# Neurotoxic Emergencies

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**KEYWORDS**

• Poisoning • Emergency • Overdose • Neurology • Toxicology

The symptoms and effects delineating a neurotoxic emergency vary depending on the viewpoint of the clinician. In general, agents causing acute life-threatening conditions have rapid mechanisms that severely disrupt major organ systems. This article focuses on agents causing rapid decompensation to a potentially life-threatening condition. The majority of these agents affect the central nervous system (CNS), thus the article is structured based on CNS effects: drug-induced and toxin-induced seizures, acute depressed mental status, and acute excited mental status. The final section highlights selected agents with primarily peripheral effects that meet the same criteria for an acute life-threatening condition.

A wide variety of poisons, toxins, drugs, chemicals, industrial agents, pesticides, and environmental agents have the potential to cause emergent neurotoxic effects. To avoid confusion, the authors use the term "xenobiotic" when discussing the various causative neurotoxic agents. A xenobiotic is a pharmacologically, endocrinologically, or toxicologically active substance not endogenously produced and therefore foreign to the organism.[1]

Neurotoxic xenobiotics produce symptoms in the victim through a wide array of different mechanisms, as shown in **Table 1**. Neurotoxic emergencies frequently affect the CNS through effects on neurotransmitters; therefore, much of this discussion focuses on the actions of specific neurotransmitters.

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**Table 1**
**Mechanisms of neurotoxic xenobiotics**

| Effect | Specific Mechanism |
|---|---|
| Cellular | Oxidative stress (free radicals, nucleophiles, or electrophiles)<br>Alteration of membrane integrity<br>Disruption of energy metabolism and/or regulation<br>Altered regulation of gene expression<br>Altered protein production<br>Disruption of intracellular ion homeostasis |
| Metabolic | Stimulation or inhibition of enzymatic function<br>Mimicking the actions of nutrients, hormones, or neurotransmitters |
| Neurotransmitter | Stimulation or blockade neurotransmitter receptors<br>Altered release, uptake, and/or storage of neurotransmitters<br>Altered neurotransmitter production or metabolism |

## DRUG-INDUCED AND TOXIN-INDUCED SEIZURES

Seizures are a manifestation of many drug and toxin exposures or withdrawal syndromes. Some overdoses may include seizure amongst a myriad of other organ system toxicities, whereas others induce seizures as the primary manifestation of toxicity. Drug-induced and toxin-induced seizures (DTS) are typically generalized seizures, with status epilepticus occurring in approximately 4% to 10% of cases.[2,3] The epidemiology and incidence of DTS are not well known because seizures are not always tracked by regional poison centers. The California Poison Control Systems have provided the best view of agents most frequently implicated in DTS through a series of investigations over the last 17 years.[2–4] Over this time period, the proportion of DTS from tricyclic antidepressants (TCA), stimulants, and theophylline fell while anticholinergic antihistamines and isoniazid remained fairly constant. Their most recent prospective series of DTS found antidepressants were most common (33%) followed by stimulants (15%), antiepileptics (12%), and anticholinergic antihistamines (10%).[2] Of note, citalopram and escitalopram were absent from their 1994 and 2003 series yet comprised 8% of cases in the most recent review.[2] A comprehensive review of toxin-related seizures was recently published.[5] This section discusses some of the more common and newer pharmaceuticals implicated in DTS.

### *Psychiatric Agents*

#### *Tricyclic antidepressants*

TCAs have multiple pharmacologic effects including serotonin and norepinephrine reuptake inhibition, central and peripheral anticholinergic and antihistamine effects, peripheral $\alpha_1$ antagonism, and fast sodium channel blockade.[6] A recent series documenting prevalence of clinical outcomes in amitriptyline overdose reported seizures in 6%, hypotension in 10%, coma in 29%, and wide QRS complex or ventricular dysrhythmia in 30%.[7] Acidemia from seizures or hypotension can decrease TCA protein binding, resulting in worsening toxicity.[8] Seizures are treated primarily with benzodiazepines. Boluses of sodium bicarbonate are useful for the cardiovascular effects of TCA poisoning by providing a sodium bolus as well as raising the serum pH.[6,8]

#### *Bupropion*

Bupropion is a mixed dopamine and norepinephrine reuptake inhibitor, well known to lower the seizure threshold in therapeutic doses and induce seizures in overdose.[9] Of all drug-induced seizures reported to a regional poison center, 14.9% were due to bupropion.[2] Another poison center review of bupropion overdoses reported