BEHAVIORAL and PSYCHOLOGICAL SYMPTOMS in DEMENTIA (BPSD)

Dr. Shah MD, MPH
Braodlawns Medical Center

DISCLOSURE

• Dr. Shah has no relevant conflicts with commercial interests to disclose

OBJECTIVES

• Factors precipitating behavioral disturbances
• How to rule out medical, environmental, and caregiving causes of behavioral problems
• Environmental and non-pharmacologic management of behavioral disturbances
• When and how to medicate
TOPICS COVERED

• Clinical Features
• Assessment and Differential Diagnosis
• Basic Approach to Treatment
• Treatments for Specific Disturbances

Activities of Daily Living

- Behavioral symptoms (Usually identified on the basis of observation of the patient)
- Physical aggression
- Screaming
- Restlessness
- Agitation/Catastrophic reactions (Verbal/Physical)
- Wandering
- Culturally inappropriate behaviors
- Sexual disinhibition
- Hoarding
- Cursing

- Psychological symptoms (Usually and mainly assessed on the basis of interviews with patients and relatives)
- Anxiety
- Depressive mood
- Apathy
- Hallucinations and delusions (Psychosis of Alzheimer's Disease)
- Misidentification syndromes
- Sundownering
- Elation
- Negativism
Behavioral symptoms

- Physical/verbal aggression, agitation, disinhibition, restlessness, wandering, culturally inappropriate behaviors, sexual disinhibition, cursing and hoarding.

Psychological symptoms

- Anxiety, depressive mood, hallucinations and delusions, apathy, Sundowning (Delirium due to known physiological condition ICD F05)
- delusional misidentification syndrome (DMS), negativism and elation.
Apathy

- Recently been recognized as one of the BPSDs
- It is different than depression, although it can be a part of depression
- When severe, it can interfere with overall functioning

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Table 1. Behavioral and psychological symptoms of dementia (from Luxenberg et al.14)

DOI: 10.1046/j.1440-1819.2000.00773.x

<table>
<thead>
<tr>
<th>Group I (most common/most distressing)</th>
<th>Group II (moderately common/moderately distressing)</th>
<th>Group III (least common/least distressing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological</td>
<td>Psychological</td>
<td>Behavioral</td>
</tr>
<tr>
<td>Delusions</td>
<td>Misorientation</td>
<td>Crying</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>Depression</td>
<td>Lack of interest</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>Behavioral</td>
<td>Repetitive questioning</td>
</tr>
<tr>
<td>Sleeplessness</td>
<td>Agitation</td>
<td>Repetitive questioning</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Culturally inappropriate behavior and expressions</td>
<td>Shadowing</td>
</tr>
<tr>
<td>Depression</td>
<td>Memory</td>
<td></td>
</tr>
<tr>
<td>Behavioral</td>
<td>Visiting</td>
<td></td>
</tr>
<tr>
<td>Physical aggression</td>
<td>Screaming</td>
<td></td>
</tr>
<tr>
<td>Wandering</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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BEHAVIORAL SYMPTOMS
BY DEMENTIA TYPE

- Frontotemporal dementia (Pick's disease): often associated with prominent disinhibition, compulsive behaviors, and social impairment
  - In severe cases, a syndrome of hyperphagia, hyperactivity, and hypersexuality may occur
- Dementia with Lewy bodies: prominent psychosis characterized by visual hallucinations
- Behavioral problems can occur in all dementia types
HOW COMMON IS BPSD

INTRODUCTION

• As many as 80%–90% of patients with dementia develop at least one distressing symptom over the course of their illness

• Behavioral disturbances or psychotic symptoms in dementia often precipitate early nursing-home placement

• Disturbances are potentially treatable, so it is vital to anticipate and recognize them early

• Present in all types of dementias

• 60% community dwelling

• 80% dementia pts in LTC
• Agitation 75%
• Wondering 60%
• Depression 50%
• Psychosis 30%
• Screaming 20%

• Caregiver stress
• ER
• Hospital Stay
• Polypharmacy
• Placement in LTC
• $ 
• QoL for pt. and the caregiver

NEUROCHEMISTRY
**TABLE 1**

<table>
<thead>
<tr>
<th>Type</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroanatomical</td>
<td>Neuritic plaques and neurofibrillary tangles in the frontal and temporal cortices are associated with (MCI), right frontal lobe atrophy is associated with (MMSE)</td>
</tr>
<tr>
<td>Neurofunctional</td>
<td>Frontal, temporal, and parietal cortical dysfunction is associated with psychotic symptoms, greater EEG delta power and the right hemisphere is associated with (MCI)</td>
</tr>
<tr>
<td>Neurochemical</td>
<td>Damage to cholinergic neurons in the frontal and temporal cortices and autonomic and serotonergic systems is associated with (MCI), higher levels of noradrenaline in the substantia nigra, lower levels of serotonin in the prefrontal cortex are associated with psychotic symptoms</td>
</tr>
<tr>
<td>Cognitive</td>
<td>Higher levels of NE in the substantia nigra, lower 5-HT levels in the presubiculum are associated with psychotic symptoms</td>
</tr>
<tr>
<td>Psychological</td>
<td>High prevalence of neocortical in the frontal, temporal, and parietal cortices is associated with (MCI), the prevalence of (MCI) alone is associated with an earlier age of onset of symptoms, the presence of (MCI) alone is associated with depressive symptoms, homocysteine for (MCI) alone is associated with depression, agitation, and motor disorders, anxiety, and sleep disorders are more frequent in individuals with (MCI) alone, low levels of 5-HT receptors are associated with depression, and aggression, dopamine receptor polymorphisms are associated with psychosis and aggression</td>
</tr>
</tbody>
</table>

CLINICAL FEATURES

• Psychiatric symptoms may develop that resemble discrete mental disorders such as depression or mania
• The course and features are more difficult to predict, and treatments are less reliably effective than in younger adults without dementia
• Neuropsychiatric symptoms such as apathy, poor self-care, or paranoia may be the first indication of dementia

CLINICAL FEATURES: AGITATION (1 of 2)

• Reflects loss of ability to modulate behavior in a socially acceptable way
• May involve verbal outbursts, physical aggression, resistance to bathing or other care needs, and restless motor activity such as pacing or rocking
• Often occurs concomitantly with psychotic symptoms such as paranoia, delusional thinking, or hallucinations

CLINICAL FEATURES: AGITATION (2 of 2)

• The word agitation is used to describe a variety of behaviors and psychologic symptoms
• Assessment of disruptive behavior must include a careful description of the nature of the symptom, when it occurs, where it develops, and if any precipitants are identified
• Overt resistance to care is most often seen in later stages of dementia, but it may be a first sign of incipient cognitive decline
ASSESSMENT

• Obtain a history from both the patient and an informant
• Elicit a clear description of the behavior:
  ➢ Temporal onset and course
  ➢ Associated circumstances
  ➢ Relationship to key environmental factors, such as caregiver status and recent stressors

DIFFERENTIAL DIAGNOSIS:
MEDICAL CAUSES

• Disturbances that are new, acute in onset, or evolving rapidly are most often due to a medical condition or medication toxicity
• An isolated behavioral disturbance in a demented patient can be the sole presenting symptom of acute conditions such as pneumonia, UTI, pain, angina, constipation, or uncontrolled diabetes
• Medication toxicity can present as behavioral symptoms alone
MANAGEMENT

- Educate caregivers
- Nonpharmacological
- Optimize current medications
- Pharmacological

CARE GIVER
DIFFERENTIAL DIAGNOSIS:
STRESS IN CAREGIVING RELATIONSHIP

• May exacerbate/cause a behavioral disturbance
• Relationships with potential for stress include:
  ➢ Inexperienced caregivers
  ➢ Domineering caregivers
  ➢ Caregivers who themselves are impaired by medical or psychiatric disturbances

A general strategy focuses on two main elements: the environment and direct caregiving

The Environment

• Maintain consistency of physical facilities and staff
• Instruct new residents and family to bring familiar items with them
• Reduce noise
• Avoid highly contrasting colors or wall papers
• Use clear, soft lighting
Caregiving

- Maintain consistency of staff and approach
- Remember that behaviors are not intentional
- Minimize a rigid schedule
- Avoid trying to reason or argue
- Daily routines

NONPHARMACOLOGICAL

Remember, the nonpharmacological interventions should be considered before or at the same time as pharmacotherapy!
TREATMENTS FOR SPECIFIC DISTURBANCES: GENERAL PRINCIPLES

• Management of pain, dehydration, hunger, and thirst is paramount
• Consider the possibility of positional discomforts or nausea secondary to medication effects
• Modify environment to improve orientation
• Good lighting, one-on-one attention, supportive care, and attention to personal needs and wants are also important

BEHAVIORAL INTERVENTIONS (1 of 3)

• Evaluate and treat underlying medical conditions
• Replace poorly fitting hearing aids, eyeglasses, and dentures
• Keep the environment comfortable, calm, and homelike with use of familiar possessions
• Provide regular daily activities and structure; refer patient to adult day care programs, if needed

BEHAVIORAL INTERVENTIONS (2 of 3)

• Assess for new medical problems
• Attend to patient’s sleep and eating patterns
• Install safety measures to prevent accidents
• Ensure that the caregiver has adequate respite
• Educate caregivers about practical aspects of dementia care and about behavioral disturbances
• Teach caregivers communication skills, how to avoid confrontation, techniques of ADL support, activities for dementia care
• Simplify bathing and dressing with use of adaptive clothing and assistive devices, if needed
• Offer toileting frequently and anticipate incontinence as dementia progresses
• Provide access to experienced professionals and community resources
• Refer family and patient to local Alzheimer’s Association
• Consult with caregiving professionals, such as geriatric case managers
OPTIMIZE CURRENT MEDICATIONS

REMOVE OFFENDING MEDICATIONS, PARTICULARLY ANTICHOLINERGIC AGENTS

- Advil PM (pain and sleep)
- Benadryl (for allergies)
- Dramamine (for motion sickness)
- Excedrin PM (for pain and insomnia)
- Pepcid AC (acid reflux)
- Sominex (for insomnia)
- Tagamet (acid reflux)
- Tylenol PM (for pain and insomnia)
Drugs That May Cause Memory Loss

- Narcotic painkillers
- Sleeping aids
- Incontinence drugs - Anticholinergics
- Antihistamines
- Cholesterol drugs
- Antidepressant drugs
- TCA

Drugs

- Regularly review medications and supplements
- Manage medications that could affect cognition
- Do frequent medication reconciliation

PHARMACOLOGICAL
ROLE OF ANTI-DEMENTIA FOR BEHAVIOR

- 868 patients were treated with memantine and 882 patients were treated with placebo.
- Patients on memantine improved by 1.99 on the NPI scale
- (95% CI -0.08 to -3.91; p = 0.041) compared with the placebo group.


<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose (mg)</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>5 - 20 mg</td>
<td>Dry mouth, falls, headache, GI symptoms, sedation, sexual dysfunction</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>8 - 40 mg</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>50 - 100 mg</td>
<td></td>
</tr>
<tr>
<td>Trazadone</td>
<td>50 - 300 mg</td>
<td></td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>2.5 - 10 mg</td>
<td>Cardiomyopathy, death, extrapyramidal symptoms, fall, metabolic syndrome, neuroleptic malignant syndrome, QT prolongation, sedation, unusual autonomic effects</td>
</tr>
<tr>
<td>Clozapine</td>
<td>25 - 125 mg</td>
<td></td>
</tr>
<tr>
<td>Paliperidone</td>
<td>0.25 - 2 mg</td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25 - 800 mg</td>
<td></td>
</tr>
<tr>
<td><strong>Cholinesterase inhibitors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donepezil</td>
<td>5 - 15 mg</td>
<td></td>
</tr>
<tr>
<td>Galantamine</td>
<td>4 - 24 mg</td>
<td></td>
</tr>
<tr>
<td>Rivastigmine</td>
<td>1.4 - 12 mg or 4.5 - 9.6 mg per day</td>
<td></td>
</tr>
<tr>
<td><strong>Memantine</strong></td>
<td>7 - 34 mg</td>
<td></td>
</tr>
<tr>
<td><strong>Muscle relaxants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carisoprodol</td>
<td>250 - 800 mg</td>
<td></td>
</tr>
<tr>
<td>Zaleplon</td>
<td>10 - 19 mg</td>
<td></td>
</tr>
</tbody>
</table>

These behaviours respond poorly, if at all, to an antipsychotic. Short-term antipsychotic use might help some patients with these behaviours.

- Disruptive vocalisations
- Disinhibited behaviours
- Voiding inappropriately
- Emotional withdrawal
- Incontinence
- Wandering
- Racing
- Repetitive behaviours
- Insomnia

https://www.veteransmates.net.au/topic-44-therapeutic-brief

### BEST PRACTICES IN PSYCHIATRY: RECOMMENDATIONS FROM THE CHOOSING WISELY CAMPAIGN

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Sponsoring organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not prescribe antipsychotic medications for behavioral and psychological symptoms of dementia in individuals with dementia without an assessment for an underlying cause of the behavior.</td>
<td>American Medical Directors Association, American Geriatrics Society, American Psychiatric Association</td>
</tr>
<tr>
<td>Do not use antipsychotics as first choice to treat behavioral and psychological symptoms of dementia.</td>
<td>American Medical Directors Association, American Geriatrics Society, American Psychiatric Association</td>
</tr>
</tbody>
</table>

Source: For more information on the Choosing Wisely Campaign, see http://www.choosingwisely.org. For supporting clinicians and to search Choosing Wisely recommendations relevant to primary care, see http://www.aaph.org/quality/recommendations/search.htm

### SOFT: KEY RECOMMENDATIONS FOR PRACTICE

<table>
<thead>
<tr>
<th>Clinical recommendations</th>
<th>Evidence rating</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonpharmacologic interventions should be used as first-line treatment for behavioral and psychological symptoms of dementia.</td>
<td>C</td>
<td>7, 13</td>
</tr>
<tr>
<td>Before initiating antipsychotic therapy in older patients, physicians should have and document a discussion with patients and caregivers about the risks and benefits of these medications.</td>
<td>C</td>
<td>2, 13, 14</td>
</tr>
<tr>
<td>The use of antipsychotics for behavioral and psychological symptoms of dementia is associated with increased mortality.</td>
<td>A</td>
<td>23, 24</td>
</tr>
<tr>
<td>Antipsychotic medications should be discontinued if there is no evidence of symptom improvement.</td>
<td>A</td>
<td>13, 29, 30</td>
</tr>
</tbody>
</table>

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SOFT evidence rating system, go to http://www.aaph.org/quality/soft
Depression

- SSRIs
- SNRIs
- Psychostimulants
- Atypical antipsychotics
- ECT, deep brain stimulation, and TMS

Anxiety, Panic, Phobias

- Antidepressants (SSRIs, SNRIs)
- Benzodiazepines
### Mania

- Mood stabilizers (anticonvulsants)

### Agitation: Identify Cause(s)

- Cognitive decline
- Depression
- Manic behavior
- Disinhibited behavior
- Anxiety, Panic, Phobia
- Psychosis

### Sleep Disturbance

- Good sleep hygiene
- Nighttime sleep aids (ambien, trazadone and melatonin)
### Wandering
- Provide daytime exercise and outdoor time
- Place a dark tape across the floor of the entrance to an area that is restricted. Door locks and security systems

### Sexual Disinhibition
- Inappropriate sexual behavior (ISB)
- Cimetidine
- sertaline + medroxyprogesterone acetate + lupron
- Estrogen patch

### Sundowning
- Selective Serotonin Reuptake Inhibitors
- Mood Stabilizers
- Benzodiazepines
- Antipsychotics
SUMMARY (1 of 2)

- The need to express basic needs such as hunger, thirst, or fatigue, which the patient cannot adequately communicate in dementia, may precipitate a behavioral disturbance
- Delirium secondary to an underlying condition such as dehydration, urinary tract infection, or medication toxicity is a common cause of abrupt behavioral disturbances in patients with dementia

SUMMARY (2 of 2)

- Medication effects on behavioral disturbances in dementia tend to be modest and should be implemented only after trying environmental and other nonpharmacologic techniques
- Antipsychotic medications may reduce agitation, and antidepressants may be helpful if symptoms of depression are evident in the patient with a behavioral disturbance

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (1 of 3)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Daily Dose</th>
<th>Uses</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>10–20mg max dose</td>
<td>Depression, anxiety (off-label)</td>
<td>GI upset, nausea, insomnia, risk of QT prolongation with doses &gt;20 mg</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>5–20 mg</td>
<td>Depression, anxiety</td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>10–40 mg</td>
<td>Depression, anxiety</td>
<td>Long half-life, greater inhibition of the cytochrome P-450 system</td>
</tr>
</tbody>
</table>
### SELECTIVE SEROTONIN REUPTAKE INHIBITORS (2 of 3)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Daily Dose</th>
<th>Uses</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxetine</td>
<td>10–40 mg</td>
<td>Depression, anxiety</td>
<td>Greater inhibition of cytochrome P-450 system, some anticholinergic effects</td>
</tr>
<tr>
<td>Sertraline</td>
<td>25-100 mg</td>
<td>Depression, anxiety</td>
<td></td>
</tr>
<tr>
<td>Vilazodone</td>
<td>10-40 mg</td>
<td>Depression, anxiety</td>
<td>Take with food, dose adjust in severe hepatic disease, reduce dose if given with CYP3A4 inhibitors</td>
</tr>
</tbody>
</table>

### SELECTIVE SEROTONIN REUPTAKE INHIBITORS (3 of 3)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Daily Dose</th>
<th>Uses</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vortioxetine</td>
<td>5-10 mg</td>
<td>Depression</td>
<td>Nausea, dizziness, fewer sexual adverse events than other SSRIs</td>
</tr>
</tbody>
</table>

### SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Daily Dose</th>
<th>Uses</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desvenlafaxine</td>
<td>25–50 mg</td>
<td>Depression, fibromyalgia</td>
<td>Nausea, hypertension, dry mouth, dizziness, headaches</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>20–60 mg</td>
<td>Depression, diabetic neuropathy</td>
<td>Nausea, dry mouth, dizziness, hypertension</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>7.5–30 mg</td>
<td>Useful for depression with insomnia and weight loss</td>
<td>Sedation, hypotension, potential for neutropenia</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>25–150 mg</td>
<td>Useful in severe depression, anxiety</td>
<td>Hypertension, insomnia</td>
</tr>
</tbody>
</table>
TRICYCLIC ANTIDEPRESSANTS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Daily Dose</th>
<th>Uses</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desipramine</td>
<td>10–100 mg</td>
<td>Severe depression, anxiety, high degree of efficacy</td>
<td>Anticholinergic effects, hypotension, sedation, cardiac arrhythmias</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>10–75 mg</td>
<td>High efficacy for depression if side effects are tolerable; therapeutic level 50–150 ng/dL.</td>
<td>Anticholinergic effects, hypotension, sedation, cardiac arrhythmias, caution with glaucoma</td>
</tr>
</tbody>
</table>

OTHER DRUGS TO TREAT DEPRESSIVE FEATURES

<table>
<thead>
<tr>
<th>Medication</th>
<th>Daily Dose</th>
<th>Uses</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>75–225 mg</td>
<td>More activating, lack of cardiac effects</td>
<td>Irritability, insomnia</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100–300 mg</td>
<td>Anxiety (off-label), insomnia (off-label)</td>
<td>Sedation, falls, hypotension</td>
</tr>
<tr>
<td>Trazodone</td>
<td>25–150 mg</td>
<td>When sedation is desirable</td>
<td>Sedation, falls, hypotension</td>
</tr>
</tbody>
</table>

TREATMENT OF MANIC-LIKE BEHAVIOR

- Symptoms resemble those of bipolar disorder (pressured speech, disinhibition, elevated mood, intrusiveness, hyperactivity, impulsivity, reduced sleep)
- The important distinction in the dementia patient is the frequent co-occurrence with confusional states and a tendency to have fluctuating mood (i.e., irritable or hostile as opposed to euphoric)
<table>
<thead>
<tr>
<th>Drug</th>
<th>Geriatric Dosage</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>200–1000 mg/day</td>
<td>Nausea, fatigue, ataxia, blurred vision,</td>
<td>Poor tolerability in older adults; must monitor CBC, LFTs, electrolytes</td>
</tr>
<tr>
<td></td>
<td>(therapeutic</td>
<td>hypo-natremia</td>
<td>q 2 weeks for first 2 months, then q 3 months</td>
</tr>
<tr>
<td></td>
<td>level 4–12 μg/mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>25–200 mg/day</td>
<td>Sedation, skin rash, rare Stevens-Johnson</td>
<td>Increased adverse events and interactions when used with divalproex,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>syndrome, dizziness, anemia</td>
<td>slow-dose titration required</td>
</tr>
<tr>
<td>Lithium</td>
<td>150–1000 mg/day</td>
<td>Nausea, vomiting, tremor, confusion,</td>
<td>Poor tolerability in older adults; toxicity at low serum levels; monitor</td>
</tr>
<tr>
<td></td>
<td>(therapeutic</td>
<td>leukocytosis</td>
<td>thyroid and renal function</td>
</tr>
<tr>
<td></td>
<td>level 0.5–0.8 mEq/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divalproex sodium</td>
<td>250–2000 mg/day</td>
<td>Nausea, GI upset, ataxia, sedation,</td>
<td>Monitor CBC, platelets, liver function tests at baseline and every 6</td>
</tr>
<tr>
<td></td>
<td>(therapeutic</td>
<td>hypo-natremia</td>
<td>months; better tolerated than other mood stabilizers in older adults</td>
</tr>
<tr>
<td></td>
<td>level 50–100 μg/mL)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The 4 agents in this table are approved by the FDA for the treatment of bipolar disorder but are off-label for treatment of manic-like behavior associated with dementia. Note FDA warning for increase in suicidal thoughts/behaviors with anticonvulsant agents.
TREATMENT OF DELUSIONS AND HALLUCINATIONS

- Delusions (fixed false beliefs) or hallucinations (sensory experiences without stimuli) typically require pharmacologic treatment if:
  - The patient is disturbed by these experiences
  - Experiences lead to disruptions in the patient's environment that cannot otherwise be controlled

- Clinical criteria for the diagnosis of Alzheimer's dementia with psychosis specifies the presence of delusions or hallucinations for at least 1 month, at least intermittently, and must cause distress for the patient

<table>
<thead>
<tr>
<th>ANTIPSYCHOTIC AGENTS (1 of 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Aripiprazole</td>
</tr>
<tr>
<td>Asenapine</td>
</tr>
<tr>
<td>Clozapine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ANTIPSYCHOTIC AGENTS (2 of 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Haloperidol</td>
</tr>
<tr>
<td>Iloperidone</td>
</tr>
<tr>
<td>Lurasidone</td>
</tr>
</tbody>
</table>
### ANTIPSYCHOTIC AGENTS (3 of 5)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
<th>Forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine</td>
<td>2.5–15 mg</td>
<td>Sedation, falls, gait disturbance</td>
<td>Weight gain, hyperglycemia</td>
<td>Tablet, rapidly dissolving tablet, IM injection</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>2–12 mg</td>
<td>EPS, sedation</td>
<td>1st generation agent</td>
<td>Tablet</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>1.5 – 12 mg</td>
<td>Sedation, fatigue, GI upset, EPS</td>
<td>Dose reduce in renal impairment</td>
<td>Sustained release tablet, depot IM long-acting injection</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25-200 mg</td>
<td>Sedation, hypotension</td>
<td>Ophthalmologic exam every 6 mo</td>
<td>Tablet, sustained release tablet</td>
</tr>
</tbody>
</table>

### ANTIPSYCHOTIC AGENTS (4 of 5)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
<th>Forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone</td>
<td>0.5–2 mg</td>
<td>Sedation, hypotension, EPS with doses &gt; 1 mg/day</td>
<td></td>
<td>Tablet, rapidly dissolving tablet, liquid concentrate, depot IM long-acting injection</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>40–160 mg</td>
<td>Higher risk of prolonged QTc interval</td>
<td>Little published information on use in older adults, Warning about increased QTc prolongation</td>
<td>Capsule, IM injection</td>
</tr>
</tbody>
</table>

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### Table 3. Clinical Signs of Common Adverse Effects Associated with Antipsychotic Agents

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Clinical signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergic effects</td>
<td>Blurred vision, confusion, constipation, dry mouth, urinary retention</td>
</tr>
<tr>
<td>Extrapyramidal symptoms</td>
<td>Muscle spasm, pseudoparkinsonism (bradykinesia, rigidity, tremor), tardive dyskinesia</td>
</tr>
<tr>
<td>Hyperpyrexia</td>
<td>Acne, galactorrhea, gynecomastia, hirsutism, reduced bone density</td>
</tr>
<tr>
<td>Neuroleptic malignant syndrome</td>
<td>Autonomic instability (hyperpyrexia, tachycardia, hypertonia, muscle rigidity)</td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
<td>Choreo, irreversible involuntary muscle spasm, myoclonus (usually in the residual phase), tics</td>
</tr>
</tbody>
</table>

Information from references 19 through 22.
ANTIPSYCHOTIC AGENTS (5 of 5)

• All of these medications have warnings about hyperglycemia, cerebrovascular events and increase in all-cause mortality in patients with dementia
• All of these medications are off-label for treatment of psychosis in dementia

TREATMENT OF MOOD DISTURBANCES

• Reduce aversive environmental stimuli
• Assess physical health comprehensively
• Try recreation programs and activity therapies
• Consider antidepressants for:
  ➢ Depression of 2 weeks’ duration resulting in significant distress
  ➢ Depressive symptoms lasting >2 months after initiation of behavioral interventions

CHOLINESTERASE INHIBITORS

• In patients with mild to moderate Alzheimer’s disease, donepezil or galantamine are better than placebo in reducing psychosis and behavioral disturbances
• In patients with dementia with Lewy bodies, who are sensitive to the EPS of antipsychotic agents, cholinesterase inhibitors have been reported to reduce visual hallucinations
MANAGING SLEEP DISTURBANCES

• Improve sleep hygiene (see next slides)
• Treat associated depression, suspiciousness, delusions
• If the above do not succeed, consider (off-label):
   Trazodone 25–50 mg at bedtime
   Mirtazapine 7.5–15 mg at bedtime
   Gabapentin is increasingly used for insomnia
   Zolpidem 5 mg at bedtime
   Zaleplon has been studied in older patients and also appears to be effective
   Melatonin available OTC
• Avoid benzodiazepines or antihistamines

SLEEP HYGIENE (1 of 2)

• Establish a stable routine for going to bed and awakening
• Pay attention to noise, light, and temperature
• Increase daytime activity and light exercise
• Reduce or eliminate caffeine, nicotine, alcohol
• Reduce evening fluid consumption to minimize nocturia

SLEEP HYGIENE (2 of 2)

• Give activating medications early in the day
• Control nighttime pain
• Limit daytime napping to periods of 20 to 30 minutes
• Use relaxation, stress management, and breathing techniques to promote natural sleep
INAPPROPRIATE SEXUAL BEHAVIOR

- First exclude underlying treatable causes
- Treat any underlying syndrome, such as a mania-like state
- Consider antiandrogens for men who are dangerously hypersexual or aggressive:
  - Progesterone: 5 mg/day orally; adjust dose to suppress testosterone well below normal
  - If patient responds, may treat with 10 mg IM depot progesterone weekly
  - Leuprolide acetate: 5–10 mg IM monthly is an alternative

INTERMITTENT AGGRESSION OR AGITATION

- Behavioral interventions: distraction, reminiscence, validation therapy, environmental modifications, caregiver education and support, music therapy, physical activity, or aromatherapy
- Behavior modification using positive reinforcement of desirable behavior
- Avoid physical restraints

CHOOSING WISELY*

- Don’t use antipsychotics as first choice to treat behavioral and psychological symptoms of dementia.
CASE 1 (1 of 3)

• An 86-year-old man has episodes of increasing psychosis and aggression over the past 2 months.
  ➢ Primary caregiver is his daughter, whom he verbally abuses and threatens; he has punched her on 3 occasions.
  ➢ Believes that his food is being poisoned
  ➢ Believes that his son, who lives 1,000 miles away, has been coming into their home and stealing
  ➢ Attempts at nonpharmacologic interventions have been unsuccessful

• History: moderate Alzheimer disease

CASE 1 (2 of 3)

Which one of the following is the most appropriate pharmacologic treatment for this patient?
A. Citalopram
B. Donepezil
C. Haloperidol
D. Risperidone
E. Valproic acid

CASE 1 (3 of 3)

Which one of the following is the most appropriate pharmacologic treatment for this patient?
A. Citalopram
B. Donepezil
C. Haloperidol
D. Risperidone
E. Valproic acid
CASE 2 (1 of 3)

- A 78-year-old woman has had disrupted sleep for the past month.
  - Her son says that she has difficulty falling asleep.
  - Once she does sleep, she awakens after about 4 hours.
- OTC antihistamines help her sleep, but she is groggy the following day.

- History: Lewy body dementia
- Physical examination: no findings that might contribute to insomnia

CASE 2 (2 of 3)

Which one of the following is the most appropriate initial treatment for this patient?
A. Mirtazapine
B. Ramelteon
C. Trazodone
D. Zolpidem
E. Melatonin

CASE 2 (3 of 3)

Which one of the following is the most appropriate initial treatment for this patient?
A. Mirtazapine
B. Ramelteon
C. Trazodone
D. Zolpidem
E. Melatonin
A 72-year-old man has hallucinations that cause him severe distress. The hallucinations are of Civil War soldiers and monkeys, and he fears they will attack him.

- In previous visits, no medical or pharmacologic (eg, anticholinergic agents) causes of psychosis were identified. Behavioral interventions were unsuccessful.
- During a particularly stressful episode, his family took him to the emergency department, where he was prescribed risperidone 0.25 mg twice daily.
  - He rapidly became more confused and markedly rigid.
  - Symptoms resolved after risperidone was discontinued.

- History: early Lewy body dementia

Which one of the following is the most appropriate treatment recommendation for this patient?

A. Clozapine
B. Haloperidol
C. Lorazepam
D. Quetiapine
E. Rivastigmine