

Thought Disorders

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PRINCIPLES

Patients with a history of mental illness have a higher rate of emergency department (ED) visits than the general population. Patients with at least one primary psychiatric visit to an ED were over four times more likely to become frequent ED users compared to patients with none.¹ Psychiatric patients accounted for almost 10% of all ED visits in 2010.²

Patients are often brought to the ED by family, police, or emergency medical service (EMS) with concerning symptoms of disorganized thought or behavior. They may express language and ideas found to be inappropriate and disruptive to accepted patterns of social interaction. Whether the issue involves thought content (delusions) or thought form (structure of thinking), the clinical impression is that of psychosis (detachment from reality and societal norms). Acutely psychotic patients raise concerns of safety for themselves and those around them.

The emergency clinician's role is to first prevent and control violent and disruptive behavior and then determine if the underlying etiology of the thought disorder is functional (psychiatric) versus organic (medical) in nature. Functional causes include schizophrenia and schizophrenia-like illness, mania or mood disorder-associated psychosis. Organic causes can mimic the psychotic behavior of functional psychosis. Medication effects, substance abuse, and certain medical disorders need to be excluded before psychosis can be attributed to an underlying psychiatric illness.

Schizophrenia often manifests as a thought disorder or psychosis. The prevalence of schizophrenia approaches 1% internationally. The incidence is approximately 1.5 new cases annually per 10,000 people. Slightly more men than women are diagnosed (1.4:1), and women tend to be diagnosed later in life.³ The mortality rate for schizophrenia is 2.5 times that of the general population and continues to grow. Migrants, urban dwellers, those with low social economic status, and those who live at higher latitude have an increased risk for the disease.

Although the etiology of schizophrenia is multifactorial, it has a substantial genetic component with 80% of the variation in the trait of the disease attributed to genetic factors.

Alterations in the dopaminergic, serotonergic, cholinergic, and glutamatergic dependent pathways have all been implicated in the pathophysiology of schizophrenia.⁴ Neuro-inflammation and white matter pathology may be associated with the disease. Neuropathological and neuroimaging studies provide consistent evidence of an association between schizophrenia and microglial activation and proliferation.⁵ Schizophrenia is also postulated to be related to environmental factors interacting with neurodevelopmental factors thereby increasing risk of the disease. Stress, perinatal hypoxia, poor nutrition, infections, vitamin D deficiency,

and zinc deficiency have all been associated with the development of schizophrenia.⁶ Evidence supports the existence of a progressive continuum of psychotic illness, beginning with unipolar depression and progressing to bipolar disease, schizoaffective psychosis, and finally schizophrenia. Research has shown that primary cerebral insults may occur early during brain development long before the illness is clinically expressed. Interactions between early neurodevelopmental disturbances and pathological events in postnatal brain maturation seem necessary to trigger the onset of overt schizophrenia.⁷

CLINICAL FEATURES

Thought disorders broadly affect mental activity and can be associated with varying degrees of functional impairment. The core psychopathology of schizophrenia and other thought disorders according to *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) includes hallucinations, delusions, disorganization, cognitive impairment, and negative symptoms.^{8,9} The positive symptoms of schizophrenia manifest in many forms, including distortion of reality. Hallucinations are the perception of a sensory process in the absence of an external source. They can be auditory, olfactory, visual, gustatory, or somatic in nature. The vast majority of people with schizophrenia experience auditory hallucinations.

Another impairment present in most schizophrenics is delusional thinking. Delusions are fixed, false beliefs that persist in the face of overwhelming contradictory evidence. Due to impaired insight, patients with thought disorders often have delusional explanations for their hallucinations. Delusions can be bizarre and clearly implausible, or they can be reasonable and understandable yet untrue.

Patients with schizophrenia typically display disorganization of behavior and thinking. Their use of disjointed speech patterns reflects their internal poor organization of thought. This results in a lack of a coherent focus of ideas. The most commonly observed abnormal speech patterns are tangentiality and circumstantiality where the narrative wanders away from the initial topic of conversation. More severe thought disorders include derailment, neologisms, word salad, and perseverations. In severe cases, there may be no understandable content and speech is utterly incomprehensible. A separate group of patients with a more extreme deficit in communication are those suffering from catatonia. This behavior includes immobility, stupor, mutism, resistance to instructions, oppositionalism, echo phenomena, and withdrawal. Although classically associated with schizophrenia because of the profound communication and thought deficiencies, more recent studies highlight a strong association of catatonia with mood and medical disorders. Despite their similar

presentations, only a minority of catatonic patients suffer with schizophrenia.¹⁰

Along with disorganization, thought disorders can be associated with significant cognitive impairment. These difficulties with attention, memory, reasoning, verbal comprehension, and decision-making usually precede the onset of positive symptoms.¹¹ These features are increasingly considered a core feature of thought disorders and not the byproduct of other symptoms or medications.

Negative symptoms represent an absence or diminution of normal cerebral processes. Negative symptoms include blunted affect, emotional withdrawal, social withdrawal, poor rapport with other people, difficulty with abstract thinking, loss of spontaneous conversation, and stereotyped thinking. The negative symptoms of schizophrenia are associated with an insidious onset of disease, fewer remissions, and poorer long-term prognosis. They are also associated with worse premorbid interpersonal skills, lower intelligence quotient (IQ), and tend to progress over time.

The development of schizophrenia involves three phases. The *premorbid phase* is characterized by the development of negative symptoms with deterioration in personal, social, and intellectual functioning. The patients are often young and may progressively withdraw from social actions. They may neglect personal appearance and hygiene. They experience deterioration of work, school, and home life. The *progressive phase* is often precipitated by a stressful event with the development of positive symptoms. The progressive phase can be said to begin when the patient develops the classical characteristics of schizophrenia mentioned earlier. Patients can become agitated or exhibit a hypervigilant withdrawal state characterized by rocking or staring and the patient may be violent and acting bizarrely. It is during the progressive phase that the patient is most likely to be brought to the ED by family, friends, police, or concerned bystanders. The *residual phase* is characterized by persistence of residual symptoms and disability. Impaired social and cognitive ability, poor hygiene, delusions, bizarre behavior, and social isolation can occur. On average, functional outcome is poor and patients may have varying levels of treatment resistance. Mortality is substantially increased due to elevated suicide risk and increased rates of poorly controlled medical comorbidities.

DIFFERENTIAL DIAGNOSIS

Medical Disorders

Numerous acute and chronic medical conditions can precipitate thought disorders (Box 100.1). Additionally, patients with underlying psychiatric disease may develop medical disorders that can exacerbate behavioral symptoms and cloud the distinction between psychiatric and organic brain disease.

Factors associated with primary medical conditions include new onset of symptoms, acute change in mental status, recent fluctuation in behavioral symptoms, onset in fifth decade of life or older, onset of symptoms after the patient has already been admitted to a medical care setting, and the presence of nonauditory hallucinations, lethargy, abnormal vital signs, and poor performance on cognitive function testing, particularly orientation to time, place, and person. Primary psychiatric conditions are more commonly associated with auditory hallucinations, a family history of psychosis, and an insidious onset in the late teens to mid-twenties. Medical delirium is common in elders; therefore, special attention should be paid to symptoms of psychosis in this population. Health care providers frequently ascribe medical delirium to other causes, such as dementia, psychosis, or depression.¹² Medical delirium can be frequently missed in elders brought to the ED for alterations in behavior.¹³

BOX 100.1

Medical Disorders That May Cause Acute Psychosis

METABOLIC DISORDERS

- Hypercalcemia
- Hypercarbia
- Hypoglycemia
- Hyponatremia
- Hypoxia

INFLAMMATORY DISORDERS

- Sarcoidosis
- Systemic lupus erythematosus
- Temporal (giant cell) arteritis

ORGAN FAILURE

- Hepatic encephalopathy
- Uremia

NEUROLOGIC DISORDERS

- Alzheimer's disease
- Cerebrovascular disease
- Encephalitis (including HIV infection)
- Encephalopathies
- Epilepsy
- Huntington's disease
- Multiple sclerosis
- Neoplasms
- Normal-pressure hydrocephalus
- Parkinson's disease
- Pick's disease
- Wilson's disease

ENDOCRINE DISORDERS

- Addison's disease
- Cushing's disease
- Panhypopituitarism
- Parathyroid disease
- Postpartum psychosis
- Recurrent menstrual psychosis
- Sydenham's chorea
- Thyroid disease

DEFICIENCY STATES

- Niacin
- Thiamine
- Vitamin B₁₂ and folate

HIV, Human immunodeficiency virus.

Patients intoxicated with drugs of abuse are often brought to the ED because of bizarre or dangerous behavior. Street drugs such as cocaine, amphetamines, bath salts, hallucinogens, and synthetic cannabis affect the serotonergic and dopaminergic pathways and can provoke psychotic reactions resembling a primary psychotic disease or can disclose latent schizophrenia.¹⁴ Certain pharmacologic agents may also cause acute psychosis and mimic a thought disorder (Box 100.2).

Psychiatric Disorders

Once medical causes have been ruled out and the etiology is believed to be psychiatric, it can be helpful to classify which type of psychosis the patient is experiencing. The DSM-5 uses four classes of information to distinguish among the various types of

BOX 100.2

Pharmacologic Agents That May Cause Acute Psychosis

ANTIANSIETY AGENTS

- Alprazolam
- Chlordiazepoxide
- Clonazepam
- Clorazepate
- Diazepam
- Ethchlorvynol

ANTIBIOTICS

- Isoniazid
- Rifampin

ANTICONVULSANTS

- Ethosuximide
- Phenobarbital
- Phenytoin
- Primidone

ANTIDEPRESSANTS

- Amitriptyline
- Doxepin
- Imipramine
- Protriptyline
- Trimipramine

CARDIOVASCULAR DRUGS

- Captopril
- Digitalis
- Disopyramide
- Methyl dopa
- Procainamide
- Propranolol
- Reserpine

DRUGS OF ABUSE

- Alcohol
- Amphetamines
- Cannabis
- Cocaine
- Hallucinogens
- Opioids
- Phencyclidine
- Sedative-hypnotics

MISCELLANEOUS DRUGS

- Antihistamines
- Antineoplastics
- Bromides
- Cimetidine
- Corticosteroids
- Disulfiram
- Heavy metals

psychosis: type of psychotic symptom, course of illness, consequences of illness, and exclusions.¹⁵ Each category can help distinguish schizophrenia from other disorders that include psychosis among their symptoms. The DSM-5 definition of schizophrenia is included in Box 100.3.

A *brief psychotic disorder* involves the sudden onset of psychotic symptoms in response to major stress and lasts from several days up to 1 month. *Peripartum psychosis* is included under the diagnosis of brief psychotic disorder. Patients with *schizophreniform*

BOX 100.3

Diagnostic Criteria for Schizophrenia From *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*

- A. Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be (1), (2), or (3):
 1. Delusions
 2. Hallucinations
 3. Disorganized speech (eg, frequent derailment or incoherence)
 4. Grossly disorganized or catatonic behavior
 5. Negative symptoms (ie, diminished emotional expression or avolition)
- B. For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning).
- C. Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (ie, active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or by two or more symptoms listed in Criterion A present in an attenuated form (eg, odd beliefs, unusual perceptual experiences).
- D. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either (1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or (2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness.
- E. The disturbance is not attributable to the physiological effects of a substance (eg, a drug of abuse, a medication) or another medical condition.
- F. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).

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disorder have similar symptoms to a brief psychotic disorder and last for longer than 1 month to less than 6 months. Up to one-third of patients with schizophreniform disorder can recover within 6 months; the other two-thirds develop clinical schizophrenia.¹⁶ Patients with *mood disorders* may develop psychotic symptoms as part of their disease. If psychotic symptoms develop during periods of mood disturbances, the diagnosis of mood disorder with psychotic features applies. If symptoms consistent with schizophrenia persist for more than 2 weeks in the absence of prominent mood episode, the diagnosis of *schizoaffective disorder* is made. Patients with *personality disorders* may occasionally develop brief psychotic episodes especially under stress. None of the aforementioned disturbances can be attributable to the effects of a substance or another medical condition.⁹

Delusional disorder is characterized by one or more delusions that are present for longer than 1 month and the criteria for schizophrenia have not been met. Patients may believe famous

people are in love with them (erotomanic) or that they have extraordinary powers or possess a special relationship with a deity or famous person (grandiose type). Other common delusions are of sexual partners being unfaithful (jealous type), that they are being malevolently treated (persecutory type), or that they have some physical defect or medical condition (somatic type). Function is not typically severely impaired, and behavior may not be bizarre apart from the impact of the delusions. Individuals may appear and behave normally if not actively discussing delusions, but social, marital, work, and legal problems can result from delusional beliefs.

DIAGNOSTIC TESTING

Diagnostic tests are indicated when a patient's clinical scenario cannot be explained by the history and physical examination alone. Often there is not enough information readily available to the clinician to accurately ensure that the patient is suffering from a thought disorder alone. The potential medical causes of thought disorders are very broad; therefore, if a medical evaluation is indicated, testing should be patient specific and based on the particular medical processes that the clinician feels may be causing or exacerbating the thought disorder. The clinical judgment of the treating physician, rather than panels of routine tests, should be used to efficiently and appropriately guide diagnostic test ordering.

The evaluation of a "first-time" psychosis or thought disorder presentation in an emergency patient differs substantially from the evaluation of a patient with chronic disease and recurrent symptoms. The evaluation for the first time thought disorder patient may include a larger, more detailed laboratory and radiological evaluation. Complete blood counts, electrolyte panels, glucose levels, thyroid function, urine testing, cortisol levels, vitamin B₁₂, methylmalonic acid levels, and rapid plasma regain (RPR) testing could be useful in certain clinical situations and ordered as needed for individual patients.

Whether to obtain neuroimaging on the initial evaluation of patients with thought disorders remains controversial. Incidental findings on computed tomography (CT) or magnetic resonance imaging (MRI) occur at similar rates to control patients and rarely lead to the discovery of clinically relevant disorders in the absence of neurological signs.¹⁷ Neuroimaging for intra-cranial injury, vasculitis, demyelinating diseases, tumor, cerebrovascular disease, or abscess may be indicated based upon findings noted on the history and physical examination. Given the long-term costs of schizophrenia, neuroimaging in a young person with a first time psychosis will exclude rare and treatable causes of psychosis and can support the diagnosis of schizophrenia, and it should be considered by the treating clinician on a case by case basis.

Ancillary testing beyond that required for medical clearance of psychiatric emergency patients rarely alters care, especially for patients with an established diagnosis of schizophrenia or other chronic thought disorders. Policies that require panels of testing prior to psychiatric admission are costly and unnecessary. One of the largest unnecessary costs is incurred with the routine use of urine drug screens, which have been found to rarely alter disposition for psychiatric patients from the ED especially when combined with a good substance abuse history.¹⁸ Greater emphasis should be placed on identifying a clinical toxidrome and history of use when attempting to determine if drugs and medications are contributing to the symptoms of psychosis.

MANAGEMENT

Patient safety and ED staff safety are a principle concern when a patient presents with aggressive and unpredictable psychotic behavior. Risk factors for violence in patients with schizophrenia

include gross excitement, prior violence, auditory hallucinations, systematization of delusions, incoherence of speech, and long duration of illness. In contrast, traits such as substance abuse and antisocial episodes are not recognized as significant violence-associated factors.¹⁹ Strategies to control disruptive and violent behavior in psychosis and thought disorders include de-escalation techniques, chemical sedation, and physical restraints.

Although chemical and physical intervention can be appropriate when patients are demonstrating dangerous behavior, non-physical intervention, such as verbal de-escalation should be considered first. The clinician should demonstrate a calm, non-judgmental demeanor while showing appropriate concern and avoiding excessive stimulation, posturing, and prolonged eye contact. The patient should be given an opportunity to express their concerns, as well as identify unmet needs that can be easily corrected (eg, inadequate pain control, communication failures, or social concerns). If available, consider recruiting trusted others (eg, family, friends, case managers) to help prevent further agitation.²⁰

When verbal de-escalation is ineffective or inappropriate, physical restraint or use of seclusion may be necessary. Risk factors for the use of restraint or seclusion include referrals initiated by a third party, patients arriving to the ED in restraints, and clinician perception of the patient as severely disruptive, already exhibiting psychosis, or experiencing a manic episode.²¹

Chemical restraint for psychomotor agitation is a common and necessary intervention. Speed of onset and reliability of delivery are two important factors to consider when selecting a route of administration of sedation in the behaviorally disturbed patient. Oral sedation is indicated when the patient can be safely verbally de-escalated, is not at imminent risk of harm to self, and agrees to take oral medications. When more expedient sedation is required, parenteral route has the advantages of immediate effect and titration of dosing. The goal of titration in this setting is the induction of rousable sleep, not unconsciousness.²²

Benzodiazepines and antipsychotics are the two medications most commonly used for chemical restraint. Using a single agent or, for more disturbed patients, a combination of the two classes, can be considered. Common agents and dosages are listed in Table 100.1.

Combined with concurrent physical restraint and the risk of previously ingested intoxicants, there is significant risk for over-sedation and respiratory compromise. The combination of haloperidol and lorazepam causes respiratory depression in up to 50% of patients with a significant number also experiencing a hypoxic event. Fortunately, most episodes are quickly corrected with verbal stimulation or airway repositioning. As a result, we recommend the use of pulse oximetry or CO₂ monitoring in chemically restrained patients to detect early signs of respiratory

TABLE 100.1

Common Drugs for Sedation

DRUG	USUAL ADULT DOSE	ADVERSE EVENTS
Midazolam	2.5 to 5 mg IM (rapid onset)	Respiratory depression Oversedation
Lorazepam	1 to 2 mg PO or IM	Hypotension
Diazepam	5 to 10 mg PO or IM (longer acting)	Paradoxical excitation reaction in patients with organic brain disease
Haloperidol	5 to 10 mg PO or IM	Increased mortality risk in elderly
Ziprasidone	10 to 20 mg PO or IM	dementia-related psychosis
Olanzapine	10 mg PO or IM	Caution in prolonged QT or history of neutropenia

IM, Intramuscular; PO, per os (by mouth).

depression.¹⁵ In addition to monitoring of airway and level of consciousness, sedated and restrained patients should have frequent behavioral monitoring. The use of physical restraints may cause excess pressure on the patient's neck, chest or abdomen, and requires ongoing direct visualization. Potentially hazardous articles and possessions should be removed from the patient's area. Restrained patients are known to forcibly remove Foley catheters without deflation of the balloon if their limbs are released prior to removal of the catheter, resulting in urethral injury.

A detailed discussion of the use of physical and chemical restraints is provided in Chapter 189.

DISPOSITION

Making an appropriate disposition for patients with decompensated thought disorders is often difficult in today's emergency medicine practice environment. Although institutional and community psychiatric resources vary widely by region, there appears to be a nationwide trend of diminishing psychiatric referral resources in the presence of rising numbers of psychiatric-related ED visits.²³ The number of inpatient psychiatric beds nationwide has decreased dramatically, and many EDs "board" psychiatric patients for extended periods of time.

Appropriate disposition is based on the etiology of the underlying psychosis, response to treatment, consideration of patient and community safety, and an appropriate outpatient follow-up plan.

Patients who are actively suicidal, dangerous to others, possess severe mental debilitation precluding self-care, or are having their

first psychotic episode should be admitted. The decision for inpatient psychiatric admission is not always precise. There may be disagreement between emergency clinicians and consulting psychiatrists regarding need for involuntary hold and final disposition, but psychiatric consultation can help confirm safety for discharge, help facilitate inpatient admission, and aid in outpatient follow-up.²⁴

Telemedicine is emerging as a technology that may ease the growing lack of adequate psychiatric resources for ED patients by facilitating urgent psychiatric consultation. A recent study demonstrated that telemedicine can be used safely and is not associated with significant differences in care when compared with face-to-face psychiatric evaluations.²⁵

Medication noncompliance is a common reason for a known schizophrenic to present to the ED with a decompensated psychotic episode. A patient whose psychosis stabilizes in the ED with medication can sometimes be safely discharged back into the community. Safe discharge planning can be accomplished provided that the patient has adequate ability to care for self and does not pose a risk of harm to self or others. Insight by the patient and judgment to adhere to an agreed course of action, including taking medication, is typically required. Patients with severe underlying psychiatric illnesses may have some degree of persistent mental disability even when optimally treated. For these patients, recruiting family or friends familiar with the patient can help establish that the patient is back to his or her baseline to ensure safety. A safe transition to the community setting requires adequate social support, including follow-up with a mental health service.²¹

KEY CONCEPTS

- Thought disorder symptoms can be precipitated by psychiatric, underlying medical, and toxicologic etiologies.
- Diagnostic testing should be patient specific and based on the particular medical processes that the clinician feels may be causing or exacerbating the thought disorder, rather than panels of routine tests.
- Consider nonphysical intervention first when appropriate, but chemical sedation and physical restraint are immediately necessary for patients who demonstrate aggressive and dangerous behavior.
- Appropriate disposition depends on the etiology of the underlying psychosis, response to treatment, and patient and community safety considerations and, more often than not, includes psychiatric consultation.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.

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CHAPTER 100: QUESTIONS & ANSWERS

- 100.1.** Which of the following pharmacologic agents have been implicated in causing acute psychosis?
- Aripiprazole, hydralazine, nitroglycerin
 - Diazepam, rifampin, captopril
 - Hydrochlorothiazide, acetaminophen, albuterol
 - Lorazepam, salsalate, rocuronium
 - Penicillin, ceftriaxone, risperidone

Answer: B. Box 100.2 provides an extensive list of other agents that may cause psychosis.

- 100.2.** Rapid tranquilization using a neuroleptic agent would be indicated in which of the following cases?
- An intoxicated schizophrenic
 - Anticholinergic psychosis
 - A lactating schizophrenic
 - A phencyclidine overdose
 - A pregnant schizophrenic

Answer: A. Neuroleptics are contraindicated in choices B to E. They should not be the sole agent for alcohol withdrawal but would be useful for acute psychotic agitation.

- 100.3.** A 45-year-old woman presents to the emergency department (ED) for a complaint of severe anxiety and unrest. Her past history is significant only for moderate schizophrenia, for which she was placed on olanzapine 2 months prior. She has been compliant. Physical examination is remarkable for the presence of anxiety, clear sensorium and orientation, and normal speech. She is restlessly pacing the room and reports being compelled to keep moving. Urine drug screen is negative. What would be the most appropriate therapy?
- Benzotropine orally
 - Lorazepam orally
 - Olanzapine intravenously
 - Psychiatry consultation
 - Ziprasidone intravenously

Answer: A. Akathisia is a state of motor restlessness characterized by a physical need to be constantly moving. The patient does not want to do so but feels compelled. It is most commonly seen in middle-aged patients within the first few months of starting treatment. It may be mistaken for an acute deterioration, but psychotic features are not increased. Treatment is with oral beta-blockers and anticholinergics (benztropine).

- 100.4.** What is the most common adverse effect seen with neuroleptic agents?
- Akinesia
 - Dystonia
 - Orthostatic hypotension
 - Pseudoparkinsonism
 - Tardive dyskinesia

Answer: B. Dystonia occurs in 1% to 5% of this patient population. The reaction occurs because of a dopaminergic pathway disruption with a resulting cholinergic predominance. Anticholinergics should be administered parenterally (Benadryl 25 to 50 mg intravenous [IV] or Cogentin 1 or 2 mg IV), followed by 48 to 72 hours of oral follow-up treatment to prevent recurrence. Patients may experience tongue protrusion (buccolingual crisis), upward eye deviation (oculogyric crisis), back arching (opisthotonus), and, rarely, laryngospasm. Symptoms may lessen with voluntary muscle action and increase with stress.

- 100.5.** A 27-year-old known schizophrenic is brought to the emergency department (ED) for altered mental status. His only known medication is clozapine, which he started 4 weeks ago with subsequent dose increases. He has no other past history. Physical examination is remarkable for a muscular black man who is somnolent and diaphoretic. He withdraws all extremities stiffly and grimaces to pain. Vital signs are temperature, 40.5° C; heart rate, 146 beats per minute; blood pressure, 205/125 mm Hg; and respiratory rate 28 breaths per

minute. Rectal examination is guaiac positive. Foley placement shows brown urine. What should be the next diagnostic maneuver?

- A. Creatine kinase level
- B. Head computed tomography (CT) scan
- C. Lumbar puncture
- D. Thyroid hormone levels
- E. Urine drug screen

Answer: A. Neuroleptic malignant syndrome is an idiopathic condition clinically similar to serotonin syndrome and malignant

hyperthermia. Milder cases may be confused with serotonin syndrome. Severe cases, related to possible hypothalamic dysfunction, present with fever, rigidity, altered mental status, autonomic instability, and elevated creatine phosphokinase (CPK) and possibly rhabdomyolysis. It is seen with both typical and atypical antipsychotics and generally occurs in the first few weeks of treatment. Complications may include hepatic/renal failure, gastrointestinal (GI) hemorrhage, and respiratory failure. Severe cases may require intravenous dantrolene or dopamine agonists (eg, bromocriptine).