ETIOLOGY AND MANAGEMENT OF AGITATION IN THE ELDERLY IN THE ACUTE CARE SETTING

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OBJECTIVES

- Formally define agitation as to have a common understanding among personnel
- Identify warning signs of agitation and relate stages of behaviors to the Behavior Activity Rating Scale (BARS)
- List potential etiologies of the acute development of agitation
- Review The ADEPT Framework for assessment and management of agitation and apply this to a patient case
- Assess nonpharmacologic treatment strategies
- Discuss when medication management for agitation is necessary and which agents are preferred

AGITATION, DEFINED

Agitation – state of motor and cognitive hyperactivity marked by inappropriate or excessive verbal or motor activity, as well as emotional excitement

Domain I – Physical / Aggressive

Domain II – Physical / Non-Aggressive

Domain III – Verbal / Aggressive

Domain IV – Verbal / Non-Aggressive

Agitation fractures the patient-provider relationship and in turn makes care for the patient more difficult and puts staff at risk

EARLY IDENTIFICATION

Warning Signs:

- Sudden Behavioral Shifts
- Changes in voice tone / inflection / cadence
- Restlessness
- Uncooperative Behavior
- Difficulty focusing or comprehending medical plans

Behavioral Activity Rating Scale (BARS)

Score	Patient Description
1	Difficult or unable to arouse
2	Asleep but responds normally to verbal or physical contact
3	Drowsy, appears sedated
4	Quiet and awake (normal level of activity)
5	Signs of overt (physical or verbal) activity, calms with re-direction/instruction
6	Extremely or continuously active, not requiring restraint
7	Violent, requires restraint

ADEPT FRAMEWORK

Developed by the American College of Emergency Physicians to serve as a guide for the care of the elderly, agitated patient

Assess – Diagnose – Evaluate
Prevent – Treat

Systematic assessment to provide a standard of care, prevent prescribing cascade and promote interdisciplinary management of agitation

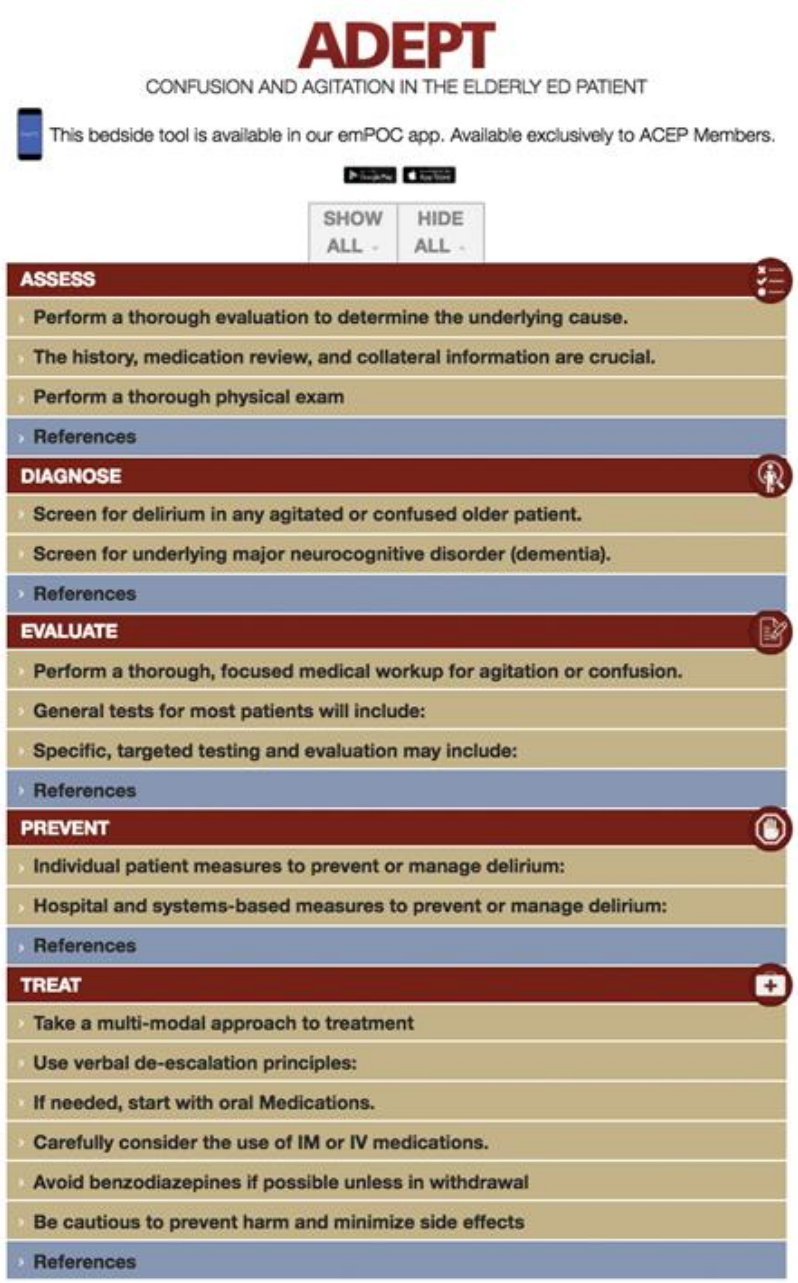


Figure 1. ADEPT tool.

ASSESS

- Determine the patient's baseline mental status if able
- Rule out life threatening conditions that could present with altered affect
  - Stroke, TIA, ICH, ACS, toxicologic causes
- Evaluate the patient for the most common causes of acute agitation in the elderly:
  - Infections
  - Neurologic Disorders
  - Metabolic/Electrolyte Disorders
  - Medication adverse effects
  - Change in Environment
  - Intoxication

DIAGNOSE

Delerium – abrupt onset with fluctuating course

- Hypoactive Delerium
- Hyperactive Delerium
- Mixed Delerium

Dementia – gradual onset, typically progressive decline

- Screen for dementia if patient is cooperative

Other Primary Psychiatric Conditions -

- Depression, BPD, schizophrenia, personality disorders

EVALUATE

- Thorough workup including objective lab parameters and subjective information from patient and/or family/caregivers
- Most patients should receive ECG, CBC, CMP, and urinalysis
  - Infectious Etiology
  - Fluid/Electrolyte status
- Patient History
  - Medication Review
  - Pain
  - Change in Environment

PREVENT

- Early identification and intervention via de-escalation strategies
- Modify environment when able, prevent overstimulation
- Provide accessibility tools (hearing aids, glasses)
- Provide opportunities for mobility, hydration, eating (if possible), having basic needs met
- Supportive care; treat pain and insomnia, prevent nausea/vomiting, provide a bowel regimen if indicated
- Reduce length of stay if possible or transfer to floor

TREAT

Non pharmacologic, acute treatment options

- Verbal deescalation
- Distraction
- Reorientation
- Reassurance

Medication Management

- Antipsychotics?
- Precedex?
- Benzodiazepines?
- Diphenhydramine?

LOW, MEDIUM, & HIGH-RISK INTERVENTIONS

Low (appropriate for all patients)

- Resume Home medications
- Environmental modification
- Verbal de-escalation
- Treat underlying conditions and symptoms

Medium (if at risk of harm to self, staff or persistent agitation)

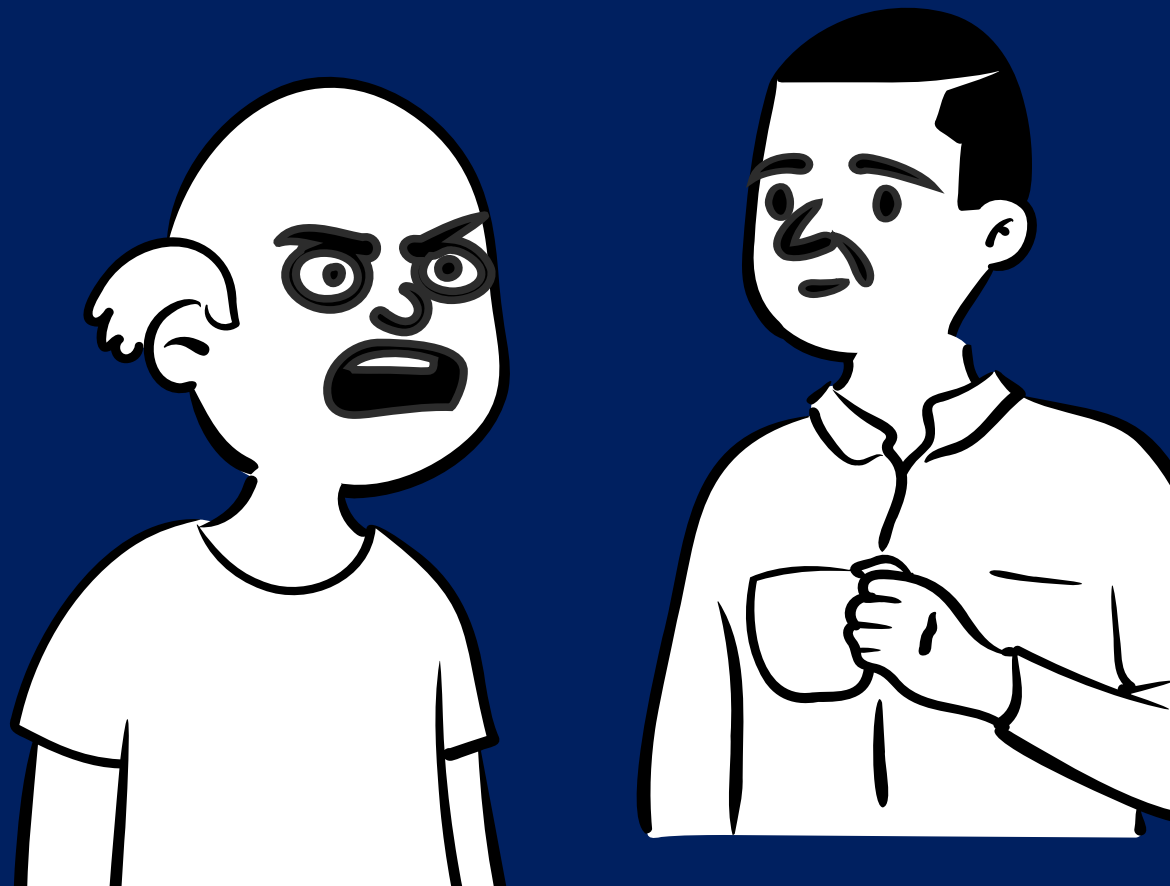
Step 1: oral medications –antipsychotics
Step 2: IM or IV medications – if not cooperative

High Risk (should be limited to severe circumstances)

Benzodiazepines – dose should be limited
Physical restraints

10 PRINCIPLES OF DE-ESCALATION

1) Respect personal space
2) Do not be provocative
3) Establish verbal contact
4) Be concise
5) Identify wants and feelings
6) Listen closely to what the patient is saying
7) Agree or agree to disagree
8) Lay down the law and set clear limits
9) Offer choices and optimism
10) Debrief the patient and staff



WHEN IS DRUG THERAPY INDICATED?

- Drug therapy in general should be approached with caution and utilized only after primary, low risk interventions are exhausted, or the patient poses a significant threat to themselves or staff

- The goal of pharmacological management is *minimal sedation* to preserve the safety of patients and staff

- Important to keep in mind that antipsychotic medications do not provide any outcome benefit in regards to length of stay, disposition, or mortality

ANTIPSYCHOTIC PEARLS

Quetiapine (PO)

- Lowest affinity for D2 receptors among atypical antipsychotics
- Sedating, orthostatic hypotension

Olanzapine (PO, ODT, IM)

- Highest anticholinergic burden among atypical antipsychotics (sedation, orthostasis)

Risperidone (PO, ODT)

- Well studied in the elderly, initial doses should be <1 mg
- Renal dosing considerations

Ziprasidone (IM)

- Highest QTc prolongation among atypical antipsychotics

Haloperidol (PO, IM)

- High potency dopamine activity; highest risk for akathisia, acute dystonia
- Greater QTC prolongation risk
- Highly anticholinergic

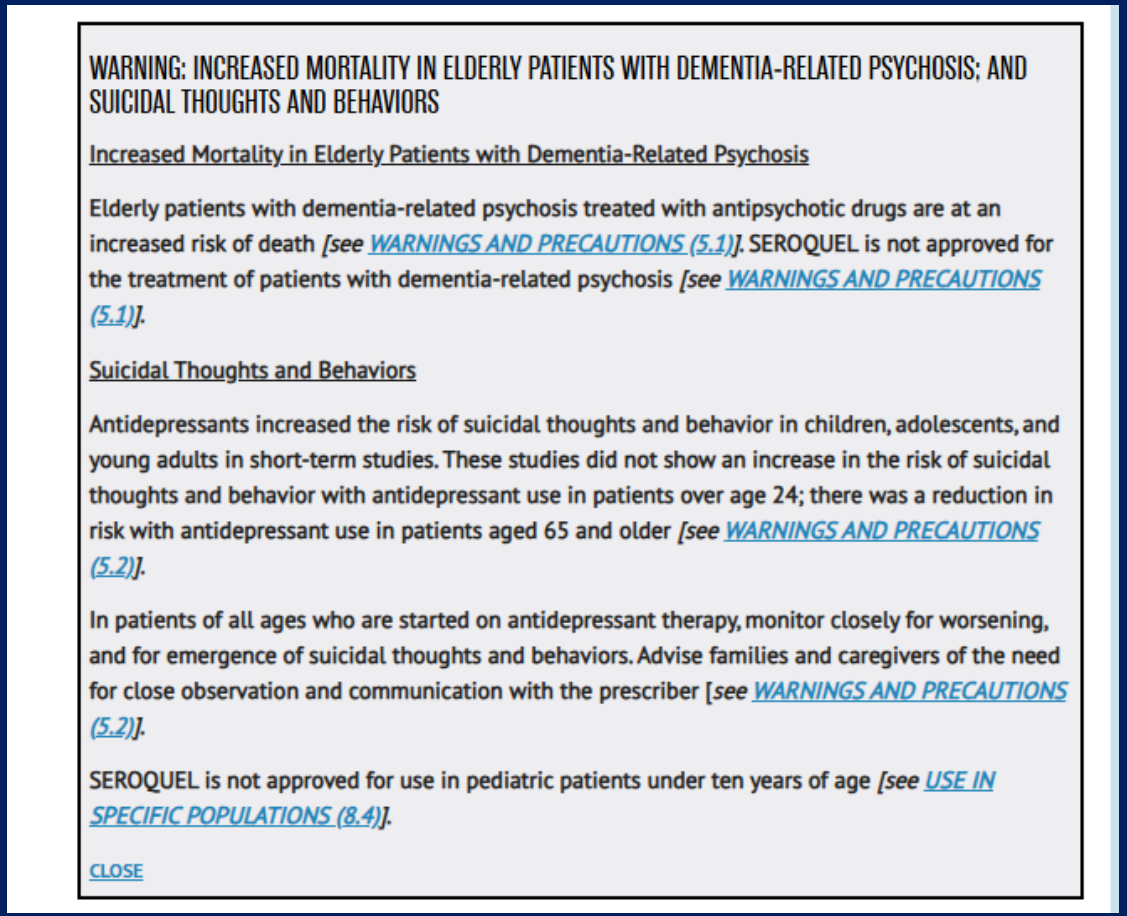
ANTIPSYCHOTIC MONITORING IN ELDERLY

Acute adverse effects:

- QTc prolongation
- Orthostasis
- Sedation

Long Term Considerations:

- Metabolic Abnormalities (Lipids, blood glucose)
- Weight Gain
- EPS risk
- Endocrine Effects



WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS; AND SUICIDAL THOUGHTS AND BEHAVIORS

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death *[see WARNINGS AND PRECAUTIONS (5.1)]*. SEROQUEL is not approved for the treatment of patients with dementia-related psychosis *[see WARNINGS AND PRECAUTIONS (5.1)]*.

Suicidal Thoughts and Behaviors

Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there was a reduction in risk with antidepressant use in patients aged 65 and older *[see WARNINGS AND PRECAUTIONS (5.2)]*.

In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber [*see WARNINGS AND PRECAUTIONS (5.2)]*.

SEROQUEL is not approved for use in pediatric patients under ten years of age *[see USE IN SPECIFIC POPULATIONS (8.4)]*.

CLOSE

DEXMEDETOMIDINE

- Central acting alpha-2 agonist – lower side effect burden
- IV Precedex has long been a preferred option in critically ill patients to achieve and maintain a light level of sedation and carry a lower risk of delirium than other sedatives
  - 4D trial for Hyperactive Delerium
- FDA Approval for SL films in treatment of agitation associated with schizophrenia or bipolar disorder, emerging evidence for use in BPSD
  - $126/dose

PHARMACOLOGIC AGENTS TO AVOID

Diphenhydramine

- Highly anticholinergic medication
  - Acutely, dry mouth, constipation, dizziness
  - Increased risk of falls, delirium, and dementia with progressive use

Benzodiazepines

- Cognitive impairment, worsened delirium, fall risk
- Long term use can lead to abuse, misuse, addiction, physical dependence
- Lorazepam and oxazepam are preferred agents in the elderly due to their minimal phase I metabolism
- Midazolam is associated with higher rates of adverse effects

PILLARS OF MEDICATION SAFETY

- Prioritize oral administration when possible
- Benzodiazepines and antipsychotic coadministration should be avoided
  - Particularly IM formulations of antipsychotics combined with benzodiazepines – olanzapine FDA warning
    - If needed, separate administration of the two by at least 1 hr and monitor closely for sedation, respiratory depression, and loss of consciousness
- Restrict use to minimum effective dose and duration
- Establish an exit strategy early in therapy

TABLE 3. Associations of formulation of antipsychotic or anxiolytic medications (Haloperidol, Olanzapine, Lorazepam) with adverse events and the need for redosing.

	Formulation	Oral	Intramuscular	Intravenous
	No. of participants	85	127	352
Any adverse events	No. of cases (%)	2 (2%)	19 (15%)	67 (19%)
	OR (95% CI)	1.00	**7.63 (1.64, 35.57)**	**10.17 (2.36, 43.79)**
Adverse respiratory events [a]	No. of cases (%)	1 (1%)	11 (9%)	27 (8%)
	OR(95% CI)	1.00	**9.49 (1.05, 85.54)**	6.59 (0.87, 50.01)
Other adverse events [b]	No. of cases (%)	1 (1%)	8 (6%)	40 (11%)
	OR (95% CI)	1.00	5.59 (0.65, 47.81)	**13.30 (1.65, 107.49)**

LONG TERM MANAGEMENT

Treatment of underlying cause hopefully should mitigate or resolve behavioral symptoms

SSRIs – particularly for concomitant depression, anxiety, panic disorders
- Evidence supporting use in behavioral and psychological signs of dementia (BPS)
- Sertraline, citalopram, and escitalopram are preferred in geriatrics
  - Minimal residual anticholinergic effects and drug interaction risks

Brexpiprazole – Alzheimer Dementia related agitation
- Generally well tolerated, caution in Parkinson's disease and Lewy body dementia

Antipsychotics – discourage routine use; reserve for refractory cases or patients with comorbid indications

APPLICATION OF ADEPT FRAMEWORK

Patient Presentation:

Mr. Harold Benson, an 82-year-old male, is brought to the ED by his daughter at 7:30 PM because of sudden agitation, pacing, yelling, and attempting to leave the house over the last 24 hours.

PMH:

- Alzheimer dementia (moderate stage)
- Hypertension
- CKD stage 3
- Osteoarthritis

Vital signs:

- BP 148/82 mmHg
- HR 102 bpm
- RR 18/min
- Temp 38.2°C (100.8°F)
- SpO_2 96% on room air

Medications

- Donepezil 10 mg daily
- Amlodipine 5 mg daily
- Ibuprofen 600 mg PRN

Clinical Course

Assess:

- Rule out: hypoxia, stroke, hypoglycemia, MI, medication toxicity
- Daughter reports no recent falls, change in affect was abrupt and started yesterday
- In conversation, patient is inattentive and has fluctuating level of engagement
- Consider: Infection? Electrolyte disturbances? Med changes?

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Clinical Course

Diagnose:

- Abrupt onset
- Fluctuating symptoms
- Altered consciousness and disorganized thinking

Likely delirium picture superimposed on existing dementia... now to evaluate how this developed

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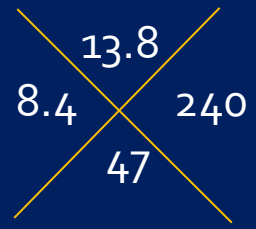
Clinical Course

Evaluate:



Physical exam shows dry mucous membranes, lungs clear to auscultation, nondistended abdomen with bowel sounds present, appears in distress

ECG shows sinus tachycardia with QTc of 430

Urinalysis negative for protein, blood, nitrates, glucose
sp gravity 1.032, dark yellow urine

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Clinical Course

Prevent:

- Quiet room
- Daughter remains at bedside
- Frequent reorientation
- Reduced noise and stimulation
- IV fluids started
- Hearing aids and glasses provided
- Staff use calm verbal de-escalation
- Consistent reassessing of needs

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Clinical Course

Meanwhile... Mr. Benson

- Has repeatedly attempted to pull out his IVs
- Continues to try to leave the treatment area and remains apprehensive with his daughter for bringing him in
- Displays high suspicion of staff
- Verbally yelled at staff during POC glucose testing and phlebotomy

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Clinical Course

Treat:

Though nonpharmacologic methods have been effective, Mr. Benson remains a danger to staff and himself. Presenting problem of dehydration/pre-renal AKI has also been addressed

Low dose, antipsychotic is indicated and Harold is amenable to taking medications by mouth

What medication choice would be appropriate?

Quetiapine? Olanzapine? Risperidone? Haldol? Lorazepam?

CONCLUSIONS

- Early identification of agitation in the elderly population is critical to promote workplace safety, patient wellbeing, and outcomes
- The ADEPT framework can be a useful tool to analyze patient scenarios and create treatment plans to aid in the treatment of acute agitation
- Nonpharmacological methods are 1st line for agitation control
- Critical thought should be used to determine whether pharmacologic therapy is necessary and as to which agent is preferred on a patient-by-patient basis
- Medication safety principles should be adhered to in the geriatric population to minimize adverse events

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Questions?