

TABLE 473e-4 PATHOPHYSIOLOGIC FEATURES AND TREATMENT OF SPECIFIC TOXIC SYNDROMES AND POISONINGS (CONTINUED)

Physiologic Condition, Causes	Examples	Mechanism of Action	Clinical Features	Specific Treatments
Cyclic antidepressants	Amitriptyline, doxepin, imipramine	Inhibition of $\alpha$ -adrenergic, dopaminergic, GABA-ergic, histaminergic, muscarinic, and serotonergic receptors; inhibition of sodium channels (see membrane-active agents); inhibition of norepinephrine and serotonin reuptake	Physiologic depression (Table 473e-2), seizures, tachycardia, cardiac conduction delays (increased PR, QRS, JT, and QT intervals; terminal QRS right-axis deviation) with aberrancy and ventricular tachydysrhythmias; anticholinergic toxidrome (see above)	Hypertonic sodium bicarbonate (or hypertonic saline) for ventricular tachydysrhythmias associated with QRS prolongation. Use of phenytoin is controversial. Avoid class IA, IC, and III antiarrhythmics. IV emulsion therapy may be beneficial in some cases.
Cholinergics				
Acetylcholinesterase inhibitors	Carbamate insecticides (aldicarb, carbaryl, propoxur) and medicinals (neostigmine, physostigmine, tacrine); nerve gases (sarin, soman, tabun, VX); organophosphate insecticides (diazinon, chlorpyrifos-ethyl, malathion)	Inhibition of acetylcholinesterase leading to increased synaptic acetylcholine at muscarinic and nicotinic cholinergic receptor sites	Physiologic depression (Table 473e-2). Muscarinic signs and symptoms: seizures, excessive secretions (lacrimation, salivation, bronchorrhea and wheezing, diaphoresis), and increased bowel and bladder activity with nausea, vomiting, diarrhea, abdominal cramps, and incontinence of feces and urine. Nicotinic signs and symptoms: hypertension, tachycardia, muscle cramps, fasciculations, weakness, and paralysis. Death is usually due to respiratory failure. Cholinesterase activity in plasma and red cells is <50% of normal in acetylcholinesterase inhibitor poisoning.	Atropine for muscarinic signs and symptoms; 2-PAM, a cholinesterase reactivator, for nicotinic signs and symptoms due to organophosphates, nerve gases, or an unknown anticholinesterase
Muscarinic agonists	Bethanechol, mushrooms ( <i>Boletus</i> , <i>Clitocybe</i> , <i>Inocybe</i> spp.), pilocarpine	Stimulation of CNS and postganglionic parasympathetic cholinergic (muscarinic) receptors		
Nicotinic agonists	Lobeline, nicotine (tobacco)	Stimulation of preganglionic sympathetic and parasympathetic and striated muscle (neuromuscular junction) cholinergic (nicotine) receptors		
Sedative-hypnotics <sup>b</sup>				
Anticonvulsants	Carbamazepine, ethosuximide, felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, phenytoin, tiagabine, topiramate, valproate, zonisamide	Potentiation of the inhibitory effects of GABA by binding to the neuronal GABA-A chloride channel receptor complex and increasing the frequency or duration of chloride channel opening in response to GABA stimulation. Baclofen and, to some extent, GHB act at the GABA-B receptor complex. Meprobamate, its metabolite carisoprodol, felbamate, and orphenadrine antagonize NDMA excitatory receptors. Ethosuximide, valproate, and zonisamide decrease conduction through T-type calcium channels. Valproate decreases GABA degradation, and tiagabine blocks GABA reuptake. Carbamazepine, lamotrigine, oxcarbazepine, phenytoin, topiramate, valproate, and zonisamide slow the rate of recovery of inactivated sodium channels. Some agents also have $\alpha_2$ agonist, anticholinergic, and sodium channel-blocking activity (see above and below).	Physiologic depression (Table 473e-2), nystagmus. Delayed absorption can occur with carbamazepine, phenytoin, and valproate. Myoclonus, seizures, hypertension, and tachyarrhythmias can occur with baclofen, carbamazepine, and orphenadrine.	Benzodiazepines, barbiturates, or propofol for seizures.
Barbiturates	Short-acting: butabarbital, pentobarbital, secobarbital			Hemodialysis and hemoperfusion may be indicated for severe poisoning by some agents (see "Extracorporeal Removal," in text).
Benzodiazepines	Long-acting: phenobarbital, primidone Ultrashort-acting: estazolam, midazolam, temazepam, triazolam Short-acting: alprazolam, flunitrazepam, lorazepam, oxazepam Long-acting: chlordiazepoxide, clonazepam, diazepam, flurazepam Pharmacologically related agents: zaleplon, zolpidem		Tachyarrhythmias can also occur with chloral hydrate. AGMA, hypernatremia, hyperosmolality, hyperammonemia, chemical hepatitis, and hypoglycemia can be seen in valproate poisoning. Carbamazepine and oxcarbazepine may produce hyponatremia from SIADH.	See above and below for treatment of anticholinergic and sodium channel (membrane)-blocking effects.
GABA precursors	$\gamma$ -Hydroxybutyrate (sodium oxybate; GHB), $\gamma$ -butyrolactone (GBL), 1,4-butanediol		Some agents can cause anticholinergic and sodium channel (membrane) blocking effects (see above and below).	
Muscle relaxants	Baclofen, carisoprodol, cyclobenzaprine, etomidate, metaxalone, methocarbamol, orphenadrine, propofol, tizanidine and other imidazoline muscle relaxants			

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