

Who's at greatest risk for delirium tremens

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Some patient traits show clear potential
for this life-threatening complication.

Ms. J, 42, was admitted to the OB-GYN service for a routine vaginal hysterectomy to treat dysfunctional uterine bleeding. In the presurgical history, she described having a few drinks daily. Shortly after a successful uncomplicated procedure, the patient became tremulous and was given several doses of lorazepam.

Two days after surgery, the patient became delirious. She complained of tactile and visual hallucinations, her level of consciousness waxed and waned, and she showed significant autonomic instability. A psychiatry consult was ordered. The consult team recommended IV fluids, IV diazepam, and haloperidol, supplemented with a multivitamin and 100 mg/d of thiamine. When the patient's delirium resolved within 4 days, a more detailed discussion revealed a history of alcohol abuse and withdrawal seizures.

It is not uncommon for a patient to develop acute alcohol withdrawal and delirium tremens (DTs) while recovering from routine surgery. Delirium tremens remains a medical emergency, even though advances have reduced its associated mortality rates (Box).¹⁻⁷

Psychiatrists who know the risk factors for DTs—also

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termed alcohol withdrawal delirium—can identify and protect patients who are susceptible to this life-threatening complication. We describe the clinical features of DTs, potential predisposing factors, theories behind its mechanisms, and strategies for preventing and managing DTs in patients experiencing alcohol withdrawal.

Clinical features

Disorientation and confusion are the hallmark features of DTs. Other clinical manifestations include vivid hallucinations, extreme tremulousness, autonomic hyperactivity, sweating, tachycardia, and agitation. Men experiencing DTs seem to demonstrate a greater degree of autonomic hyperactivity than women.⁸

Symptoms usually arise in the alcoholic patient between the third and fifth days of abstinence but have been known to occur several weeks after a patient's last drink. Symptoms usually resolve within a few days⁹ but have been known to resolve within hours in some patients and to persist for several months in others.¹⁰

Differential diagnosis. Clinicians often fail to differentiate alcohol hallucinosis from DTs. Alcohol hallucinosis—which occurs in 3 to 10% of patients with severe alcohol withdrawal¹¹—manifests as auditory, visual, or tactile hallucinations with a clear sensorium. Patients experiencing DTs also may experience hallucinations but with confusion, disorientation, and severe autonomic hyperactivity. Unlike DTs, alcohol hallucinosis is not fatal.⁹

DTs also should be differentiated from:

- other causes of delirium, such as medication or infection. If the cause is identified and removed, the delirium should gradually resolve.
- Wernicke's encephalopathy—caused by glucose exposure in the thiamine-deficient alcoholic—which is characterized by confusion, ophthalmoplegia, and ataxia.

Completing a thorough history and physical exam, talking to family members, and reviewing past medical charts are often the best ways to differentiate DTs from other conditions.

What causes DTs?

Vitamin deficiencies were initially thought to cause alcohol withdrawal.³ More recent evidence points toward multiple neuroadaptive changes in the brain associated with chronic alcohol exposure.¹² Although numerous neurotransmitter sys-

Box

DTs: MORTALITY RATE AS HIGH AS 15%

Approximately 1.5 to 2 million Americans seek treatment for alcohol abuse or dependence each year.¹ As many as 71% of these patients manifest symptoms of alcohol withdrawal.² Of those individuals who experience alcohol withdrawal, delirium tremens (DTs) may occur in up to 5%.^{3,5} Utilizing these percentages, it can be estimated that as many as 50,000 to 70,000 individuals develop DTs each year in the United States alone.

Although the incidence of DTs can be assumed to be relatively low, the condition should be considered a medical emergency. Studies list mortality rates for DTs as high as 15% and as low as 2 to 3%.^{7,8}

tems may play a role in alcohol withdrawal, recent research has focused on glutamate¹³ and gamma-aminobutyric acid (GABA).¹⁴

The brain seems to compensate for alcohol's enhancement of GABA (inhibitory) neurons by up-regulating excitatory neurons (glutamate). Alcohol has been shown to have some effects on neurons.¹⁵ The implication is that withdrawing alcohol triggers an "excitatory state" until the brain can readjust the fine balance between excitation and inhibition, a process that takes weeks to months. Some changes may never reverse because of the neurotoxic effects of alcohol and alcohol withdrawal.

Repeated alcohol exposure and withdrawal may lead to neuroadaptive changes in the brain and to more severe withdrawal symptoms, such as DTs. Repeated alcohol withdrawal episodes can produce a kindling effect. As outlined by Becker, kindling occurs "when a weak electrical or chemical stimulus, which initially causes no overt behavioral responses, results in the appearance of behavioral effects, such as seizures, when it is administered repeatedly."¹⁶ Thus, repeated alcohol withdrawal worsens future episodes and eventually leads to alcohol withdrawal seizures.

Whereas most of these theories apply to alcohol withdrawal, they are also compatible with the neuronal mechanisms that may underlie DTs. Alcohol withdrawal and DTs share the presence of a "hyperactive state." Most likely, DTs is the progression to more severe or pronounced neuroadaptive



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Table 1

RISK FACTORS FOR DELIRIUM TREMENS

Comorbid medical illness (with electrolyte, fluid abnormalities)*

History of delirium tremens*

Blood alcohol level >300 mg/dL on presentation*

Presentation after an alcohol withdrawal seizure*

Older age*

Longer history of alcohol dependence

Intense alcohol craving

Abnormal liver function

* Supported with studies and/or in the medical literature

Source: Saitz R. Introduction to alcohol withdrawal. *Alcohol Health Res World* 1998;22(1):5-12.

Table 2

STRATEGIES TO PREVENT AND TREAT DELIRIUM TREMENS

Assess risk for DTs with a thorough history, including collaborative family information and medical charts

Admit patients with a history of serious withdrawal symptoms or potential for inpatient detoxification (based on degree of tolerance)

Check complete lab values (chemistry panel, liver function tests including ALT and AST, complete blood count, blood alcohol level, GGT, and others if relevant), and correct any fluid, vitamin, or electrolyte abnormalities

Treat comorbid medical conditions

Differentiate DTs from alcohol hallucinosis, other causes of delirium, and Wernicke's encephalopathy

Consider giving benzodiazepines along with low-dose neuroleptics, if appropriate, and monitor for disinhibition/confusion and extrapyramidal symptoms, respectively

Place the patient in a low-stimulation environment with frequent monitoring

changes seen in mild to moderate alcohol withdrawal. One could certainly imagine that the possible neurotoxic effects of alcohol, alcohol withdrawal, and repeated detoxifications could sensitize the CNS to the more severe symptoms seen in DTs. Infection and metabolic abnormalities may also enhance the progression. Unfortunately, why some but not all patients experiencing alcohol withdrawal progress to DTs is unknown.

Predisposing risk factors

Past withdrawal complicated by seizures or DTs is the single best predictor of future alcohol withdrawal symptoms.¹⁷ Also consider the following patients to be at elevated risk:

- any individual who presents with a blood alcohol level >300 mg/dl or after experiencing a withdrawal seizure⁹
- patients with comorbid medical conditions, such as electrolyte abnormalities, infection, or poorly treated cardiovascular or respiratory diseases
- older persons, who tend to be susceptible to delirium associated with hospitalization, medical illnesses such as urinary tract infections or pneumonia, or use of certain medications.¹⁸

Potential risk factors for developing DTs are summarized in *Table 1*.¹ Although few studies have been done, clinicians can use these factors as a guide for aggressively preventing DTs in at-risk patients.

Managing and preventing DTs

Management. Drug therapy is considered crucial to quell withdrawal symptoms and reduce the risk of death.¹⁹ Patients usually are treated with one of several benzodiazepines (such as chlordiazepoxide, diazepam, oxazepam, or lorazepam) to decrease autonomic instability and reduce seizure risk during acute alcohol withdrawal. Although dosages of these medications are estimated based on drinking history, some general starting ranges are often used in clinical practice:

- chlordiazepoxide, 50 to 100 mg tid
- lorazepam, 1 to 2 mg every 4 hours
- oxazepam, 15 to 30 mg qid
- diazepam, 10 to 20 mg tid/qid.

Treating DTs often requires the use of IV benzo-

diazepines because of their quick onset of action and benefit for acutely agitated patients who have difficulty taking medications by mouth.

Prevention. Correcting fluid and electrolyte abnormalities may be critical in preventing DTs (Table 2). In one study of patients who died while experiencing DTs, only 25% received adequate fluid replacement, which can be as much as 6 liters per day.²⁰ Ideally, comorbid conditions should be addressed early in presentation and before DTs develop.²¹

High-dose benzodiazepine therapy does not completely protect a patient from DTs or reduce its duration,²² but it may reduce mortality. A meta-analysis of prospective, placebo-controlled trials reported a risk reduction of 4.9 cases of DTs per 100 patients treated with benzodiazepines. Mortality also seems to have been reduced in patients with DTs who were treated with sedative hypnotics.⁹ Benzodiazepines may cause increased confusion and disinhibition, as is frequently seen when patients with dementia are treated with these agents.²³

Neuroleptics such as haloperidol have been used to prevent and treat DTs, but studies of their ability to reduce mortality have produced inconsistent results. What's more, neuroleptics can reduce the seizure threshold and produce extrapyramidal symptoms.²³ Atypical antipsychotics may offer a safer alternative, although more studies are needed to evaluate whether they decrease the occurrence and severity of DTs.

In summary, a rational approach to preventing and treating DTs is to:

- manage comorbid medical illnesses, and correct fluid and electrolyte abnormalities
- place the patient in a safe, low-stimulation environment with frequent monitoring
- use benzodiazepines judiciously.

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Related resources

- ▶ National Institute on Alcohol Abuse and Alcoholism.
- ▶ www.niaaa.nih.gov
- ▶ Shaw GK. Detoxification: the use of benzodiazepines. *Alcohol Alcohol* 1995;30(6):765-70 (a thorough review of benzodiazepine use in alcohol withdrawal).

DRUG BRAND NAMES

Chlordiazepoxide • Librium	Lorazepam • Ativan
Diazepam • Valium	Oxazepam • Serax
Haloperidol • Haldol	

DISCLOSURE

The authors report no financial relationship with any company whose products are mentioned in this article, or with manufacturers of competing products.

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Delirium tremens (DTs) is a medical emergency in patients experiencing alcohol withdrawal. Risk factors include older age, history of DTs and seizures, and medical comorbidity. Correcting electrolyte and fluid imbalances can prevent DTs, and careful use of benzodiazepines may avert delirium and reduce the risk of death.

BottomLine