ABSTRACT

- **Objective:** To review the diagnosis and treatment of alcohol (ethanol) withdrawal.
- **Methods:** Historical overview and evidence review.
- **Results:** The prevalence of ethanol abuse and related medical complaints is significant, accounting for as much as 14.3% of U.S. health care expenditures in 1998. The detection of the ethanol withdrawal state can be extremely challenging and can involve the process of rapid exclusion of numerous other similarly presenting disease states. The pathophysiology of ethanol withdrawal can be generally viewed as the opposite of ethanol intoxication at the central nervous system neurotransmitter level. While the treatment of ethanol toxicity is largely supportive, the treatment of ethanol withdrawal is more complex but does address neurotransmitter and neuroreceptor treatment. Benzodiazepines are generally recommended as a first-line pharmacologic approach.
- **Conclusion:** Diagnosis and treatment of alcohol withdrawal syndrome is challenging. Management approaches continue to evolve.

Alcohol is a common drug of abuse that has significant effects on society. The total economic costs of alcohol abuse in the United States were estimated to be $185 billion in 1998 [1]. Diagnostic criteria for ethanol abuse include physical dependence symptoms (such as tolerance and withdrawal) and psychological symptoms (such as craving) [2].

Although there are descriptive reports of ethanol withdrawal symptoms from the mid-18th century [3], the first recorded clinical observations linking ethanol abstinence to ethanol withdrawal were those of Victor and Adams in 1955 [4]. Isabell provided the first documented clinical observations of delirium tremens (DT) and ethanol-induced withdrawal seizures that same year [5]. The prevalence of ethanol (alcohol) withdrawal symptoms in the general population has been estimated to be 5% [6]. Recent epidemiological research supports this, showing a DSM-IV alcohol dependence prevalence rate of 3.8% [7].

PATHOPHYSIOLOGY

An obvious prerequisite to the manifestation of ethanol withdrawal is the establishment of ethanol dependence and tolerance. Biochemically, ethanol exerts its effect on the central nervous system mainly as a depressant [8]. The resulting biochemical changes that result from chronic use of ethanol mainly manifest themselves in the form of influence over the neurotransmitters γ-aminobutyric acid (GABA) and glutamate.

GABA is the main central nervous system (CNS) inhibitory transmitter. GABA exerts its effect on the CNS by increasing inhibitory tone via the chloride channel on the nerve cell membrane [9]. Ethanol acts as a GABA agonist, causing decreased CNS excitability. Clinically, this decreased CNS excitability results in sedation, cognitive dysfunction, and poor motor coordination. Furthermore, the chronic use of ethanol results in a downregulation of GABA receptors [10]. Downregulation of receptors is a decrease in the number of receptors on a cell membrane. The downregulation of GABA receptors on the CNS cell membranes from chronic ethanol use results in the requirement of increasingly larger doses of ethanol to achieve the same euphoric and inhibitory effect, a phenomenon known as tolerance [11]. The downregulation of GABA receptors may also partially explain the clinical examples of patients being awake and functional at very high blood ethanol concentrations that would induce coma or death in nontolerant individuals [11]. With the removal of ethanol in the chronic user, the CNS inhibition is released, and there is an increase in CNS excitation due to the decrease of both circulating GABA and receptor downregulation. This CNS excitation results in the clinical spectrum of ethanol withdrawal.

From the Medical College of Wisconsin, Milwaukee, WI.
A second important CNS biochemical pathway alteration involves glutamate as an excitatory neurotransmitter. Endogenous glutamate acts on the N-methyl-D-aspartate (NMDA) receptors in the CNS, causing influx of calcium into a voltage-gated and ligand-dependent calcium channel [11]. The influx of calcium results in cell depolarization, causing CNS stimulation. Ethanol acts as an NMDA receptor antagonist, thereby inhibiting CNS tone below threshold; an excess of NMDA receptor hyperactivity and production of glutamate ensues [11]. The resultant hyperactivity in the CNS is manifested in many ways, including catecholamine hyperactivity. This type of receptor hyperactivity results in the clinical picture of altered mental status, hyperthermia, hyperactive muscle activity, seizures, and other forms of CNS excitation. An effect via ethanol withdrawal on the CNS catecholamine concentrations is also observed. Initially, acute and chronic ethanol intake results in an increase in dopamine extracellular levels by the disinhibition of GABA receptors [12]. This increase in dopamine may initially account for some of the positive effects of ethanol (euphoria) and also craving for ethanol. The continued dopamine excess then results in increased metabolism into norepinephrine by dopamine β-hydroxylase. Ethanol withdrawal also affects dopaminergic CNS transmission. A high plasma level of the metabolite of dopamine, homovallinic acid, has been observed in patients with clinical ethanol withdrawal [13]. The CNS catecholamine system is also affected by ethanol withdrawal, not only by a increase in dopamine but by an impairment of the action of α-2 receptor activity (an effect that some pharmacological imidazole drugs such as dexmedetomidine may improve). The final effect is also an excess of CNS dopamine and norepinephrine levels, further contributing to the clinical manifestation of ethanol withdrawal via dysautonomic regulation.

In summary, the ingestion of ethanol on a chronic basis results in a constellation of CNS biochemical changes associated with dependence and tolerance. Tolerance is partially the result of the downregulation of GABA receptors with the upregulation of NMDA receptors and production of excess glutamate. With the removal or decreased concentration of ethanol, a reversal of the above ensues, resulting in CNS excitation.

**MORTALITY**

Monte and coworkers determined a 6.6% incidence of death in their ethanol withdrawal patient population [14]. They determined that patients presenting with advanced liver disease (cirrhosis), needing intubation (especially for pneumonia), other chronic underlying disease states, and presentation with DTs, the most serious and potentially deadly complication of ethanol withdrawal, had a much higher risk of dying. Among those experiencing DTs, the mortality rate is approximately 5% [15,16].

**CLINICAL DIAGNOSIS**

**History of Abuse**

A basic tenet for a patient to have the constellation of ethanol withdrawal symptoms is that he is physically addicted to ethanol. Therefore, the practitioner should seek to obtain a history of ethanol abuse. In the acutely ill patient, this determination may be challenging [17]. Further, outpatients may be unwilling to divulge the fact that they are ethanol dependent, or may not even consider themselves tolerant. The practitioner should attempt to obtain the following historical data: estimation of consumption (type of alcohol consumed, volume, frequency, drinking pattern); level of dependency (daily drinking, early in the day drinking, previous...
medical ethanol detoxification interventions, priority of ethanol in the patient’s life); and negative outcomes of drinking (social, financial, legal) [18].

**Clinical Features**

A common method by which to clinically define alcohol withdrawal is via the DSM-IV classification (Table 1). A scheme described by Victor and Adams in 1953 [4] stratifies patients by clinical features into mild, moderate, and severe withdrawal categories. A modified version of this scheme is seen in Table 2.

Early and mild ethanol withdrawal symptoms can be masked by various concomitant disease processes including trauma or medical or underlying psychiatric illness. Furthermore, concomitant use of cardiac or other medications that alter vital signs can be problematic. Common examples of cardiac medications that may “normalize” otherwise unstable vital signs include beta and calcium channel blockers. Some common disease states that can be clinically similar to ethanol withdrawal are seen in Table 3. Toxins that can mimic ethanol withdrawal are listed in Table 4 [22].

**Rating Scales**

The use of rating scales has been recommended to assess the severity of ethanol withdrawal. Such scales include the CIWA, CIWA-AD, and CIWA-Ar developed by Sullivan and coworkers [23]. An appropriate ethanol withdrawal rating scale must possess the following characteristics: (1) good interobserver reliability; (2) can be applied by trained nurses, (3) detects and quantifies the important clinical signs and symptoms of withdrawal; (4) provides an additive score as an index of severity; (5) can give a prognosis for treatment; (6) allows for serial clinical assessments; (7) assesses response to ongoing therapy. The most commonly used scale is the revised CIWA-Ar (Clinical Institute Withdrawal Assessment Scale for Alcohol) (Table 5).

The CIWA-Ar can be administered at the bedside in about 2 minutes [23]. The scale measures 10 symptoms, with each criterion rated on a scale from 0 to 7, except for “orientation and clouding of sensorium,” which is rated on scale of 0 to 4. Scores of 0 to 9 indicate absent to minimal withdrawal. Scores of 10 to 19 indicate mild to moderate withdrawal (marked autonomic arousal); and scores of 20 or more indicate severe withdrawal (impending DTs). A shorter, more simplified scale for measuring severity, the SHOT (sweating, hallucinations, orientation, and tremor) was developed by Gray et al [24] for use in the emergency department. The developers found the scale takes 1 minute to administer versus 5 minutes for the CIWA-Ar [24].

Rating scale scores can be used to guide selection of treatment setting. Many authors recommend outpatient detoxification if the CIWA-Ar score is 8 to 10 and the prerequisites seen in Table 6 are met. Some authors recommend against using withdrawal rating scales to determine eligibility for inpatient or outpatient treatment [31].

**PHARMACOTHERAPY**

Benzodiazepines are the drug of first choice for treatment of ethanol withdrawal. The medical provider must further consider the pharmacokinetics of each differing benzodiazepine. Lorazepam has been recommended in patients with liver disease and the elderly due to its lack of pharmacologically active metabolites [32]. Lorazepam...
undergoes simple glucuronidation for its in vivo deactivation. Another candidate mentioned in the ethanol literature with similar properties to lorazepam is oxazepam. There has been interest in using other medications that do not have the sedative and potentially addictive side effects attributed to benzodiazepines. One commonly recommended drug for outpatient management is carbamazepine. Malcolm and coworkers compared carbamazepine to lorazepam in patients with low to moderate withdrawal and found similar results in the suppression of withdrawal [33]. Other literature, including a Cochrane review, supported this view [34,35].

A less commonly used drug class used for the treatment of both outpatient and inpatient ethanol withdrawal is barbiturates. Most studies compare the efficacy of barbiturates, specifically phenobarbital, to benzodiazepines [36]. While the efficacy of treating ethanol withdrawal with either type of GABA agonist is logical, the concern of more pronounced hypotension and apnea with intravenous phenobarbital in the inpatient setting has limited its use.

Other drugs have been suggested, such as valproic acid, tiapride, baclofen, lamotrigine, topiramate, gabapentin, tiagabine, and vigabatrin. At this time, there are limited data to recommend these therapies.

**MANAGEMENT**

**Treatment of Minor Withdrawal**

Minor withdrawal can be treated in the inpatient or outpatient setting. One review recommends the use of oral benzodiazepines for “days to 1 week” [31]. Classically, mild withdrawal should resolve in 24 to 48 hours. Review of the literature reveals no consensus on the duration of outpatient benzodiazepine type or treatment.

### Table 3. Medical Disease States Similar to Ethanol Withdrawal

<table>
<thead>
<tr>
<th>Encephalitis</th>
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<tbody>
<tr>
<td>Hypomagnesemia</td>
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<tr>
<td>Meningitis</td>
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<tr>
<td>Neuroleptic Malignant Syndrome</td>
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<tr>
<td>Pneumonia</td>
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<tr>
<td>Serotonin Syndrome</td>
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<td>Thyrotoxicosis</td>
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### Table 4. Toxins that Mimic Ethanol Withdrawal

<table>
<thead>
<tr>
<th>Amphetamines</th>
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<tbody>
<tr>
<td>Anticholinergics</td>
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<tr>
<td>Carbamates (pesticides)</td>
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<tr>
<td>Cocaine</td>
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<tr>
<td>Lithium</td>
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<tr>
<td>Organophosphates</td>
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<tr>
<td>Salicylates</td>
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<tr>
<td>Theophylline</td>
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</table>


### Outpatient Treatment

The initial overall goal for outpatient medical treatment is to prevent withdrawal seizures and to treat minor withdrawal symptoms. For the outpatient setting, Solomon and coworkers proposed a 5-day fixed-schedule benzodiazepine treatment regimen [Table 7] for those patients who qualify for outpatient ethanol detoxification (Table 6) [37]. In their study comparing lorazepam and chlordiazepoxide, both drugs were equally efficacious in suppression of ethanol withdrawal symptoms, especially seizures.

As in this study, most of the literature stresses the use of a fixed pharmacologic schedule for outpatient detoxification. There have been limited studies examining symptom-triggered outpatient therapy as an alternative. A recent Danish study by Elholm and coworkers examined self-administered symptom-triggered oral chlordiazepoxide use in a small number of heavily controlled subjects and found similar overall safety in the symptom-triggered group and the fixed-schedule group [38]. At the present time, most outpatient detoxification units do not have the resources to monitor patients in a symptom-triggered outpatient manner. Furthermore, the safety issue of excessive use still exists, and symptom-triggered outpatient therapy cannot be recommended. More vigorous studies in real-world settings should be undertaken before sending home patients with a variable amount of benzodiazepines to “treat their symptoms.” The overall consensus is that symptom-triggered therapy is not compatible with outpatient therapy.

There is controversy with respect to the treatment of ethanol withdrawal seizures on an outpatient basis. The current thought is that classic ethanol withdrawal seizures are self-limited if the patient stops drinking...
In spite of this, there is no consensus on whether or not to offer the patient alcohol-related seizure prophylaxis. What is certain, however, is that using phenytoin to treat and prevent ethanol withdrawal seizures is not efficacious [41].

**Inpatient Treatment**

Patients with seizures, alcohol hallucinosis, or DT require prolonged observation and/or hospital admission. Once the determination for hospitalization is made, the ethanol withdrawal patient may be further stratified into an ICU setting. About 5% of patients who exhibit ethanol withdrawal will progress to DTs [42]. Ferguson et al identified certain risk factors that increase the chance of progression (Table 8) [16]. The criteria listed in Table 9 have been suggested as guidelines for when to admit to the ICU [43].

Treatment of inpatient ethanol withdrawal involves both supportive care and pharmacologic treatment with GABA agonists. Supportive care is similar to that of all patients who present with dehydration, electrolyte imbalance, nausea and vomiting, and comorbid disease [44–46].

Most patients with moderate to severe ethanol withdrawal present with hypovolemia due to the diuretic properties of ethanol and the lack of concurrent hydration. Hypovolemia may be associated with disorders in serum sodium. The most concerning is hyponatremia, which can be more commonly observed in beer drinkers, due to the high volume of fluid [4]. Cautious restoration of a low serum sodium is warranted, with slow correction of no more than 8 to 10 mmol/L per day [47].

Benzodiazepines are first-line inpatient pharmacotherapy [48–52] and are recommended for all types of ethanol withdrawal including seizures, hallucinosis, and DT. Choice among the different agents is guided by duration of action, rapidity of onset, and cost [51]. Most clinicians use the benzodiazepine they are most comfortable with based on the caveats with respect to treating elderly patients and those with liver disease.

The literature for the pharmacologic treatment of ethanol withdrawal has shifted from a fixed schedule to a symptom-triggered approach [53–57]. Evidence suggests that symptom-triggered therapy results in the administration of less total medication and a shorter duration of treatment. One of the benefits of this type of treatment may be more aggressive supportive and nursing care. An example symptom-triggered protocol by Mayo-Smith and coworkers is seen in Table 10 [54].

The suggested protocol by Mayo-Smith and colleagues contains many caveats and exclusions, including no specific guidelines as to how much medication to provide when symptoms are not controlled, exclusion of patients who cannot take oral medications, and exclusion of patients that have comorbid medical, cognitive, and psychiatric disease [53–57]. One small study by Weaver and coworkers observed that in a general medical inpatient population with mild to moderate ethanol withdrawal, there was no difference in outcome between the fixed and symptom-triggered treatment arms [58]. It remains to be demonstrated in other populations whether generalized guidelines can be used. Another concern is the use of symptom-triggered therapy in patients who do not meet appropriateness criteria [59,60]. In a study by Hecksel et al, fewer than half of the patients receiving symptom-triggered therapy met the CIWA-AR appropriateness.

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**Table 5. CIWA-Ar Scale (modified)**

1. Agitation (0–7)
2. Anxiety (0–7)
3. Auditory disturbances (0–7)
4. Clouding of sensorium (0–4)
5. Headache (0–7)
6. Nausea/vomiting (0–7)
7. Paroxysmal sweats (0–7)
8. Tactile disturbances (0–7)
9. Tremor (0–7)
10. Visual disturbances (0–7)

**Table 6. Prerequisites for Outpatient Ethanol Withdrawal Treatment**

- Willingness to participate
- No significant comorbid medical, psychiatric, cognitive, poly-substance abuse issues
- Reliable transportation to outpatient provider clinics
- Ability to take oral medications
- Absence of pregnancy
- Adequate community and or family support

Adapted from reference 25–30.
criteria for this type of therapy (ie, recent ethanol use and intact verbal communication).

Resistant Alcohol Withdrawal Syndrome

One clinical question that remains unclear is that of “resistant alcohol withdrawal syndrome” [61–64]. This syndrome has variable definitions, the most common being lack of control of withdrawal symptoms and/or continued abnormal vital signs in the face of high benzodiazepine doses. It is unclear when to resort to other pharmacological adjuncts when the patient is not responding to conventional doses of benzodiazepines. In the study by Hack and coworkers, the definition of resistant alcohol withdrawal was one in which a total of 50 mg of diazepam was given intravenously in titrated doses over 1 hour [65]. With the caveat of the lack of a specific pharmacological endpoint to add another sedative adjunct to benzodiazepine ethanol withdrawal resistance, numerous medications have been proposed for treatment [66]. The most common include phenobarbital, propofol, and dexmedetomidine. All 3 medications are given as infusions with or without an initial bolus. All require intensive care type monitoring, especially for sedation causing cessation of respiratory drive.

While benzodiazepines affect the frequency of chloride channel opening on the GABA complex, barbiturates increase the duration of the channel opening. The recommended dose of phenobarbital is variable and can range from commonly recommended loading and infusion doses used in treatment of seizures to smaller titrated doses [67,68]. One commonly recommended dose is 10–20 mg/kg IV at a maximum rate of 1 mg/kg minute.

Propofol (2,6 diisopropylphenol) is also a commonly recommended medication for benzodiazepine resistance. Propofol and benzodiazepines exert their effect in a similar manner, having an agonistic effect on GABA receptors, and an antagonistic effect on NMDA receptors. Propofol does not do not exert its effect on the chloride channel similar to benzodiazepine or phenobarbital [69]. Propofol may also have an additional effect as an agonist on glutamate receptors [70]. The patient is given an initial bolus dose of 0.5 mg/kg every 10 seconds titrated to effect, to a total dose of 2.5 mg/kg. The continuous infusion dose for sedation is 25–75 ug/kg/min IV, and higher doses may result in a general anesthetic state [71]. The most common side effects of propofol are again similar to the other commonly used sedatives, including hypotension and respiratory depression. Hypotension can usually be treated with crystalloid IV bolus/infusions and decreasing the drip rate. Propofol has a 3-compartment model of dissipation, allowing for its short effect time. The first phase is that of rapid distribution of the drug from the blood to both the spinal and supraspinal nerve synapses for both GABA and NDMA receptors. This effect should last less than 10 minutes for a clinical sedative effect for a bolus infusion. The second phase is that of rapid clearance of the propofol from the blood compartment taking 30 to 50 minutes for bolus doses. The third phase is that of slow return of the drug from the poorly perfused non-nervous system body tissue into the blood, with a half-life of up to 480 minutes [69].

Dexmedetomidide is a lipophilic imidazole derivative approved for use in 1999. It has a very high affinity for α2 adrenergic receptors and low affinity for α1 receptors. Similar drugs with central α2 activity include clonidine and tetrahydrolzoline, a component

<table>
<thead>
<tr>
<th>Day</th>
<th>Lorazepam</th>
<th>Chlordiazepoxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2 mg po TID</td>
<td>30 mg po TID</td>
</tr>
<tr>
<td>2</td>
<td>2 mg po in AM, 1 mg at noon, 2 mg at bedtime</td>
<td>20 mg po TID</td>
</tr>
<tr>
<td>3</td>
<td>1 mg po TID</td>
<td>15 mg po TID</td>
</tr>
<tr>
<td>4</td>
<td>1 mg po BID</td>
<td>10 mg po TID</td>
</tr>
<tr>
<td>5</td>
<td>1 mg po once daily</td>
<td>10 mg po BID</td>
</tr>
<tr>
<td>6</td>
<td>Stop</td>
<td>Stop</td>
</tr>
</tbody>
</table>

Table 7. Outpatient Treatment

Adapted from reference 37.

<table>
<thead>
<tr>
<th></th>
<th>Delirium Tremens Risk Factors</th>
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</thead>
<tbody>
<tr>
<td>Age older than 30 years</td>
<td></td>
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<tr>
<td>History of previous DTs</td>
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<tr>
<td>Chronic heavy ethanol abuse (not defined)</td>
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<tr>
<td>Concurrent significant illness</td>
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<tr>
<td>Withdrawal symptoms with a still measurable ethanol blood level</td>
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<tr>
<td>Presenting to the medical provider after a long period of abstinence</td>
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Table 8. Delirium Tremens Risk Factors

Adapted from reference 16.
of over-the-counter eye drops (Visine). Clonidine has been used in patients with concurrent opiate and ethanol withdrawal and in patients with hypertension in withdrawal. Dexmedetomidate’s central presynaptic α2 agonistic effects include decreasing norepinephrine release at the locus ceruleus, leading to non-GABA mediated sedation [72]. The result of this type of sedation can be a decrease in autonomic dysfunction (tachycardia and hypertension) and anxiety. Most of the studies on this drug are of the case report or series variety [72,73]. The dose of dexmedetomidate is 1.0 μg/kg bolus, with a continuous infusion of 0.2–1.0 μg/kg/hr. One touted advantage to this drug is respiratory stability, along with simultaneous treatment of co-existing opiate withdrawal. At this time, most case series use the dexmedetomidate as an adjunct drug, along with a benzodiazepine, to combat withdrawal. It remains to be seen if an α agonist can be the sole treatment agent in a GABA- and NMDA-altered alcohol withdrawal patient.

One common clinical question that is asked regards the use of ethanol to treat ethanol withdrawal symptoms. It is thought that the most common form of treating ethanol withdrawal is that of self treatment, without the benefit of medical evaluation [74]. The older medical literature has recommendations using both oral and intravenous ethanol to attempt gradual withdrawal. At this time no ethanol withdrawal clinical practice guidelines recommend its use. Other authorities do not recommend the use of ethanol due the potential of further enabling the underlying ethanol abuse disorder with delay in rehabilitation and continued treatment with essentially a multiorgan toxin (eg, cirrhosis, gastritis, bone marrow suppression) [75,76].

Wernicke’s Encephalopathy, Glucose, and Thiamine

It is well known that patients with chronic ethanol abuse have a high associated incidence of thiamine (vitamin B1) deficiency [77]. The concern is that the antemortem diagnosis of this disease process is difficult and easily missed, possibly resulting in permanent neurological damage (Wernicke’s encephalopathy or Korsakoff syndrome). Therefore, the recommendation has been to give thiamine both acutely and chronically in an attempt to prevent this malady. Furthermore, it is recommended that thiamine be given before glucose in the undifferentiated confused patient, again in order to “avoid” iatrogenic precipitation of Wernicke’s. Therefore, several authors have recommended that the thiamine be given first, before a carbohydrate load (especially glucose), in order to avoid iatrogenic precipitation of Wernicke’s encephalopathy [78]. What is clear is that prolonged use of carbohydrates (loading) without adequate thiamine administration can either precipitate or exacerbate Wernicke’s encephalopathy [78]. There is no proof, or logical metabolic explanation for the acute precipitation of Wernicke’s with

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**Table 9. Indications for ICU Admission for the Treatment of Alcohol Withdrawal**

<table>
<thead>
<tr>
<th>Indications</th>
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<tbody>
<tr>
<td>History of cardiac disease (heart failure, arrhythmia, angina, myocardial ischemia, recent myocardial infarction)</td>
</tr>
<tr>
<td>Hemodynamic instability</td>
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<tr>
<td>Marked acid-base disturbances</td>
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<tr>
<td>Severe electrolyte disturbances requiring aggressive replacement</td>
</tr>
<tr>
<td>Respiratory insufficiency (hypoxia, hypercapnia, severe hypoxia, pneumonia, COPD, asthma)</td>
</tr>
<tr>
<td>Gastrointestinal (GI) pathology (pancreatitis, GI bleeding, hepatic insufficiency, peritonitis)</td>
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<tr>
<td>Persistent hyperthermia (temperature ≥ 39°C/103°F), One study observed that over half of the patients that died of DTs had significant hyperthermia [16].</td>
</tr>
<tr>
<td>Laboratory evidence of rhabdomyolysis</td>
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<tr>
<td>Renal insufficiency with or without increased fluid requirements</td>
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<tr>
<td>Need for frequent or high doses of sedatives or an intravenous infusion to control symptoms</td>
</tr>
</tbody>
</table>

Adapted from reference 43.

**Table 10. Pharmacotherapy Regimens for Alcohol Withdrawal**

Example symptom-triggered protocol: Administer CIWA-Ar and administer 1 of the following if score is > 8 (doses are oral and should be adjusted for parenteral use)

- Chlordiazepoxide 50–100 mg
- Diazepam 10–20 mg
- Lorazepam 2–4 mg

Repeat every hour until score is < 8, then every 4 hours

Example fixed-schedule regimens:

- Chlordiazepoxide, 4 doses of 50 mg, then 8 doses of 25 mg
- Diazepam, 4 doses of 10 mg, then 8 doses of 5 mg
- Lorazepam, 4 doses of 2 mg, then 8 doses of 1 mg


3. Sutton T. Tracts on delirium tremens, on peritonitis, on some other internal inflammatory affections, and on gout. London: T. Underwood; 1813.


CONCLUSION

The exact toxic and metabolic etiology of ethanol withdrawal have yet to be fully elucidated. What is known biochemically about ethanol withdrawal enables the clinician to combat the syndrome with available GABA agonists, NMDA antagonists, and catecholamine antagonists. The clinical diagnosis and treatment of ethanol withdrawal, while at times obvious, can also be very difficult, especially in the face of comorbidities. Various rating scales have been proposed but do not accommodate all presentations of ethanol withdrawal, especially in those patients with comorbidities and polysubstance withdrawal. There also remains some controversy as to the appropriate types of pharmacotherapy for this syndrome; however it is agreed that benzodiazepines are the first-line therapy. There are many suggestions for adjunctive pharmacologic care, and dexmedetomidate may represent a new efficacious treatment opportunity. Overall, the treatment of ethanol abuse and withdrawal is constantly evolving.

Corresponding author: Richard Tovar, MD, Medical College of Wisconsin, Milwaukee, WI 53226.

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