this vapor also can cause eye pain and nausea. Exocrine glands in the nose, mouth, and pharynx are next exposed to the vapor, and cholinergic overload here causes increased secretions, rhinorrhea, excess salivation, and drooling. Toxin then interacts with exocrine glands in the upper airway, causing bronchorrhea, and with bronchial smooth muscle, causing bronchospasm. This combination of events can result in hypoxia.

Once the victim has inhaled, vapor can passively cross the alveolar-capillary membrane, enter the bloodstream, and incidentally and asymptomatically inhibit circulating cholinesterases, particularly free butyrylcholinesterase and erythrocyte acetylcholinesterase, both of which can be assayed. Unfortunately, the results of this assay may not be easily interpretable without a baseline, since cholinesterase levels vary enormously between individuals and over time in an individual, healthy patient.

Usually the first organ system to become symptomatic from bloodborne nerve agent exposure is the gastrointestinal tract, where cholinergic overload causes abdominal cramping and pain, nausea, vomiting, and diarrhea. After the gastrointestinal tract becomes involved, nerve agents will affect the heart, distant exocrine glands, muscles, and brain. Because there are cholinergic synapses on both the vagal (parasympathetic) and sympathetic sides of the autonomic input to the heart, one cannot predict how heart rate and blood pressure will change once intoxication has occurred. Remote exocrine activity will include oversecretion in the salivary, nasal, respiratory, and sweat glands—the patient will be "wet all over." Bloodborne nerve agents will overstimulate neuromuscular junctions in skeletal muscles, causing fasciculations followed by frank twitching. If the process goes on long enough, ATP in muscles will eventually be depleted and flaccid paralysis will ensue.

In the brain, since the cholinergic system is so widely distributed, bloodborne nerve agents will, in sufficient doses, cause rapid loss of consciousness, seizures, and central apnea leading to death within minutes. If respiration is supported, status epilepticus that does not respond to usual anticonvulsants may ensue (Chap. 445). If status epilepticus persists, neuronal death and permanent brain dysfunction may occur. Even in mild nerve-agent intoxication, patients may recover but may experience weeks of irritability, sleep disturbance, and nonspecific neurobehavioral manifestations.

The time from exposure to development of the full-blown cholinergic crisis after nerve agent vapor inhalation can be minutes or even seconds, yet there is no depot effect. Since nerve agents have a short circulating half-life, if the patient is supported and, ideally, treated with antidotes, improvement should be rapid, without subsequent deterioration.

Liquid exposure to nerve agents results in different speeds and orders of symptom onset. A nerve agent on intact skin will partially evaporate and partially begin to travel through the skin, causing localized sweating and then, when it encounters neuromuscular junctions, localized fasciculations. Once in muscle, the agent will cross into the circulation and cause gastrointestinal discomfort, respiratory distress, heart rate changes, generalized fasciculations and twitching, loss of consciousness, seizures, and central apnea. The time course will be much longer than with vapor inhalation; even a large, lethal droplet can take up to 30 min to exert an effect, and a small, sublethal dose could progressively take effect over 18 h. Clinical worsening that occurs hours after treatment has started is far more likely with liquid than with vapor exposure. In addition, miosis, which is practically unavoidable with vapor exposure, is not always present with liquid exposure and may be the last manifestation to develop in this situation; such a delay is due to the relative insulation of the pupillary muscle from the systemic circulation.

Unless the cholinesterase is reactivated by specific therapy (oximes), its binding to the enzyme is essentially irreversible. Erythrocyte acetylcholinesterase activity recovers at ~1% per day. Plasma butyrylcholinesterase recovers more quickly and is a better guide to recovery of tissue enzyme activity.

TREATMENT NERVE AGENT INTOXICATION

Acute nerve agent poisoning is treated by decontamination, respiratory support, and three antidotes: an anticholinergic, an oxime, and an anticonvulsant (Table 262e-3). In acute cases, all these forms of therapy may be given simultaneously.

DECONTAMINATION

Decontamination of a vapor is formally unnecessary; however, in the Tokyo subway attack, sarin vapor trapped in patients' clothing caused miosis in 10% of emergency personnel. Removal of clothing would have prevented most of these instances. Expedient decontamination methods for CWAs are available. For soap and water decontamination, the skin surface and hair are washed in warm or tepid water at least three times, or the exposed individual showers for 2 min, washing with soap and rinsing. The rapid physical removal

TABLE 262e-3 ANTIDOTE RECOMMENDATIONS AFTER EXPOSURE TO NERVE AGENTS

	Antidotes		
Patient's Age	**Mild/Moderate Effects[a]**	**Severe Effects[b]**	**Other Treatment**
Infants (0–2 years)	Atropine (0.05 mg/kg IM or 0.02 mg/kg IV) *and* 2-PAM Cl (15 mg/kg IM or IV slowly)	Atropine (0.1 mg/kg IM or 0.02 mg/kg IV) *and* 2-PAM chloride (25 mg/kg IM or 15 mg/kg IV slowly)	Assisted ventilation after antidotes for severe exposure
Child (2–10 years)	Atropine (1 mg IM or 0.02 mg/kg IV) *and* 2-PAM Cl[c] (15 mg/kg IM or IV slowly)	Atropine (2 mg IM or 0.02 mg/kg IV) *and* 2-PAM chloride[c] (25 mg/kg IM or 15 mg/kg IV slowly)	Repeat atropine (2 mg IM, or 1 mg IM for infants) at 5- to 10-min intervals until secretions have diminished and breathing is comfortable *or* airway resistance has returned to nearly normal.
Adolescent (>10 years)	Atropine (2 mg IM or 0.02 mg/kg IV) *and* 2-PAM Cl[c] (15 mg/kg IM or IV slowly)	Atropine (4 mg IM or 0.02 mg/kg IV) *and* 2-PAM Cl[c] (25 mg/kg IM or 15 mg/kg IV slowly)	
Adult	Atropine (2–4 mg IM or IV) *and* 2-PAM Cl (600 mg IM or 15 mg/kg IV slowly)	Atropine (6 mg IM) *and* 2-PAM Cl (1800 mg IM or 15 mg/kg IV slowly)	Phentolamine for 2-PAM-induced hypertension (5 mg IV for adults; 1 mg IV for children) Diazepam for convulsions (0.2–0.5 mg IV for infants <5 years; 1 mg IV for children >5 years; 5 mg IV for adults).
Elderly, frail	Atropine (1 mg IM) *and* 2-PAM Cl (10 mg/kg IM or 5–10 mg/kg IV slowly)	Atropine (2–4 mg IM) and 2-PAM Cl (25 mg/kg IM or 5–10 mg/kg IV slowly)	

[a]Mild/moderate effects include localized sweating, muscle fasciculations, nausea, vomiting, weakness, and dyspnea. [b]Severe effects include unconsciousness, convulsions, apnea, and flaccid paralysis. [c]If the calculated dose exceeds the adult IM dose, adjust accordingly.

Abbreviation: 2-PAM Cl, 2-pralidoxime (or Protopam®) chloride.

Source: State of New York, Department of Health.