



ToxTalks:

A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

In Partnership with the UVA Division of Medical Toxicology – Department of Emergency Medicine

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Caffeine

Background

Caffeine is a methylxanthine and natural stimulant found in the leaves, seeds, and fruits of over 60 plant species. It is the most widely consumed psychoactive substance worldwide and is generally safe at typical dietary doses. However, the increasing availability of highly concentrated caffeine products including pills, pre-workout supplements, and energy drinks has led to a growing number of clinically significant poisonings.

Caffeine exposure is nearly universal, with most adults consuming between 100 and 300 mg daily through coffee, tea, and other beverages. Most cases of clinically significant toxicity occur in the setting of intentional overdose, misuse of supplements, or accidental ingestion of concentration formulations. Pediatric exposures most often occur due to exploratory ingestion of tablets or concentrated liquid caffeine products, while adolescents and young adults represent a growing population of energy drink and supplement-related toxicity. Although fatalities remain rare, severe poisonings are well-documented and typically involve large, concentrated ingestions.

Mechanism of Action

Caffeine's primary mechanism is blockade of adenosine receptors, which removes inhibition of neurotransmitter release leading to increased sympathetic tone and circulating catecholamines. At higher serum concentrations, caffeine inhibits phosphodiesterase and causes accumulation of intracellular cyclic AMP, further enhancing myocardial contractility and metabolic activity. High concentrations of epinephrine and norepinephrine in the



Caffeine supplement available from [Target](#)



Blue Ridge Poison Center at UVA Health | 1-800-222-1222

bloodstream leads to tachycardia, hypertension, tremor, and metabolic abnormalities and elevated intracellular calcium leads to cardiac excitability and seizure risk. Together, these mechanisms cause a clinical picture closely resembling theophylline toxicity characterized by sympathetic overactivation, metabolic derangements, and dysrhythmias. In severe toxicity, there is beta-2 adrenergic receptor agonist effects that can lead to systemic vasodilation and hypotension.

Pharmacokinetics and Toxicokinetics

Caffeine is rapidly absorbed from the gastrointestinal tract, with peak serum concentrations typically occurring within 30 to 60 minutes of ingestion. It is both lipid and water soluble, with an oral bioavailability of almost 100%. Liquid and powdered formulations may be absorbed even more quickly, contributing to sudden onset of symptoms in large ingestions. Caffeine also readily crosses the blood-brain barrier, placenta, and into breast milk. It is primarily hepatically metabolized and produces paraxanthine, theobromine, and theophylline. Under normal conditions, the elimination half-life ranges from 3 to 7 hours, but this may be significantly prolonged in overdose, pregnancy, liver disease, and neonates. In massive ingestions, saturation of metabolism and altered clearance can lead to prolonged toxicity and delayed clinical deterioration. The relatively low protein binding and small molecular weight of caffeine make it amenable to extracorporeal removal, which may be considered in severe poisoning.

Clinical Manifestations

The clinical presentation of caffeine toxicity reflects progressive sympathetic overactivation and metabolic stimulation. Patients with mild toxicity typically present with anxiety, restlessness, tremor, palpitations, nausea, and insomnia. As toxicity worsens, persistent tachycardia, agitation, hypertension, diaphoresis, and electrolyte abnormalities such as hypokalemia become more prominent. Severe toxicity can manifest as seizures, metabolic acidosis, rhabdomyolysis, life-threatening ventricular dysrhythmias, and hemodynamic instability. Seizures may occur abruptly and without warning in massive ingestions. Ventricular dysrhythmias represent the most dangerous complication and are the leading cause of death in caffeine poisoning. Both the ventricular dysrhythmias and systemic vasodilation in severe toxicity can lead to hypotension.

Diagnosis and Management

Diagnosis is primarily clinical and relies on a thorough history including current medications and supplements, and recognition of the hyperadrenergic toxicity. Hypokalemia is the most frequently observed laboratory abnormality resulting from beta-adrenergic stimulation and intracellular potassium shifts. Hyperglycemia, lactic acidosis, hypophosphatemia, and elevated creatine kinase can also be seen. Serum caffeine concentrations can be measured in specialized laboratories but are not necessary for diagnosis or management.

Management of caffeine toxicity centers on supportive care, control of sympathetic excess, and prevention of life-threatening complications. Patients should be placed on continuous cardiac monitoring with early establishment of intravenous access. Airway protection and hemodynamic stabilization should be prioritized in patients with severe agitation, seizures, or cardiovascular instability.

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Activated charcoal may be considered in recent large ingestions if the airway is protected, as caffeine binds well to charcoal and enterohepatic recirculation may prolong absorption in large overdoses. Intravenous fluids are important to support renal clearance, correct dehydration, and reduce the risk of rhabdomyolysis and [hypotension](#). Electrolyte abnormalities, especially hypokalemia, should be corrected because low potassium increases the risk of ventricular dysrhythmias. Benzodiazepines are the mainstay of treatment and should be administered early to control agitation, seizures, and sympathetic overactivity. Hemodialysis should be considered in severe cases involving massive ingestion, refractory dysrhythmias, persistent seizures, severe metabolic acidosis, or hemodynamic instability.

For assistance 24/7, please consult the Blue Ridge Poison Center: 1-800-222-1222. Healthcare providers may also use the dedicated HCP line: 1-800-451-1428.

