Management of Acute Agitation and Delirium in Adults

The following charts provide information to help guide pharmacotherapy for acute agitation and/or delirium, when necessary. Mild to moderate agitation may respond to verbal de-escalation or calm surroundings.[5,7] Assess oxygen saturation, glucose level, and electrolytes.[5] Consider infection as a possible cause.[5] Treat the patient with meds if the patient is a danger to themselves or others, or is not calm enough to be medically evaluated.[7] Consider oral options if the patient can cooperate and quick onset is not imperative, and intramuscular over intravenous (unless the patient already has IV access).[18,20] A toolbox offering strategies and resources for preventing and treating delirium is also provided.

Management of Acute Agitation in Adults by Clinical Scenario

Clinical Scenario	Suggested Options or Resources
Alcohol **intoxication**	• Consider an antipsychotic.[7] Try to **avoid** benzodiazepines due to risk of respiratory depression.[7] • Ketamine is an emerging option.[21] Consider it second-line.[4] • Consider alcohol withdrawal (below) instead of intoxication if a patient with a history of alcohol use has a low or undetectable alcohol level or withdrawal symptoms such as delirium, sweating, tachycardia, or tremors.[7]
Alcohol **withdrawal**	• Use a benzodiazepine first-line to control symptoms and prevent seizures from withdrawal.[28] • If the patient is cooperative, use an oral benzodiazepine (e.g., chlordiazepoxide, diazepam, lorazepam); otherwise, use a parenteral benzodiazepine (e.g., lorazepam or midazolam [faster onset]).[4,7,24] o For **oral dosing** for alcohol withdrawal, see our chart, *Outpatient Alcohol Detox and Relapse Prevention*. o For **parenteral dosing** for alcohol withdrawal, see our FAQ, *Management of Inpatient Alcohol Withdrawal*.
Delirium *Continued…*	• Treat/address underlying causes (e.g., hypoxia, hypoglycemia, infection, medications, electrolyte disturbances).[7] o Consider withdrawal from alcohol (see above), tobacco (provide nicotine replacement), or chronic meds (e.g., benzodiazepines) as potential causes.[7] o Review the patient's home med list to identify less well-known potential causes of withdrawal delirium. For example, there are published case reports of delirium in patients withdrawn from SSRIs, SNRIs, baclofen, gabapentin, pregabalin, and antipsychotics. • If neither alcohol nor benzodiazepine withdrawal is suspected, an antipsychotic is usually the drug of choice.[7] o Antipsychotics are widely used for ICU delirium, even though clinical trials have not proven benefit. This may be a function of study design, and benefit for patients with hyperactive or mixed delirium cannot be ruled out.[53] o Available data suggest the risk of adverse reactions (including QT prolongation) is relatively low with short-term use of antipsychotics in patients treated for delirium when close monitoring and dose titration are used.[53] • Dexmedetomidine is suggested for delirium in ventilated patients if agitation is interfering with weaning and extubation [Evidence level B-1][37,54] • Ketamine is an emerging option.[21] Consider it second-line.[4]

Clinical Scenario	Suggested Options or Resources
Delirium, continued	• See our toolbox below, *Preventing and Treating Delirium in Inpatients*, for more information.
Dementia	• Assess for pain or other treatable causes.[8] • Lean toward an antipsychotic vs a benzodiazepine in the elderly, due to fall risk.[10] o Risperidone has the most data in this population.[8,10] o Olanzapine is also effective for agitation.[10] o For emergency treatment of delirium or aggression, haloperidol is another option.[10] o For agitation in patients with Parkinson's disease or Lewy body dementia, quetiapine is the preferred antipsychotic.[18] • Warnings about excess mortality associated with the use of antipsychotics in patients with dementia are based on studies of several weeks' duration.[8] Harm may come to the patient or others from withholding antipsychotics in an acute situation.[8]
Psychosis or Mania	• If the patient is cooperative, use an **oral** antipsychotic (e.g., risperidone, olanzapine).[4,7] o Orally disintegrating tablets do NOT have an advantage over PO tablets unless the patient has trouble swallowing.[26] • Parenteral antipsychotic options include droperidol, olanzapine, aripiprazole, or haloperidol.[6,30,42] • Consider adding a benzodiazepine (e.g., lorazepam 1 to 2 mg, midazolam [faster onset]):[4,7,26] o for more rapid effect.[3] o if the response to the initial dose of antipsychotic is insufficient (giving a benzodiazepine is preferred to repeating the antipsychotic dose).[26] o **Note**: use of parenteral olanzapine with parenteral benzodiazepines is not recommended in labeling, but see "Olanzapine" row below for additional information.[12] • Dexmedetomidine sublingual film is an emerging option for patients with agitation due to schizophrenia or bipolar disorder. See "Dexmedetomidine" row below for additional information.
Stimulant intoxication (e.g., methamphetamine)	• Generally use a benzodiazepine first-line.[7] o For psychotic symptoms, consider an atypical antipsychotic.[7] • Ketamine is an emerging option.[21] Consider it second-line.[4]
Traumatic brain injury	• Evidence is limited.[41] • Consider olanzapine, o Avoid haloperidol; may impede neurologic recovery.[41] • Benzodiazepines are commonly used, except in cases of alcohol or benzodiazepine withdrawal, but some evidence suggests that they might impede neurologic recovery, and increase length of stay and duration of amnesia.[41]

Clinical Scenario	Suggested Options or Resources
Unknown cause	• **With psychotic symptoms** (see above): o Antipsychotic (PO if cooperative).[7] o Add a benzodiazepine (oral or parenteral) if the antipsychotic is not effective.[7] • Lorazepam or midazolam (faster onset).[4] • **Without psychotic symptoms**: o Consider a benzodiazepine if alcohol withdrawal is suspected (see above).[7] • Ketamine is an emerging option.[13] Consider it second-line.[4]

-Continue to the next page for a Comparison of Therapeutic Options for Acute Agitation in Adults-

Comparison of Therapeutic Options for Acute Agitation in Adults

Drug	Administration Tips/Comments
Dexmedetomidine, sublingual	• Consider a **sublingual** or **buccal** dose of 120 mcg (film) for mild or moderate agitation, or 180 mcg (film) for severe agitation, in adults with schizophrenia or bipolar disorder.[11] Two additional half doses may be given, 2 hours apart.[11] Max total dose in 24 hours is 240 mcg (mild to moderate agitation) or 360 mcg (severe agitation).[11] • Only use the 120 mcg dose for patients 65 years or older. Dose should be reduced in liver impairment.[36] • **Efficacy**: o May start to act as early as 20 minutes but take up to 2 hours for full effect.[38] o Has not been compared to other agents and was only studied in cooperative patients with mild to moderate agitation.[36,38,40] • **Safety**: o Adverse effects include bradycardia, QT prolongation, hypotension, dizziness, somnolence, and oral paresthesia or numbness.[36] o Avoid in patients at risk for torsades de pointes (e.g., baseline QT prolongation, use of other QT-prolonging drugs).[36]
Droperidol	• **Efficacy**: o Onset similar to olanzapine (e.g., median time to sedation <15 minutes).[19,14,25,39] May require fewer repeat doses or additional agents than olanzapine.[39] o May be more effective than haloperidol or ziprasidone.[16,19,20] • **Safety**: o May pose lower risk of side effects than midazolam or ziprasidone.[7,20] o Associated with shorter length of stay vs olanzapine or haloperidol, perhaps due to its shorter duration of action.[16] o Olanzapine may be the safer choice if the patient has QT prolongation risks (e.g., bradycardia, other QT-prolonging meds), or there is concern for extrapyramidal side effects.[29] o Some experts would avoid droperidol in the elderly due to paucity of data in this population.[18]
Haloperidol *Continued…*	• If the patient is cooperative, use **PO** haloperidol 5 mg.[7] May repeat in 15 minutes.[7] • If parenteral dosing is needed, consider starting with 5 mg **IM**.[7] Single doses higher than 7.5 mg to 10 mg are not more effective for most patients and may have more side effects.[6] May repeat in 15 minutes.[7] • Can give **IV** (off-label) if access is available and benefits of rapid sedation outweigh risks. If given IV, start with 1 to 2 mg. May repeat in 15 minutes.[11] Push over several minutes to decrease the risk of side effects (e.g., hypotension, arrhythmias, movement disorders).[11] Continuous ECG monitoring recommended.[11] • Most patients respond to one to three doses.[3] Maximum total dose in 24 hours is 20 mg PO/IM (5 to 10 mg IV).[7]

Drug	Administration Tips/Comments
Haloperidol, continued	• **Efficacy**: o May take longer to work (~20 minutes) than midazolam, olanzapine, or droperidol (e.g., mean/median time to sedation >20 minutes [Evidence level B-3].[16,17,19,24] • **Safety**: o Avoid in patients at risk for torsades de pointes (e.g., baseline QT prolongation, use of other QT-prolonging drugs).[1,7] Risk is highest with IV administration.[7] o Higher risk of akathisia, dystonia, or parkinsonism than olanzapine, risperidone, or ziprasidone.[7] o Do NOT use the extended-release IM injection (haloperidol decanoate).
Ketamine	• Ketamine (e.g., 4 to 5 mg/kg IM [maximum 500 mg/dose] or 1 mg/kg IV) is emerging as an option:[13,21] o to get combative adults under control quickly [Evidence level B-1].[13,21] o when antipsychotics and/or benzodiazepines fail.[4] • **Efficacy**: o May work in as little as five minutes, but relatively short duration of action may require redosing or the addition of a second agent.[24] • **Safety**: o Risks include tachycardia, hypertension, emergence reactions requiring benzodiazepines, laryngospasm, hypersalivation, vomiting, and respiratory depression requiring intubation.[4] o Concern for worsening psychosis.[4] Little data in patients with schizophrenia.[13,24] o Some experts suggest avoiding in the elderly due to paucity of data in this population, and risk of worsening agitation.[18]
Midazolam	• Consider midazolam 2.5 to 5 mg IM or IV, alone or with droperidol, to get agitated adult patients under control quickly (e.g., <10 minutes).[14,17,18,22] • **Efficacy**: o May work faster than IM antipsychotics (haloperidol, olanzapine, ziprasidone) [Evidence level B-3],[17,22] but may require repeat dosing due to shorter duration of action.[16] o May work almost 15 minutes faster than IM lorazepam.[35] • **Safety**: o Increased risk of respiratory depression requiring airway management vs droperidol.[32.] o May be safer than haloperidol in regard to cardiovascular or extrapyramidal adverse effects.[17] o Risk of paradoxical excitation in elderly.[18]

Drug	Administration Tips/Comments
Olanzapine	• If patient is cooperative, use **PO** olanzapine 5 to 10 mg. May repeat in 2 hours. Maximum total dose in 24 hours is 20 mg.[7] An orally disintegrating tablet is available. • **IM** dose is 10 mg. May repeat in 20 minutes. Maximum total dose in 24 hours is 30 mg.[7] Do NOT use the extended-release IM injection (*Zyprexa Relprevv*). • Can give **IV** (off-label) if access is available and benefits of rapid sedation outweigh risks. May be as effective as droperidol.[23] Consider a conservative starting dose of 2.5 to 5 mg IV. May repeat in five minutes [Evidence level B-3 and B-1].[2,14] A dose of 10 mg, followed by a dose of 5 mg after five minutes if needed, has been studied.[14] • Requires reconstitution.[12] • **Efficacy**: o Time to sedation similar to droperidol (i.e., median time to sedation <15 minutes) [Evidence level B-1].[14] o More effective than haloperidol [Evidence level B-3].[19] • **Safety**: o Some experts recommend monitoring for **respiratory depression** for at least an hour after use, especially in cases of alcohol intoxication.[2] o Use of parenteral olanzapine with parenteral benzodiazepines is not recommended in the product labeling due to risk of excessive sedation and cardiorespiratory depression based on post-marketing reports.[12,33] However, other data suggests that olanzapine may not be riskier than other antipsychotics in regard to respiratory depression.[22,31,33] o Do NOT use the extended-release IM injection (*Zyprexa Relprevv* [US]).[12]
Quetiapine	• Often used for ICU delirium and preferred for patients with Parkinson's disease or Lewy body dementia.[18,53] • For patients with Parkinson's disease or Lewy body dementia, consider a dose of 12.5 mg to 25 mg.[18] • Consider starting with 50 mg twice daily (12.5 to 50 mg per day in elderly).[44]
Risperidone	• Initial dose is 2 mg (oral; 0.5 to 1 mg in elderly).[7,18] May repeat in 2 hours. Maximum total dose in 24 hours is 6 mg.[7] • An orally disintegrating tablet is available.
Ziprasidone	• No advantage over other options. • Initial dose is 10 to 20 mg IM. May repeat every two hours (10 mg) or four hours (20 mg). Maximum total dose in 24 hours is 40 mg.[15] • Appears to pose a relatively high risk of QT prolongation.[15] Avoid in patients at risk of torsades de pointes.[1] • May take three to five minutes to reconstutite.[27] Can store reconstituted solution for up to seven days in the refrigerator, or 24 hours at room temperature if protected from light.[15] • A hazardous drug (i.e., requires special handling in people of childbearing potential due to reproductive risk).[12,34] • Relatively expensive.

-Continue to the next page for a toolbox for Preventing and Treating Delirium in Adults-

Preventing and Treating Delirium in Inpatients

Goal	Suggested Strategies or Resources
Identify patients at high risk of delirium.	• Risk factors can be categorized as predisposing factors or precipitating factors.[9] The more predisposing factors a patient has, the more susceptible they are to precipitating factors.[9] o Predisposing risk factors include:[1,9] • Age ≥65 years • Dementia or cognitive impairment (or history of) • Functional impairment, poor vision, or poor hearing • Depressive symptoms • Laboratory abnormalities • Alcohol abuse • Multiple comorbidities • Precipitating risk factors include:[9] • Medications (e.g., sedatives, anticholinergics) • Surgery, anesthesia (especially hip fracture repair or heart surgery) • Pain • Anemia, • Infection • Acute illness or acute exacerbation of chronic illness • Risk factors with the strongest association for delirium in ICU patients are:[37] o benzodiazepine use o blood transfusion o advanced age o dementia o history of coma o more severe illness (e.g., pre-ICU emergency surgery or trauma, high APACHE score)
Review medications and make recommendations to reduce the risk of delirium. *Continued…*	• Attempt to reduce the use of medications, especially psychoactive medications and others associated with delirium (e.g., anticholinergics, benzodiazepines, and opioids).[1,9,43] o See our chart, *Drugs with Anticholinergic Activity*, for help identifying anticholinergic medications. o Try to discontinue a medication any time a new long-term medication is started.[45] • If needed, use the lowest effective dose of medications that could cause delirium.[44] • Ensure sedatives are used for a specific indication, targeting a light level of sedation.[37]

Goal	Suggested Strategies or Resources
Review medications and make recommendations to reduce the risk of delirium, continued	○ When appropriate, consider dexmedetomidine (*Precedex*) or propofol over benzodiazepines for sedation in mechanically ventilated pateints.[37] (This recommendation does not apply to benzodiazepines for patients with delirium associated with alcohol withdrawal.[46]) ○ See our chart, *Meds for ICU Analgesia and Sedation*, for more information on choosing and safely using sedatives. • Recommend regimens for pain control when needed, using a multi-modal approach incorporating nonpharmacological interventions, non-opioid analgesics, regional anesthesia if appropriate, and the lowest effective doses of opioids if they are necessary.[37] ○ See our chart, *Meds for ICU Analgesia and Sedation*, for more information on choosing and safely using analgesics. • Look for meds that may cause constipation or dehydration. Recommend an effective bowel regimen and hydration such as IV fluids as appropriate.[1] • Schedule medication administration to prevent disturbing a normal sleep-wake cycle, if possible.[1] • Avoid starting medications such as antipsychotics, melatonin, or ramelteon for prophylaxis of delirium due to a lack of evidence for the practice.[37,47] Cholinesterase inhibitors may be harmful.[53]
Use non-drug measures to prevent delirium.	• Implement non-drug preventive measures, such as:[37] ○ providing patients with visible clocks ○ making sure patients' glasses and/or hearing aids are accessible ○ encourage mobility (e.g., physical therapy) ○ supporting a normal sleep-wake cycle (avoid nursing care interventions during sleeping hours; control light, noise and activity to mimic normal day/night schedule) • Use of the ABCDEF bundle (e.g., optimizing pain control, minimizing sedative use, early mobility, etc) in ICU patients is associated with less delirium.[37]
Watch for symptoms and screen regularly using a validated tool. *Continued…*	• Symptoms of delirium include:[48] ○ reduced clarity of awareness of the environment, with a reduced ability to focus, sustain, or shift attention, that may present as lethargy or distractibility ○ a change in cognition such as memory deficit, disorientation, or speech disturbance, or a perceptual disturbance (e.g., hallucinations) • There are three types of delirium:[48] ○ Hyperactive delirium: with restlessness, agitation, hallucinations, behavioral disturbances ○ Hypoactive delirium: with lethargy, reduced motor activity, unintelligible speech, and lack of interest ○ Mixed • The onset of symptoms is typically acute (i.e., hours to days).[48] Delirium has been described as "acute brain failure."[9] • The course of symptoms is typically fluctuating.[48] • Use a validated tool regularly (e.g., once per shift) to assess for delirium.[37]

Goal	Suggested Strategies or Resources
Watch for symptoms and screen regularly, continued	○ A quick screening tool such as MOTYB (ask the patient to recite the months of the year backward, and consider "passing" the test as making it to July without an error) may be used in general medical patients to trigger further assessment.[49,50] ○ Screening tools for ICU patients include the Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC), available at https://www.icudelirium.org/medical-professionals/delirium/monitoring-delirium-in-the-icu. ○ Tools for non-ICU patients (e.g., Delirium Triage Screen [DTS]) are available at https://www.icudelirium.org/medical-professionals/adult-non-icu-care-monitoring-delirium. ○ Healthcare professionals should receive initial and ongoing training on use of these tools.[51] Materials to help train healthcare professionals to administer the tests are available on these sites. • Consider assessing ICU patients at least once every nursing shift (e.g., every eight to 12 hours), or when patient's clinical condition changes.[52]
Recommend drug treatment for delirium when needed.	• For agitation, see our chart, *Management of Acute Agitation in Adults by Clinical Scenario*, above. • Consider use of the Richmond-Agitation Sedation Scale to help guide treatment (https://www.mdcalc.com/richmond-agitation-sedation-scale-rass) to identify patients who are agitated or combative.
Discontinue drug treatment for delirium as appropriate.	• Medications to treat delirium are typically needed for one week or less.[1] • Consider stopping drug treatment (tapering if necessary) once symptoms are controlled.[44,51] • Evaluate the need for continuing antipsychotics daily.[51] About 20% of patients who start an antipsychotic medication for delirium during an ICU stay continue on the drug after discharge from the hospital.[55] Continuing antipsychotics unnecessarily can increase the risk of drug side effects and increase costs.[37]
Consult resources for updated information on the prevention and treatment of delirium.	• **American Delirium Society** (https://www.americandeliriumsociety.org/) • **ICU Delirium and Cognitive Impairment Study Group** (http://www.icudelirium.org) • **Canadian Coalition for Seniors' Mental Health** (https://ccsmh.ca/) • **American Geriatrics Society** (https://www.americangeriatrics.org/) • **Society of Critical Care Medicine** (https://www.sccm.org/Home)

Abbreviations: ECG = electrocardiogram; ICU = intensive care unit; IM = intramuscular; IV = intravenous; PO = oral; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004 Feb 1;69(3):548-56.
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