</td>
<td>4</td>
<td>3.8% (29/764)</td>
<td>1.5% (7/466)</td>
</tr>
<tr>
<td>Olanzapine²</td>
<td>5</td>
<td>1.3% (15/1178)</td>
<td>0.4% (2/478)</td>
</tr>
</tbody>
</table>

- In US, letters to health care professionals were sent and warning added in prescribing information.
- UK Committee on Safety of Medicines guideline:
  - Avoid use in behavioral and psychological symptoms associated with dementia.
  - Limited to short-term and under-specialist advice for the management of acute psychotic conditions with risperidone.
  - Consider risk in treating patients with previous history of stroke or transient ischemic attack and assess cerebrovascular disease risk factors including hypertension, diabetes, smoking, and atrial fibrillation.

Risk of Death in Elderly Patients: Atypical vs Conventional Antipsychotics

Deaths per person/year

Days after initiation of medicine

Conventional antipsychotics
Atypical antipsychotics

CATIE Trial of Atypical Antipsychotics in AD

- Modest benefits
- Risks of increased mortality and morbidity are not sufficient to justify therapy

Dementia Antipsychotic Withdrawal Trial (DART-AD): long term follow-up

- 128 patients randomized to 12 months of antipsychotic vs placebo though followed up to 54 months
- Risperidone 67%, haloperidol 26% and other first generation antipsychotics 7%

DART-AD Trial Results

- 76.6% cumulative probability survival in placebo treated patients vs a 70.3% survival in patients treated with antipsychotics at 12 months
- 71% cumulative probability of survival vs 46% survival at 24 months
- 59% cumulative probability of survival vs 30% at 36 months
- 53% cumulative probability of survival vs 26% at 42 months
- Effect of this study has been a 50% decrease in antipsychotics since 2004!!
Atypical Antipsychotics Do Have a Place

- Where there is a medical need for the drugs
- Where comorbidity permits
- Where the risk/benefit of alternatives is equally high
- Remembering, though, that symptom control does not always equate to quality of life for the person being treated
- Should not use in the following: wandering, restlessness, mild agitation, unsociability, fidgeting, nervousness, poor self care, indifference or uncooperativeness
- Must rule out a physical cause first
- Do not use for an excessive duration or without adequate monitoring
- Do not use in excessive doses or in combination with another antipsychotic
Summary

- People 65 years and older are increasing rapidly, thus those with cognitive impairment are growing as well
- Behavioral metaphors help determine the medications we choose to treat cognitively impaired seniors who exhibit agitation or aggression
- Avoid older antipsychotic class, as these are ineffective in chronic use and have marked toxicity
- Atypical antipsychotic agents are effective and safer than the older agents in the acute/chronic rx of agitation/aggression in dementia/delirium
- Antidementing agents, anticonvulsants, antidepressants may be effective and safer alternatives to antipsychotic agents