REGION 11 CHICAGO EMS SYSTEM PROTOCOL	Title: Acetylcholinesterase Inhibitors Exposure – BLS/ALS
	Section: Toxins and Environmental
	Approved: EMS Medical Directors Consortium
	Effective: August 15, 2024

ACETYLCHOLINESTERASE INHIBITORS EXPOSURE (CARBAMATES, NERVE AGENTS, ORGANOPHOSPHATES) – BLS/ALS

I. PATIENT CARE GOALS

1. Rapid recognition of the signs and symptoms of confirmed or suspected acetylcholinesterase inhibitor (AChEI) agents such as carbamates, nerve agents, or organophosphates exposure followed by expeditious and repeated administration of atropine, the primary antidote.

2. Carbamates and organophosphates are commonly active agents in commercial insecticides.

3. Accidental carbamate exposure rarely requires treatment.

4. Activate HAZMAT response to evaluate any potential chemical exposure.

II. PATIENT PRESENTATION

Acetylcholinesterase Inhibitors may include nerve agents, weapons of mass destruction (WMD), carbamate organophosphate, or insecticide pesticide

A. Inclusion Criteria

1. 'DUMBELS' is a mnemonic tool used to describe the signs and symptoms of acetylcholinesterase inhibitor agent poisoning. All patient age groups are included where the signs and symptoms exhibited are consistent with the toxidrome of 'DUMBELS':

    a. **D**iarrhea
    b. **U**rination
    c. **M**iosis/Muscle weakness
    d. **B**ronchospasm/Bronchorrhea/Bradycardia (the killer Bs)
    e. **E**mesis
    f. **L**acrimation
    g. **S**alivation/Sweating

B. Exclusion Criteria

None

III. PATIENT MANAGEMENT

A. Assessment

1. Don the appropriate PPE.

2. Remove the patient's clothing and wash the skin with soap and warm water.

    a. Acetylcholinesterase inhibitor agents can be absorbed through the skin.
    b. Contaminated clothing can provide a source of continued exposure to the toxin.

3. Rapidly assess the patient's respiratory status, mental status, and pupillary status.

4. Administer the antidote atropine immediately for confirmed or suspected acetylcholinesterase inhibitor agent exposure.

5. Administer oxygen as appropriate with a target of achieving 94–98% saturation and provide airway management.

6. Establish intravenous access, if possible.

7. Apply a cardiac monitor, if available.

8. The heart rate may be normal, bradycardic, or tachycardic.

9. Clinical improvement should be based upon the drying of secretions and easing of respiratory effort rather than heart rate or pupillary response.

10. Continuous and ongoing patient reassessment is critical.

B. Patient Symptoms

1. Acetylcholinesterase inhibitor agents are highly toxic chemical agents and can be rapidly fatal.

2. Patients with low-dose chronic exposures may have a more delayed presentation of symptoms.

3. Antidotes (atropine and pralidoxime) are effective if administered before circulation fails.

4. The patient may develop:

    a. Miosis (pinpoint pupils)
    b. Bronchospasm
    c. Bradycardia
    d. Vomiting
    e. Excessive secretions in the form of:
        i. Tearing

ii. Salivation
iii. Rhinorrhea
iv. Diarrhea
v. Urination
vi. Bronchorrhea

5. Penetration of an acetylcholinesterase inhibitor agent into the central nervous system (CNS) will cause:

   a. Headache
   b. Confusion
   c. Generalized muscle weakness
   d. Seizures
   e. Lethargy or unresponsiveness

6. Estimated level of exposure based upon signs and symptoms:

   a. Mild
      i. Miosis alone (while this is a primary sign in vapor exposure, it may not be present is all exposures)
      ii. Miosis and severe rhinorrhea
   b. Mild to moderate (in addition to symptoms of mild exposure)
      i. Localized swelling
      ii. Muscle fasciculations
      iii. Nausea and vomiting
      iv. Weakness
      v. Shortness of breath
   c. Severe (in addition to symptoms of mild to moderate exposure)
      i. Unconsciousness
      ii. Convulsions
      iii. Apnea or severe respiratory distress requiring assisted ventilation
      iv. Flaccid paralysis

7. Onset of symptoms can be immediate with an exposure to a large amount of the acetylcholinesterase inhibitor.

   a. There is usually an asymptomatic interval of minutes after liquid exposure before these symptoms occur.
   b. Effects from vapor exposure occur almost immediately.

8. Signs and symptoms with large acetylcholinesterase inhibitor agent exposures (regardless of route):

   a. Sudden loss of consciousness
   b. Seizures

c. Copious secretions
d. Apnea
e. Death

9. Obtain an accurate exposure history (as patient may become unconscious before arrival at the Emergency Department):

   a. Time of ingestion or exposure
   b. Route of exposure
   c. Quantity of medication or toxin taken (safely collect all possible medications or agents).
   d. Alcohol or other substance use or ingestions.
   e. Pertinent cardiovascular history or other prescribed medications for underlying disease.

10. The patient can manifest any of the signs and symptoms of the 'DUMBELS' toxidrome based on the route of exposure, agent involved, and concentration of the agent:

    a. Vapor exposures will have a direct effect on the eyes and pupils causing miosis.
    b. Patients with isolated skin exposures will have normally reactive pupils.
    c. Certain acetylcholinesterase inhibitor agents can place the patient at risk for both a vapor and skin exposure.

C. Treatment and Interventions

1. Medications:

   a. Atropine
      i. Atropine is the primary antidote for organophosphate, carbamate, or nerve agent exposures. Repeated doses should be administered liberally to patients who exhibit signs and symptoms of exposure or toxicity.
      ii. Atropine may be provided in multi-dose vials, pre-filled syringes, or autoinjectors.

   b. Pralidoxime chloride (2-PAM)
      i. Pralidoxime chloride is a secondary treatment and should be given concurrently to reactivate acetylcholinesterase.
      ii. Pralidoxime chloride may be provided in a single dose vial, pre-filled syringes, or auto-injectors.
      iii. Auto-injectors typically contain 600 mg of pralidoxime chloride.
      iv. To be beneficial to the patient, a dose of pralidoxime chloride should be administered shortly after the nerve agent or organophosphate poisoning as it has minimal clinical effect if administration is delayed.

   c. Benzodiazepines

i. Benzodiazepines are administered as an anticonvulsant for those patients who exhibit seizure activity (see Seizures – ALS Protocol for doses and routes of administration).
ii. Benzodiazepines may be provided in multi-dose or single-dose vials, pre-filled syringes, or auto-injectors.
iii. CANA® (Convulsive Antidote Nerve Agent) is a commercially available auto-injector that contains 10 mg of diazepam.

d. Duodote®
   i. A commercially available auto-injector of nerve agent/organophosphate antidote.
   ii. Duodote® is one auto-injector that contains 2.1 mg of atropine and 600 mg of pralidoxime chloride.

e. ATNAA® (Antidote Treatment Nerve Agent Auto-injector)
   a. An auto-injector of nerve agent/organophosphate antidote that is typically in military supplies
   b. ATNAA® is one auto-injector that contains 2.1 mg of atropine and 600 mg of pralidoxime chloride
   c. ATNAA® may be seen in civilian supplies assets when Duodote® is unavailable or in short supply

f. CHEMPACK
   i. Federal cache of nerve agent antidotes that is managed by the Centers for Disease Control and Prevention (CDC) and offered to states that voluntarily agree to maintain custody and security of CHEMPACK assets.
   ii. These are forward-deployed at sites determined by states that are part of the program such as hospitals and EMS centers.
   iii. Deployment of CHEMPACKs is reserved for events where the nerve agent/organophosphate exposure will deplete the local or regional supply of antidotes.
   iv. There are two types of CHEMPACK containers:
      A. EMS Containers: CHEMPACK assets for EMS contain a large portion of autoinjectors for rapid administration of antidotes by EMS clinicians of all levels of licensure/certification. They contain enough antidote to treat roughly 454 patients.
      B. Hospital Containers: CHEMPACK assets contain a large portion of multidose vials and powders for reconstitution — they contain enough antidote to treat roughly 1,000 patients.

2. Medication Administration:

a. Atropine, in large and potentially multiple doses, is the antidote for an acetylcholinesterase inhibitor agent poisoning.
b. Atropine should be administered immediately followed by repeat doses until the patient's secretions resolve.

c. Pralidoxime chloride (2-PAM) is a secondary treatment and, when possible, should be administered concurrently with atropine.
d. The stock of atropine and pralidoxime chloride available to EMS clinicians is usually not sufficient to fully treat a patient with an acetylcholinesterase inhibitor agent exposure; however, EMS clinicians should initiate the administration of atropine and, if available, pralidoxime chloride.
e. Seizures should be treated with benzodiazepines.
f. The patient should be emergently transported to the closest appropriate medical facility as directed by medical direction.

3. Recommended Doses (see dosing tables below). The medication dosing tables that are provided below are based upon the severity of the clinical signs and symptoms exhibited by the patient. There are several imperative factors to note:

   a. For organophosphate or severe acetylcholinesterase inhibitor agent exposure, the required dose of atropine necessary to dry secretions and improve the respiratory status may exceed 20 mg. Atropine should be administered rapidly and repeatedly until the patient's clinical symptoms diminish. Atropine must be given until the acetylcholinesterase inhibitor agent has been metabolized.
   b. Because Duodote® auto-injectors contain pralidoxime chloride, they should not be used for additional dosing of atropine beyond the recommended administered dose of pralidoxime chloride.
   c. All the medications below can be administered intravenously in the same doses cited for the intramuscular route. However, due to the rapidity of onset of signs, symptoms, and potential death from acetylcholinesterase inhibitor agents, intramuscular administration is highly recommended to eliminate the inherent delay associated with establishing intravenous access.
   d. The antidotes can be administered via the intraosseous route. However, due to the rapidity of onset of signs, symptoms, and potential death from acetylcholinesterase inhibitor agents, intramuscular administration remains the preferable due to the inherent delay associated with establishing intraosseous access and the limited use of this route of administration for other medications.

C. Patient Safety Considerations

1. Continuous and ongoing patient reassessment is critical.

2. Clinical response to treatment is demonstrated by the drying of secretion and the easing of respiratory effort.

3. Initiation of and ongoing treatment should not be based upon heart rate or pupillary response.

4. Precautions for pralidoxime chloride administration:

a. Although Duodote® and ATNAA® contain atropine, the primary antidote for an acetylcholinesterase inhibitor agent poisoning, the inclusion of pralidoxime chloride in the auto-injector can present challenges if additional doses of atropine are warranted by patient condition and other formulations of atropine are unavailable:
   i. Pediatrics: An overdose of pralidoxime chloride may cause profound neuromuscular weakness and subsequent respiratory depression.
   ii. Adults: Especially for the geriatric patient, excessive doses of pralidoxime chloride may cause severe systolic and diastolic hypertension, neuromuscular weakness, headache, tachycardia, and visual impairment.
   iii. Geriatrics: Patients may have underlying medical conditions, particularly impaired kidney function or hypertension, the EMS clinician should consider administering the lower recommended adult dose of intravenous pralidoxime chloride.

5. Considerations during the use of auto-injectors:

   a. If an auto-injector is administered, a dose calculation prior to administration is not necessary.
   b. For atropine only auto-injectors, additional auto-injectors should be administered until secretions diminish.
   c. Mark 1 kits, Duodote® and ATNAA® have not been approved for pediatric use by the Food and Drug Administration (FDA), but they can be considered for the initial treatment for children of any age with severe symptoms of an acetylcholinesterase inhibitor agent poisoning especially if other formulations of atropine are unavailable.
   d. Pediatric Atro-Pen® auto-injectors are commercially available in a 0.25 mg autoinjector (yellow) and a 0.5 mg auto-injector (red). Atro-Pen® auto-injectors are commercially available in a 1 mg auto-injector (blue) and a 2 mg auto-injector (green).
   e. A pralidoxime chloride 600 mg auto-injector may be administered to an infant that weighs greater than 12 kg.

IV. NOTES/EDUCATIONAL PEARLS

A. Key Considerations

1. Clinical effects of acetylcholinesterase inhibitor agents:

   a. The clinical effects are caused by the inhibition of the enzyme acetylcholinesterase which allows excess acetylcholine to accumulate in the nervous system.
   b. The excess accumulated acetylcholine causes hyperactivity in muscles, glands, and nerves.

2. Organophosphates insecticides:

   a. Can be legally purchased by the general public.

b. Organophosphate pesticides penetrate tissues and bind to the patient's body fat producing a prolonged period of illness and ongoing toxicity even during aggressive treatment.

3. Nerve agents:

a. Traditionally classified as weapons of mass destruction (WMD).
b. Not readily accessible to the general public.
c. Extremely toxic and rapidly fatal with any route of exposure.
d. GA (tabun), GB (sarin), GD (soman), GF, and VX are types of nerve agents and are WMDs.
e. Nerve agents can persist in the environment and remain chemically toxic for a prolonged period of time.

Table 1. Mild Acetylcholinesterase Inhibitor Agent Exposure

Patient	Atropine Dose (Weight) IM or via Auto-injector
Infant: 0–2 years of age	0.05 mg/kg IM or via auto-injector (i.e., *0.25 and/or 0.5 mg auto-injector(s)*)
Child: 3–7 years of age (13–25 kg)	1 mg IM or via auto-injector (i.e., *one 1 mg or two 0.5 mg auto-injectors)*
Child: 8–14 years of age (26–50 kg)	2 mg IM or via auto-injector (i.e., *one 2 mg or two 1 mg auto-injectors)*
Adolescent/Adult	2 mg IM or via auto-injector
Pregnant Women	2 mg IM or via auto-injector
Geriatric/Frail	1 mg IM or via auto-injector
Adapted from: *U.S. Department of Health and Human Services, ASPR, National Library of Medicine, Chemical Hazards Emergency Medical Management: Nerve Agents— Prehospital Management, https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=523&toxid=93*	

Table 2. Mild to Moderate Acetylcholinesterase Inhibitor Agent Exposure

Patient (Weight)	Atropine Dose IM or via Auto-injector	Pralidoxime Chloride Dose IM or via 600 mg Auto-injector
Infant: 0–2 years of age	0.05 mg/kg IM or via auto-injector (i.e., *0.25 mg and/or 0.5 mg auto-injector)*	15 mg/kg IM
Child: 3–7 years of age (13–25 kg)	1 mg IM or via auto-injector (i.e., *one 1 mg auto-injector or two 0.5 mg auto-injectors)*	15 mg/kg IM **OR** One auto-injector (600 mg)
Child: 8–14 years of age (26–50 kg)	2 mg IM or via auto-injector (i.e., *one 2 mg auto-injector or two 1 mg auto-injectors)*	15 mg/kg IM **OR** One auto-injector (600 mg)
Adolescent/ Adult	2–4 mg IM or via auto-injector	600 mg IM **OR** One auto-injector (600 mg)
Pregnant Women	2–4 mg IM or via auto-injector	600 mg IM **OR** One auto-injector (600 mg)
Geriatric/Frail	2 mg IM or via auto-injector	10 mg/kg **IM** **OR** One auto-injector (600 mg)

Adapted from: *U.S. Department of Health and Human Services, ASPR, National Library of Medicine, Chemical Hazards Emergency Medical Management: Nerve Agents— Prehospital Management, https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=523&toxid=93*

Table 3. Severe Acetylcholinesterase Inhibitor Agent Exposure

Patient (Weight)	Atropine Dose IM or via 600 mg Auto-injector	Pralidoxime Chloride Dose IM or via Auto-injector
Infant: 0–2 years of age	0.1 mg/kg IM or via auto-injector (i.e., *0.25 mg and/or 0.5 mg auto-injector)*	45 mg/kg **IM**
Child: 3–7 years of age (13–25 kg)	0.1 mg/kg IM **OR** 2 mg via auto-injector (i.e., one 2 mg auto-injector or four 0.5 mg auto-injectors)	45 mg/kg **IM OR** One auto-injector (600 mg)
Child: 8–14 years of age (26–50 kg)	4 mg IM or via auto-injector (i.e., *two 2 mg auto-injectors or four 1 mg auto-injectors)*	45 mg/kg **IM OR** Two auto-injectors (1200 mg)
Adolescent: 14 years of age or older	6 mg IM or via auto-injector (i.e., *three 2 mg auto-injectors)*	Three auto-injectors (1800 mg)
Adult	6 mg IM or via auto-injector (i.e., *three 2 mg auto-injectors)*	Three auto-injectors (1800 mg)
Pregnant Women	6 mg IM or via auto-injector (i.e., *three 2 mg auto-injectors)*	Three auto-injectors (1800 mg)
Geriatric/Frail	2–4 mg IM or via auto-injector (i.e., *one to two 2 mg auto-injectors)*	25 mg/kg IM **OR** two to three auto-injectors (1200 mg–1800 mg)

Adapted from: *U.S. Department of Health and Human Services, ASPR, National Library of Medicine, Chemical Hazards Emergency Medical Management: Nerve Agents— Prehospital Management, https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=523&toxid=93*

Table 4. Guidance for the Treatment of Seizures Secondary to Acetylcholinesterase Inhibitor Agent Exposure

Patient	Diazepam	Midazolam
Infant (0–2 y/o)	0.2–0.5 mg/kg IM Repeat q 2–5 minutes	0.2 mg/kg IM Repeat prn in 10 minutes
	0.2–0.5 mg/kg IV q 15–30 minutes May repeat twice as needed	May repeat dose once
	Total maximum dose: 5 mg	Total maximum dose: 0.4 mg/kg
Child (3–13 y/o)	0.2–0.5 mg/kg IM Repeat q 2–5 minutes	0.2 mg/kg IM Not to exceed 10 mg Repeat prn in 10 minutes
	0.2–0.5 mg/kg IV q 15–30 minutes May repeat dose twice if needed	May repeat dose once
	Total maximum dose: 5 mg if less than 5 years	Total maximum dose: 0.4 mg/kg Not to exceed 20 mg
	Total maximum dose: 10 mg if age 5 years or older 1 CANA® auto-injector	
Adolescent: 14 y/o or older	2–3 CANA® auto-injectors	0.2 mg/kg IM Total maximum dose of 10 mg Repeat prn in 10 minutes
	5–10 mg IV q 15 minutes	May repeat dose once
	Total maximum dose: 30 mg	Total maximum dose: 20 mg
Adult	2–3 CANA® auto-injectors	10 mg IM Repeat prn in 10 minutes
	5–10 mg IV q 15 minutes	May repeat dose once
	Total maximum dose: 30 mg	Total maximum dose: 20 mg
Pregnant Women	2–3 CANA® auto-injectors	10 mg IM Repeat prn in 10 minutes
	5–10 mg IV q 15 minutes	May repeat dose once
	Total maximum dose: 30 mg	Total maximum dose: 20 mg
Geriatric	2–3 CANA® auto-injectors	10 mg IM Repeat prn in 10 minutes
	5–10 mg IV q 15 minutes	May repeat dose once
	Total maximum dose: 30 mg	Total maximum dose: 20 mg

Adapted from: *U.S. Department of Health and Human Services, ASPR, National Library of Medicine, Chemical Hazards Emergency Medical Management: Nerve Agents — Prehospital Management, https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=523&toxid=93*

EMS CHEMPACK Medications

Description	Quantity (in boxes)	Amount per box
ATNAA (Atropine 2.1 mg/Pralidoxime 600mg)	6	200
Atropen (Atropine Autoinjector) 0.5 mg	1	144
Atropen (Atropine Autoinjector) 1mg	1	144
Atropine Sulfate 0.4 mg/mL - 20 mL	1	100
Diazepam 10mg Autoinjector	2	150
Pralidoxime 1g vial - 20mL (once reconstituted)	1	276
Siezalam (Midazolam 5mg/mL vial - 10mL	1	50
Sterile Water for Injection vial - 20mL	1	100