

# In Vino Veritas?

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**A 50-year-old man with a history of mental illness and alcohol abuse is found unconscious in front of his house.**

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**A** 50-year-old man with a history of depression, bipolar disorder, and alcohol abuse presents to the ED after he was discovered unconscious in front of his house. It was unclear if he had fallen or had been assaulted, but there were no external signs of trauma. Upon presentation, patient smelled strongly of alcohol. His initial vital signs were: blood pressure (BP), 68/42 mm Hg; heart rate, 110 beats/min; respiratory rate, 20 breaths/min; temperature, afebrile. Oxygen saturation was 96% on room air. On physical examination, he was awake but confused. He denied being in pain and stated that he drank “half a bottle of wine” earlier that evening. The patient further admitted to smoking a pack of cigarettes daily and drinking alcohol, but denied illicit drug use. There was a small laceration on the right middle finger, an abrasion on the right shoulder, a 5-cm ecchymotic area on his left lower back, and striking generalized diffuse blanching erythema of the skin of his face, chest, and back. Based on persistent hypotension, a bedside focused assessment with sonography for trauma examination was performed, which showed no intra-abdominal fluid.

### How can alcohol use affect trauma-induced hypotension?

Alcohol consumption among trauma patients is very common, with studies reporting a use rate of 47% at the time of injury,<sup>1</sup> along with a high level of substance dependence in this population.<sup>2</sup> Intoxication adds a layer of obfuscation to evaluating an injury by impairing the patient’s ability to feel pain, localize injury, and generate a normal response to hypotension.

Animal studies of acute hemorrhage have found that acute alcohol intoxication inhibits the normal release of the vasoactive agents epinephrine, norepinephrine, and vasopressin.<sup>3</sup> Ethanol also inhibits the secretion of antidiuretic hormone, resulting in an impaired ability to expand intravascular volume and increasing fluid and packed RBC requirements in intoxicated trauma patients.<sup>3</sup>

In addition to the effect of ethanol itself, other alcohol-related issues can cause hypotension in these patients. These include adrenal failure, thiamine deficiency, hy-

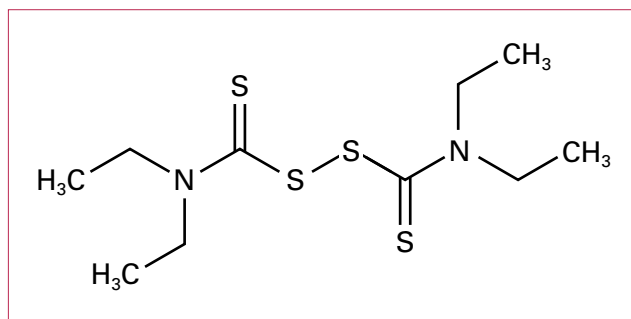
poglycemia, dehydration, pancreatitis, gastrointestinal bleeding, alcoholic cardiomyopathy, sepsis, or concurrent drug use.

### Case continuation

During the workup, the patient vomited a large amount of wine-colored emesis, which was negative for gastric occult blood. His systolic BP slowly increased after aggressive crystalloid infusion. When stable, he was taken for a computed tomography scan, which revealed normal brain, cervical spine, chest, abdomen, and pelvis. Although there was no history of drug overdose, a call to a local pharmacy revealed that patient had been prescribed the antipsychotic olanzapine (Zyprexa), fluoxetine (Prozac), and disulfiram (Antabuse).

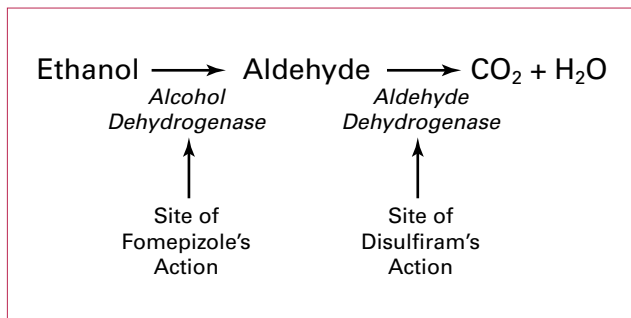
### What is disulfiram, and what are its clinical effects?

The effects of disulfiram (bis[diethylthiocarbamoyl] disulfide) (Figure 1) were first observed in 1937 when rubber workers exposed to the chemical experienced unpleasant side effects after drinking alcohol.<sup>4</sup> It was approved in 1951 by the US Food and Drug Administration under the brand name Antabuse as an aversive therapy to treat alcoholism.<sup>4</sup>



**Figure 1** Molecular structure of disulfiram (bis[diethylthiocarbamoyl] disulfide)

Disulfiram inhibits aldehyde dehydrogenase, preventing the second step in alcohol metabolism. This effect results in the accumulation of acetaldehyde (Figure 2). If a patient ingests any form of ethanol while taking disulfiram,



**Figure 2** Disulfiram inhibits acetaldehyde dehydrogenase; treatment with fomepizole inhibits alcohol dehydrogenase.

ram—including inadvertent ingestion (eg, cough syrups, sauces)—the accumulation of acetaldehyde causes multiple adverse effects, known as “disulfiram-ethanol syndrome.”

Symptom severity depends on the amount of alcohol ingested and includes headache, flushing of the skin, sweating, nausea, vomiting, palpitations, dyspnea, and hypotension.<sup>5,6,7</sup> Severe complications include dysrhythmias, myocardial infarction, acute congestive heart failure, coma, convulsions, and death.<sup>6,7</sup> The risk of an adverse effect may last days or weeks after the last dose of disulfiram. Therefore, careful patient selection for treatment of alcoholism with disulfiram is very important, as it requires very motivated patients who will be adherent with the treatment regimen.<sup>8</sup>

### What is the treatment for a patient with a disulfiram-ethanol reaction?

Supportive care and fluid resuscitation are often sufficient to treat disulfiram-ethanol-associated hypotension. If a vasopressor is indicated, norepinephrine is preferred over dopamine.<sup>9</sup> (Dopamine requires conversion by dopamine beta  $\beta$ -hydroxylase to form norepinephrine to exert its effects, and this enzyme is inhibited by diethyl-dithiocarbamate, a metabolite of disulfiram.<sup>9</sup>)

In cases of severe disulfiram-ethanol reactions, fomepizole (4-methylpyrazole, 4-MP) may stop or slow progression of illness in patients with elevated blood ethanol concentrations.<sup>10</sup> Fomepizole inhibits alcohol dehydrogenase (the first metabolic step), and consequently ethanol’s entry into its metabolic pathway (Figure 2).

### What other agents cause similar reactions when combined with ethanol?

Other xenobiotics, including cephalosporins, chloramphenicol, griseofulvin, nitrofurantoin, sulfonyleureas, and chloral hydrate, can lead to a disulfiram-like reaction when combined with alcohol. In addition, coprine from *Coprinus atramentarius*, the so-called inky cap mushroom, can lead to a disulfiram-like reaction. This most commonly occurs with ingestion of alcohol following a meal containing this otherwise edible mushroom. Similar reactions have also been described in patients with exposures dithiocarbamate pesticides and thiram fungicides combined with ethanol consumption—the latter observed in golfers over 50 years ago.<sup>11</sup>

### Case Concluded

Since the patient’s BP improved overnight with supportive care, his course in the intensive care unit was brief. The following day, he was transferred to the floor and was seen by a representative from substance abuse services. He was warned against using alcohol while on disulfiram therapy, and was discharged on hospital day 3 with primary care and psychiatric follow up.

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