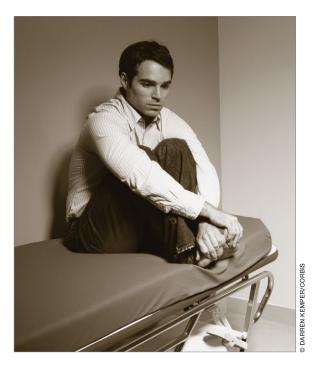




Dr. Brown talks about treatment options for acute psychosis

How to stabilize an acutely psychotic patient



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In psychiatric emergencies, use a stepwise approach to provide safe, effective treatment

cute psychosis is a symptom that can be caused by many psychiatric and medical conditions. Psychotic patients might be unable to provide a history or participate in treatment if they are agitated, hostile, or violent. An appropriate workup may reveal the etiology of the psychosis; secondary causes, such as medical illness and substance use, are prevalent in the emergency room (ER) setting. If the patient has an underlying primary psychotic disorder, such as schizophrenia or mania, illness-specific intervention will help acutely and long-term. With agitated and uncooperative psychotic patients, clinicians often have to intervene quickly to ensure the safety of the patient and those nearby.

This article focuses on the initial evaluation and treatment of psychotic patients in the ER, either by a psychiatric emergency service or a psychiatric consultant. This process can be broken down into:

- triage or initial clinical assessment
- initial psychiatric stabilization, including pharmacologic interventions and agitation management
- · diagnostic workup to evaluate medical and psychiatric conditions
- further psychiatric evaluation
- determining safe disposition.1

Triage determines the next step

Initial clinical assessment and triage are necessary to select the appropriate immediate intervention. When a patient arrives in the ER, determine if he or she requires urgent medical attention. Basic initial screening should include:

vital signs

- finger stick blood glucose
- medical history
- signs or symptoms of intoxication or withdrawal
- signs of trauma (eg, neck ligature marks, gunshot wounds, lacerations)
- asking the patient to give a brief history leading up to the current presentation.

A review of medical records may reveal patients' medical and psychiatric history and allergies. Collateral documentationsuch as ambulance run sheets or police reports-may provide additional information. If no immediate medical intervention is warranted, determine if the patient can wait in an open, unlocked waiting area or if he or she needs to be in an unlocked area with a sitter, a locked open area, or a secluded room with access to restraints. In general, psychotic patients who pose a threat of harm to themselves or others or cannot care for themselves because of their psychosis need locked areas or observation.

Initial psychiatric stabilization

Agitation is diagnostically unspecific but can occur in patients with psychosis. Psychotic patients can become unpredictably and impulsively aggressive and assaultive. Rapid intervention is necessary to minimize risk of bodily harm to the patient and those around the patient. Physicians often must make quick interventions based on limited clinical information. It is important to recognize early signs and symptoms of agitation, including:

- restlessness (pacing, fidgeting, hand wringing, fist clenching, posturing)
- irritability
- · decreased attention
- inappropriate or hostile behaviors.²

Pharmacologic interventions. The initial goals of pharmacologic treatment are to calm the patient without oversedation, thereby allowing the patient to take part in his or her care and begin treatment for the primary psychotic illness.3,4 Offering oral medications first and a choice of medications may help a patient feel more in control of the situation. If a patient has to be physically restrained,

pharmacotherapy may limit the amount of time spent in restraints.

Medication choice depends on several factors, including onset of action, available formulation (eg, IM, liquid, rapidly dissolving), the patient's previous medication response, side effect profile, allergies or adverse reactions to medications, and medical comorbidities.3 If a patient has a known psychotic illness, it may be helpful to administer the patient's regular antipsychotic or anxiolytic medication. Some medications, such as lithium, are not effective in the acute setting and should be avoided. Additionally, benzodiazepines other than lorazepam or midazolam should not be administered IM because of erratic absorption.

Antipsychotics can be used for psychotic patients with or without agitation. Benzodiazepines may treat agitation, but are not specific for psychosis. Haloperidol can be used to treat acute psychosis and has proven efficacy for agitation. Benzodiazepines can decrease acute agitation and have efficacy similar to haloperidol, but with more sedation.⁵ A combination of lorazepam and haloperidol is thought to be superior to either medication alone.6 Lorazepam helps maintain sedation and decreases potential side effects caused by haloperidol. Consensus guidelines from 2001 and 2005 recommend combined haloperidol and lorazepam for first-line treatment of acute agitation.3,7 High-potency antipsychotics such as haloperidol have an increased risk for extrapyramidal symptoms (EPS), particularly acute dystonic reactions-involuntary, sustained muscle contractions—in susceptible patients (eg, antipsychotic-naïve patients); consider starting diphenhydramine, 25 to 50 mg, or benztropine, 0.5 to 2 mg, to prevent EPS from high-potency antipsychotics (Algorithm 1, page 12).

Second-generation antipsychotics (SGAs) increasingly have been used for managing acute agitation in patients with an underlying psychotic disorder. Guidelines from a 2012 American Association for Emergency Psychiatry workgroup recommend using an SGA as monotherapy or in combination with another medication instead of haloperidol to treat agitated patients with a known psychotic disorder.8 Clinical pol-



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Clinical Point

Early signs of agitation include restlessness, irritability, decreased attention, and inappropriate or hostile behaviors





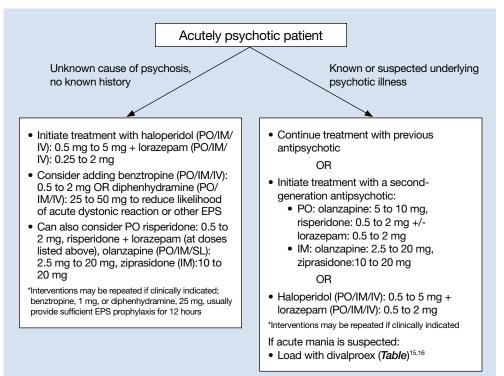
Acute psychosis

Clinical Point

IM ziprasidone and olanzapine have a relatively rapid onset of action, which makes them reasonable choices in the acute setting

Algorithm 1

Treating acute psychosis: Choosing pharmacologic agents



EPS: extrapyramidal symptoms; PO: by mouth; SL: sublingual

icy guidelines from the American College of Emergency Physicians recommend antipsychotic monotherapy for agitation and initial treatment in patients with a known psychiatric illness for which antipsychotic treatment is indicated (eg, schizophrenia).9 For patients with known psychotic illness, expert opinion recommends oral risperidone or olanzapine.^{3,8} The combination of oral risperidone plus lorazepam may be as effective as the IM haloperidol and IM lorazepam combination.¹⁰ Patients who are too agitated to take oral doses may require parenteral medications. Ziprasidone, olanzapine, and aripiprazole are available in IM formulations. Ziprasidone, 20 mg IM, is well tolerated and has been shown to be effective in decreasing acute agitation symptoms in patients with psychotic disorders.¹¹ Olanzapine is as effective as haloperidol in decreasing agitation in patients with schizophrenia, with lower rates of EPS.¹² In a double-blind, placebo-controlled trial, psychotic symptoms in patients with schizophrenia or schizoaffective disorder decreased within 2 hours of IM olanzapine administration.¹³ Both IM ziprasidone and olanzapine have a relatively rapid onset of action (within 30 minutes), which makes them reasonable choices in the acute setting. Olanzapine has a long half-life (21 to 50 hours); therefore, patients' comorbid medical conditions, such as cardiac abnormalities or hypotension, must be considered. If parenteral medication is required, IM olanzapine or IM ziprasidone is recommended.8 IM haloperidol with a benzodiazepine also can be considered.3

Coadministration of parenteral olanzapine and a benzodiazepine can lead to severe orthostatic hypotension and cardiac or respiratory depression and should be avoided in geriatric patients.¹⁴ Finally, it is important to rule out presentations that may worsen with antipsychotic treatment, including phencyclidine (PCP) toxicity (could worsen dystonic reactions), anticholinergic delirium, neuroleptic malignant syndrome (NMS), or catatonia.



Divalproex dosing for patients with acute psychosis and mania

	Initial dose	Titration
Acute mania ¹⁵	Divalproex delayed-release: 750 mg/d Divalproex extended-release: 20 mg/kg/d	Increase to clinical effectiveness or maximum serum level of 125 µg/mL
Exacerbation of psychosis ¹⁶	Divalproex: 15 mg/kg/d (in 2 doses)	Increase to clinical effectiveness over 12 days or maximum dosage of 30 mg/kg/d

If a patient does not respond to the initial dose of a medication, the dose may be repeated. However, doses should not be repeated until a patient is so sedated that he or she cannot take part in his or her care, or until he or she has developed significant EPS.

In addition to antipsychotics, consider loading with oral divalproex for patients who are acutely psychotic in the context of a manic episode (Table). 15,16 Higher serum divalproex levels—target serum levels >94 µg/mL—are associated with greater efficacy as measured by change from baseline in Mania Rating Scale or Young Mania Rating Scale scores compared with placebo.¹⁵ For acutely psychotic schizophrenia patients, there is evidence of benefit with initial treatment with divalproex combined with an SGA. In a randomized, double-blind study, patients treated with divalproex plus olanzapine or risperidone showed quicker initial resolution of psychotic symptoms compared with olanzapine or risperidone monotherapy, but no better long-term benefit.16 Clinicians may consider this welltolerated combination after an appropriate medical workup. This finding of early benefit was not replicated with divalproex extended-release.17

Side effects and adverse reactions.

Treatment with antipsychotics may cause QTc interval prolongation, which can lead to increased risk for torsades de pointes and sudden death due to ventricular fibrillation. However, there have been few cases of torsades de pointes after oral haloperidol and none with IM haloperidol compared with at least 30 cases of torsades de pointes after IV haloperidol treatment. Torsades de pointes after risperidone, olanzapine, or ziprasidone treatment has not been reported.18

Hypotension and bradycardia may occur in patients treated with olanzapine; however, these signs occur less frequently in agitated patients.18 Antipsychotic treatment increases risk for EPS, including acute dystonia, akathisia (subjective restlessness with desire to move), and parkinsonism (shuffling gait, resting tremor, rigidity and bradykinesia), as well as NMS.

Nonpharmacologic interventions. Verbal intervention to try to de-escalate an agitated, psychotic patient should be attempted first; however, this is not always possible. Other behavioral interventions include offering a meal, blanket, or pillow, or other comforting options to decrease the patient's anxiety associated with psychosis.2 However, if agitated psychotic patients continue to display aggressive behaviors and pose a risk of harm to themselves or those around them, physical restraints should be considered because the clinician must balance protecting the patient's rights with others' safety. If physical restraints are used, medication also should be administered. Remove physical restraints as soon as safely possible; the Joint Commission has established standards for minimizing harm when using physical restraints.19

Diagnostic workup

Once a patient is medically stable in the ER, begin further workup of the etiology of the psychosis (Algorithm 2, page 14). All patients should have a physical exam, provided they are calm and in behavioral control. Monitor vital signs; patients at risk of withdrawal from substances should be monitored more frequently. Although there is no established standard for "medical clearance" of a psy-



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Clinical Point

Verbal de-escalation should be attempted first; other interventions include offering a meal or blanket to decrease the patient's anxiety



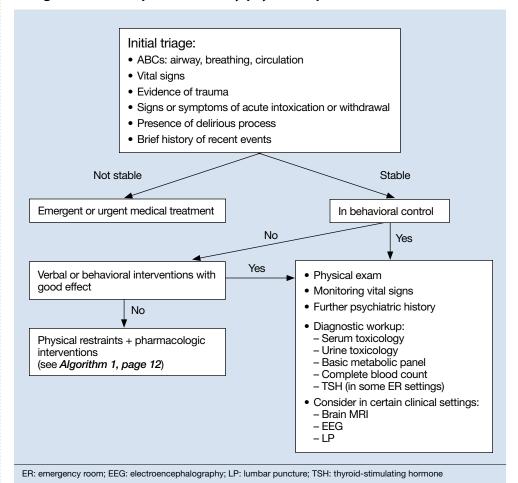
Acute psychosis

Clinical Point

Psychosis in a delirious patient may be characterized by poorly formed delusions and visual hallucinations

Algorithm 2

Diagnostic workup of an acutely psychotic patient



chiatric patient,20 all patients should undergo basic laboratory tests, including basic metabolic panel, complete blood count, and urine toxicology. The extent of the workup is determined by the clinical situation and suspected cause of psychosis.21

If you suspect delirium, the underlying medical etiology must be identified and treated. Up to 40% of hospitalized patients with delirium may have psychosis.²² Psychosis in a delirious patient may be characterized by poorly formed delusions and visual hallucinations. Delirious patients often are inattentive, easily distracted, and disoriented, with a fluctuating clinical course. Patients with psychosis generally do not have impaired attention and are alert with intact memory. However, acutely psychotic patients may be quite disorganized and uncooperative, which makes it difficult to distinguish between these 2 diagnoses. Serial exams may help clarify the clinical picture. It is important to remember that patients with a history of a psychotic disorder may have a superimposed delirium.

In young patients (age 18 to 30) with newonset psychosis, consider drug-induced psychosis; PCP, lysergic acid diethylamide, and methamphetamine intoxication and withdrawal can lead to psychotic presentations. Additionally, comorbid substance use is common among patients with primary psychotic disorders. One study found 37% of first-episode psychotic patients misused drugs or alcohol, similar to the lifetime rate of patients with chronic psychotic disorders.23,24 Check urine and serum toxicology screens and obtain relevant substance use history. Brain MRI may be considered for patients with first presentation of psychosis;

however, there is little evidence to support head CT imaging unless there is known head trauma.²⁵ Electroencephalography and lumbar puncture can be considered if clinically indicated.

Further psychiatric evaluation

Obtaining a psychiatric history is necessary to determine the etiology of the acute psychotic presentation. The timing and duration of psychotic symptoms are key. Acute symptom onset with fluctuating course and impaired attention suggests a delirious process. A gradual decline in functioning over several months to years in a young person suggests a first episode of a psychotic disorder (eg, schizophrenia). Drug abuse is common among young persons with a psychotic disorder and a positive drug screen for a psychogenic substance does not exclude a primary psychotic disorder.

If a patient has a history of schizophrenia, bipolar disorder, or psychotic depression, acutely worsening psychosis may be considered an acute or chronic presentation. Even in patients diagnosed with a psychotic illness, it is necessary to determine the cause of symptom exacerbation. Medication nonadherence (which can be partial), substance use, psychosocial stressors, or underlying medical illness should be considered. Collateral information from family or friends may be crucial to understanding a patient's presentation.

Safe disposition

Patients who pose a risk of harm to themselves or others or who are so impaired by their psychosis that they cannot care for themselves generally should be admitted to an inpatient psychiatric facility. For some psychotic patients who are agreeable to treatment and not prone to violence, less restrictive settings—such as a crisis intervention unit or respite facility-may be appropriate. A patient with first-episode psychosis could be admitted for further diagnostic clarification and treatment initiation. Manic patients often have no insight into their illness and may need hospitaliza-

Related Resources

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Drug Brand Names

Aripiprazole · Abilify Benztropine • Cogentin Diphenhydramine • Benadryl Divalproex • Depakote Haloperidol • Haldol Lithium • Eskalith, Lithobid

Lorazepam • Ativan Midazolam • Versed Olanzapine • Zvprexa Risperidone • Risperdal Ziprasidone • Geodon

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tion for containment and assurance of medication adherence. Goals of inpatient care include initiating or resuming pharmacologic treatment to reduce psychotic symptoms and beginning the recovery process. Response rates—defined as ≥20% improvement in total score on a psychopathology scale such as the Positive and Negative Syndrome Scale—will vary, but can take ≥4 weeks in some patients with first-episode schizophrenia.26 However, most patients will be stabilized and ready for discharge before 4 weeks. Family education and alliance building with the patient and family are important during hospitalization.

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Clinical Point

Timing and duration of psychotic symptoms are key; gradual decline in functioning suggests a first episode of a psychotic disorder

continued



Acute psychosis

Clinical Point

Even in patients diagnosed with a psychotic illness, it is necessary to determine the cause of symptom exacerbation

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Bottom Line

Acute psychosis has many possible causes, including psychiatric illness, medical conditions, and substance intoxication. An appropriate workup and treatment are key to stabilize and ensure the safety of an acutely psychotic patient in the emergency setting. Consider pharmacotherapy, such as haloperidol, secondgeneration antipsychotics, and benzodiazepines, and other interventions such as de-escalation.