Target Audience: Emergency Medicine Residents, Medical Students

Primary Learning Objectives:

1. Recognize signs and symptoms of organophosphate exposure
2. Describe safe and effective decontamination strategies for patients with organophosphate exposures
3. Describe the roles (including the indications, contraindications, and efficacy) of antidotes and other therapeutic interventions used in the care of patients with organophosphate exposure

Secondary Learning Objectives: detailed technical/behavioral goals, didactic points

1. Describe the pathophysiology of organophosphates exposure
2. Compare organophosphate exposures with other toxicities that cause bradycardia, miosis, and hypotension, especially with regard to the differences and similarities in presentation, diagnosis, and management
3. Discuss the priorities for emergency stabilization of the patient with an organophosphate exposure

Critical actions checklist:

1. Recognize the cholinergic toxidrome.
2. Administer atropine.
3. Administer pralidoxime.
4. Treat seizures with benzodiazepines.
5. Protect the airway.
6. Admit to the MICU.

Environment:

1. Room Set Up – ED critical care area
    a. Manikin Set Up – Mid or high fidelity pediatric simulator, simulated sweat
    b. Props – Standard ED equipment

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CASE SUMMARY

SYNOPSIS OF CASE

This is a case of a 27-year-old man who presents with vomiting, weakness, diaphoresis, and altered mental status. He is a depressed man who ingested a bottle of pesticide (parathion) he purchased over the Internet after researching ways to commit suicide. He will seize shortly after arriving to the emergency. He will also have signs of severe cholinergic poisoning. He will need large doses of atropine and benzodiazepines. He will need to be intubated and admitted to the ICU.

SYNOPSIS OF HISTORY

This 27-year-old man has had ongoing depression and previous psychiatric admissions. He bought a very potent organophosphate on-line and drank the entire 12-ounce bottle. Shortly after ingestion he called 911 because he regretted his actions. The paramedics do not know why they were summoned. They note he is weak, he has vomited twice, and lost control of his bowels, but otherwise they have no details.

SYNOPSIS OF PHYSICAL

On arrival the patient will be intermittently agitated, followed by sedation. His pupils are pinpoint, and he is diaphoretic. He will vomit, lose both bowel and bladder control. He is bradycardic and salivating. His breath sounds are coarse, and his oxygen saturations are low. He will worsen and become obtunded and seize soon after his ED arrival.

SCORING GUIDELINES

The case will test the examinee's ability to recognize a cholinergic toxidrome and to treat it.

Score up the examinee's performance if:

- considering and verbalizing decontamination, though this is not critical for the scenario
- using rocuronium or vecuronium for RSI rather than succinylcholine, which is relatively contraindicated in organophosphate exposures
- using valium as the benzodiazepine of choice
- obtaining pseudocholinesterase levels or RBC cholinesterase levels, but they won't make a difference without having a baseline level

Score down the examinee's performance if:

- not rapidly escalating atropine dosing (may double every 5 minutes)
- attempting or verbalizing orogastric lavage (nasogastric lavage aspiration is a reasonable action, but will not cause improvement in patient's exam)
- activated charcoal is given before the patient is intubated (it is not needed in this case, but is not unreasonable if the airway is first protected)

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CRITICAL ACTIONS

1. **Recognize the cholinergic toxidrome**

   The patient will have vomiting, bradycardia, diaphoresis, miosis, and urinary/bowel incontinence. This should be an easily recognized toxidrome for all residents who should show realization by stating the fact and by ordering atropine. Once recognized, treatment of the toxidrome should begin immediately.
   Cueing Guideline: The nurse can ask if the doctor knows what is causing the patient's symptoms.

2. **Administer atropine**

   Bradycardia may prompt the examinee to administer atropine, but atropine dosing does not follow standard ACLS doses. The dose may start out as 1 mg, but should be doubled every 5-10 minutes and continue until bronchorrhea has stopped. Tachycardia is not an indication to stop atropine in this setting. There is no maximum dose of atropine in organophosphate exposures/overdoses.
   Cueing Guideline: The nurse can ask if the doctor would like to do anything about the worrisome heart rate (especially if an ECG has been ordered and provided to the participant) or other symptoms of cholinergic crisis.

3. **Administer pralidoxime**

   Pralidoxime, or 2-PAM, should be given as soon as possible after recognizing the cholinergic toxidrome. The dose in adults is 1-2g IV over 15-30 minutes. Following this, a drip of 200-500mg/hr should be started. The examinee may need dosing help from the pharmacy or poison center, which should be allowed for this scenario.
   Cueing Guideline: The nurse can ask if the doctor would like to do anything about the worrisome heart rate or other symptoms of cholinergic crisis (especially after atropine is given).

4. **Treat seizures with benzodiazepines**

   The patient will have a seizure during the case. While diazepam is often considered the benzodiazepine of choice, any benzodiazepine in the case will be acceptable (diazepam 5-10mg IV, lorazepam 2-4 mg IV, midazolam 2-4 mg IV). Other antiepileptics, such as phenytoin, will not be needed nor effective.
   Cueing Guideline: The nurse can ask if the doctor would like to do anything about the seizures when they occur.

5. Protect the airway (perform endotracheal intubation)

Protect the airway, especially as the patient's ability to protect the airway worsens as the case moves forward. Due to copious secretions and bronchorrhea the patient will need endotracheal intubation. If this is not performed before the patient has a seizure, it will need to be done shortly after. Any RSI regimen is acceptable, though succinylcholine is relatively contraindicated.
Cueing Guideline: Nurse asks the doctor if he is concerned about this patient's airway given the patient's mental status.

6. Admit to the MICU

Admit to the MICU. Patient will not be stable for any other destination. This patient will need ICU admission. Any attempt to admit elsewhere will be blocked by accepting physician.
Cueing Guideline: The nurse can ask the doctor if anyone has called the pediatric intensivist to arrange for a definitive disposition decision.

Critical Actions Checklist[1]

Resident Name	
Case Description	

Skills measured **Core competencies: PC** Patient care, **MK** Medical knowledge, **IC** Interpersonal and communication skills **P** Professionalism, **PB** Practice-based learning and improvement **SB** Systems-based practice	Very Unacceptable		Unacceptable		Acceptable		Very Acceptable	
Data Acquisition (D) PC MK I	1	2	3	4	5	6	7	8
Problem Solving (S) PC MK PB	1	2	3	4	5	6	7	8
Patient Management (M) PC MK IC P PB SB	1	2	3	4	5	6	7	8
Resource Utilization (R) PC PB SB	1	2	3	4	5	6	7	8
Health Care Provided (H) PC SB	1	2	3	4	5	6	7	8
Interpersonal Relations (I) IC P	1	2	3	4	5	6	7	8
Comprehension of Pathophysiology (P) MK PB	1	2	3	4	5	6	7	8
Clinical Competence (C) PC MK IC P PB SB	1	2	3	4	5	6	7	8

Critical Actions

Yes	No		Comments:
		Recognize the cholinergic toxidrome	
		Administer atropine	
		Administer pralidoxime	
		Treat seizures with benzodiazepines	
		Protect the airway (perform endotracheal intubation)	
		Admit to the MICU	

Yes	No	
		Dangerous actions

[1] Modified ABEM Oral Certification Examination checklist and scoresheet

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HISTORY

Age: 27

Sex: Male

Name: Dave Davidson

Method of Transportation: Ambulance

Person giving information: Patient. If participant actively searches, he/she will find a contact number for patient's mother in his wallet. His mother can provide additional information.

Presenting complaint: Weakness, vomiting, incontinence

Onset and Description of Complaint: Weakness, vomiting, diaphoresis, incontinence over the last 1-2 hours.

Past Medical History: Depression

Medications: None

Habits: Smokes cigarettes, no alcohol or drugs

Family Medical History: Non-contributory

Social History: Lives alone locally, unemployed

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PLAY OF CASE GUIDELINES

This is a case of an otherwise healthy 27-year-old man with a history of depression who intentionally ingested an unknown quantity of parathion, an organophosphate. The case will test the examinee's ability to detect a cholinergic toxidrome and to treat it.

1. The patient will arrive looking ill.

2. Paramedics will state that they do not know why there were summoned; the call was for a "sick person." Medics will tell you that he has vomited and is incontinent, but will not have any details regarding the nature of his illness (i.e., the bottle of parathion he drank).

3. The examinee may be given a phone number or contact information for the patient and his mother if they actively search or assign a team member. This contact (mother) will share his depressed state and can be dispatched to the patient's home where they will find the bottle of parathion.

4. This case should be apparent clinically that he has a cholinergic toxidrome. He will need to be treated with atropine and pralidoxime. If his atropine doses are not titrated up quickly, he will remain bradycardic and continue to have bronchorrhea with poor oxygenation.

5. If he is not intubated immediately on ED arrival or after seizing, his oxygen saturations will drop further, and he will vomit and aspirate.

6. The examinee may contact the poison center and may be prompted to give pralidoxime, including the dose.

Required Actions within the First Two Minutes

- A/B: Supplemental oxygen; prepare for definitive airway management (endotracheal intubation)
- C: Peripheral IV access ordered/inserted; order ECG and other serum diagnostics (ABG/VBG, electrolytes, etc.); recognize bradycardia
- D: point-of-care serum glucose (for patient with altered sensorium)
- E: expose patient
- Initial (empiric) supportive interventions for airway, breathing, circulation, and mental status until organophosphate exposure is deduced, recognized, or confirmed by history

Branch Points

- **IF NO ATROPINE IS ORDERED WITHIN THE FIRST TWO MINUTES WITH SUCCESSIVELY INCREASING DOSES (e.g., 1 mg, 2 mg, 4 mg, 8 mg…),** then the patient becomes more confused and obtunded, develops worse bradycardia and respiratory distress, and ultimately develops respiratory failure.
- **IF NO POINT-OF-CARE GLUCOSE IS ORDERED WITHIN THE FIRST TWO MINUTES,** patient becomes more confused and obtunded**.**
- **IF NALOXONE ADMINISTRATION IS ORDERED,** there will be no effect from this intervention.
- **INITIAL INTERVENTIONS TO IMPROVE HYPOXIA OTHER THAN ENDOTRACHEAL INTUBATION (e.g., NON-REBREATHER MASK) WILL NOT IMPROVE THE HYPOXIA (the oxygen saturation will decrease). THE PATIENT WILL CONTINUE TO WORSEN UNTIL ENDOTRACHEAL INTUBATION IS PERFORMED.**
- **IF NO ENDOTRACHEAL INTUBATION IS PERFORMED INITIALLY,** the respiratory and heart rates will continue to worsen and the patient will become more hemodynamically unstable **– OR –** the patient will vomit.
- **NOTE: ALTHOUGH THE CLASSIC TEACHING FOR ORGANOPHOSPHATE POISIONING INCLUDES BRADYCARDIA, TACHYCARDIA (FROM SYMPATHETIC STIMULATION – FROM THE PATIENT'S DESIRE TO BREATHE) MAY OFFSET THE SEVERITY OF THE BRADYCARDIA. AT FACULTY DISCRETION, ADJUST THE HEART RATE ACCORDINGLY.**

Following intubation, Vital Signs are:
BP: 80/60 mmHg P: 60/minute R: use ventilator rate settings T: 37.2C (98.9F)
POx: 90% (adjust as escalating doses of atropine are given and with successful intubation)

Required Actions over the Next Four Minutes

- Cholinergic crisis from suspected organophosphate exposure should be recognized by this time
- Patient will seize regardless of any of the prior interventions up to this time
- Diagnostics should be returned as ordered
- Hypoxia and bronchorrhea (respiratory failure) should be treated by this time (endotracheal intubation, atropine)
- Treatment for the other sequelae of organophosphate poisoning (e.g., bradycardia) should be initiated at this time (see **NOTE** above)
- Toxicology consultation should be considered at this time

Branch Points

- **WHEN SEIZURE IS RECOGNIZED,** benzodiazepines should be given. If benzodiazepines (e.g., diazepam 5-10mg IV, lorazepam 2-4 mg IV, midazolam 2-4 mg IV) are not given, the patient will seize again.
- **IF ORGANOPHOSPHATE EXPOSURE IS RECOGNIZED,** then pralidoxime should be ordered and administered.
- **PRALIDOXIME, OR 2-PAM, SHOULD BE GIVEN AS SOON AS POSSIBLE AFTER RECOGNIZING THE CHOLINERGIC TOXIDROME. THE DOSE IN ADULTS IS 1-2G IV OVER 15-30 MINUTES. FOLLOWING THIS, A DRIP OF 200-500MG/HR SHOULD BE STARTED.**
- **IF THE EXAMINEE DOES NOT ADMINISTER PRALIDOXIME, THE PATIENT WILL DEVELOP RESPIRATORY DIFFICULTIES WITH MORE SECRETIONS AND LESS EFFICACY OF THE ATROPINE.**
- **NURSE MAY PROMPT FOR THE MICU CONSULTATION** if not already requested.

Following seizure, Vital Signs are:
BP: 80/60 mmHg P: 60/minute R: use ventilator rate settings T: 37.2C (98.9F)
POx: 90% (adjust as escalating doses of atropine are given)

Required Actions over the Remainder of the Case

- Organophosphate exposure and toxicity should have been recognized by this time
- Diagnostics should be returned as ordered
- Hypoxia and bradypnea (respiratory failure) should have been treated by this time
- Treatment for the bradycardia and hypotension should have been initiated at this time
- Toxicology consultation should have been considered at this time
- MICU consultation for definitive disposition and placement

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INITIAL PHYSICAL EXAM

Vital Signs: BP: 90/65 mmHg P: 38/minute R: 20/minute T: 37.2C (98.9F)
POx: 90% (on non-rebreather mask)

General Appearance: Diaphoretic, incontinent, drooling

HEENT: AC, NT. Pupils 2mm, NR. Lacrimating. Copious oral secretions. TMs clear. Nose clear. Neck supple.

Lungs: Tachypneic, coarse BS throughout.

CV: Bradycardic. Distal pulses present. No edema.

Abdomen: Soft, NT, non-distended. Hyperactive BS.

Extremities: Atraumatic.

Rectal: Neg

GU: Incontinent of urine and stool

Back: Unremarkable.

Skin: Diaphoretic.

Neurological: Drowsy, intermittently following some commands, slurred speech, 3/5 strength in all extremities, no clonus, some fasciculations.

Other: No alert bracelets

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STIMULUS INVENTORY

#1	Complete blood count
#2	Basic metabolic panel
#3	Urinalysis
#4	Liver function tests
#5	Venous blood gas
#6	Creatinine phosphokinase
#7	Toxicology
#8	Coagulation studies
#9	Point-of-care serum glucose
#10	ECG

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LAB DATA & IMAGING RESULTS

Stimulus #1	
Complete Blood Count (CBC)	
WBC	18,000/mm^3
Hemoglobin	12.5 g/dL
Hematocrit	36%
Platelets	115,000/mm^3
Differential	
PMNLs	80%
Lymphocytes	9%
Monocytes	7%
Eosinophils	4%

Stimulus #2	
Basic Metabolic Profile (BMP)	
Sodium	135mEq/L
Potassium	4.0mEq/L
Chloride	106 mEq/L
Bicarbonate	20 mEq/L
Glucose	100 mg/dL
BUN	48 mg/dL
Creatinine	1.0 mg/dL

Stimulus #3	
Urinalysis	
Color	Yellow
Specific gravity	1.030
Glucose	Negative
Protein	Negative
Ketones	Negative
Leuk. Esterase	Negative
Nitrites	Negative
WBC	0-2/hpf
RBC	0-2/hpf

Stimulus #4	
Liver Function Tests	
AST	145 U/L
ALT	180 U/L
Alk Phos	60 U/L
T. Bilirubin	0.8 mg/dL
Albumin	4 mg/dL
Protein	7 mg/dL

Stimulus #5	
Venous Blood Gas	
pH	7.34
pCO_2	28 mm Hg
pO_2	40 mm Hg
HCO_3	20 mEq/L

Stimulus #6	
Creatine phosphokinase	
CPK	758 U/L

Stimulus #7	
Toxicology	
Salicylate	< 4 mg/dL
Acetaminophen	< 10 mcg/mL
Ethanol	Undetectable
Urine drug screen	
Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Negative
Opiates	Negative
TCAs	Negative
THC	Negative

Stimulus #8	
Coagulation Studies	
INR	1.0
PTT	32 seconds

Stimulus #9
Point-of-care serum glucose
95 mg/dL

Stimulus #10	
ECG	Sinus bradycardia

Stimulus #1

Complete Blood Count (CBC)

WBC	18,000/mm^3
Hemoglobin	12.5 g/dL
Hematocrit	36%
Platelets	115,000/mm^3
Differential	
PMNLs	80%
Lymphocytes	9%
Monocytes	7%
Eosinophils	4%

Stimulus #2

Basic Metabolic Profile (BMP)

Sodium	135mEq/L
Potassium	4.0mEq/L
Chloride	106 mEq/L
Bicarbonate	20 mEq/L
Glucose	100 mg/dL
BUN	48 mg/dL
Creatinine	1.0 mg/dL

Stimulus #3

Urinalysis

Color	Yellow
Specific gravity	1.030
Glucose	Negative
Protein	Negative
Ketones	Negative
Leuk. Esterase	Negative
Nitrites	Negative
WBC	0-2/hpf
RBC	0-2/hpf

Stimulus #4

Liver Function Tests

AST	145 U/L
ALT	180 U/L
Alk Phos	60 U/L
T. Bilirubin	0.8 mg/dL
Albumin	4 mg/dL
Protein	7 mg/dL

Stimulus #5

Venous Blood Gas

pH	7.34
pCO_2	28 mm Hg
pO_2	40 mm Hg
HCO_3	20 mEq/L

Stimulus #6

Creatine phosphokinase

CPK	758 U/L

Stimulus #7

Toxicology

Salicylate	< 4 mg/dL
Acetaminophen	< 10 mcg/mL
Ethanol	Undetectable

Urine drug screen

Amphetamines	Negative
Benzodiazepines	Negative
Cocaine	Negative
Opiates	Negative
TCAs	Negative
THC	Negative

Stimulus #8

Coagulation Studies

INR	1.0
PTT	32 seconds

Stimulus #9

Serum glucose

95 mg/dL

Stimulus #10

ECG	Sinus bradycardia

Organophosphates Teaching Note

Overview

Organophosphates (OPs) are a diverse group of lipophilic pesticides and insecticides. They include veterinary preparations as well. Pesticide poisonings are a common cause of poisoning deaths. OP toxicity results from ACh accumulation throughout the nervous system and causes overstimulation of muscarinic and nicotinic receptors.

Symptoms

1. OPs produce cholinergic toxicity via excess acetylcholine and stimulation of muscarinic and nicotinic receptors. Muscarinic symptoms are commonly described by "SLUDGE and the Killer B's" (Salivation, Lacrimation, Urination, Defecation, Gastric distress, Emesis) and BBB (Bradycardia, Bronchorrhea, Bronchospasm). An alternative mnemonic is DUMBBELS (Defecation-Diaphoresis, Urination, Miosis, Bronchorrhea, Bradycardia, Emesis, Lacrimation, Salivation).
2. Nicotinic symptoms (tachycardia, fasciculations, muscle weakness) also occur. A mnemonic for nicotinic effects is "MTWThF" like the days of week (Mydriasis/Muscle cramps, Tachycardia, Weakness, Twitching, HTN/Hyperglycemia, and Fasciculations).
3. Finally, CNS manifestations may also occur (drowsiness, coma, seizures).
4. Deaths are usually from acute respiratory failure resulting from muscarinic, nicotinic, and CNS effects on respiration.

Mechanism of Toxicity

Several mechanisms may be involved:

1. Acetylcholinesterase (AChE) Inhibition: OPs or their active metabolites phosphorylate and inhibit the enzyme AChE which is responsible for degrading the neurotransmitter acetylcholine (ACh). ACh accumulates at nerve endings, resulting in excessive stimulation of nicotinic and muscarinic receptors in the central and peripheral nervous systems and neuromuscular junctions, causing the symptoms described above. OPs are considered *irreversible* cholinesterase inhibitors because they permanently inactivate AChE (known as "aging").
2. Neuropathy Target Esterase (NTE) Inhibition: Some OPs or their metabolites bind irreversibly to endogenous NTE. The resulting NTE inhibition is associated with axonal degeneration and causes delayed onset peripheral neuropathy. Note that the degree of NTE inhibition does not correlate with the degree of ACh inhibition.
3. Other Cholinesterase Inhibitors: Butyrylcholinesterase (plasma cholinesterase or pseudocholinesterase) and erythrocyte cholinesterase (RBC cholinesterase) may also be inhibited, but the clinical significance is unknown.

Treatment

Address the ABC's and provide meticulous supportive care. The key to treatment is to dry the excessive secretions that may result in respiratory distress. The principle agent is atropine. High doses may be required for long periods. Dosing regimens of 1-2 mg IV, then doubling the dose, and doubling the dose, etc., until controlling the excessive bronchial secretions. Atropine may also correct bradycardia. It will not reverse nicotinic manifestations such as fasciculations or paralysis. Benzodiazepines may be given for seizures and fasciculations. Pralidoxime should be given in severe cases. It is most effective when started within 24-36 hours of exposure, but late administration may be beneficial. In severe poisoning prolonged administration may be required. Pralidoxime reactivates cholinesterase that has been inhibited by organophosphates if aging has not yet occurred. It acts primarily at nicotinic sites, but it will also reduce muscarinic and possibly CNS symptoms.

Key Points

- Prompt decontamination is key.
- Wear appropriate PPE when handling contaminated clothing and grossly contaminated patients.
- Symptom onset is usually within minutes to hours of exposure, but it may be delayed, especially following skin exposure.
- Observe asymptomatic patients for several hours depending on the compound involved and routes of exposure.
- Observe symptomatic patients for at least 24 hours after symptom resolution and antidote discontinuation.
- Symptoms can be divided into muscarinic (SLUDGE and the killer B's); nicotinic (MTWHF), and CNS effects (headache, drowsiness, seizures, coma).
- Deaths are usually from acute respiratory failure.
- Direct treatment at decontamination, airway protection, and ventilation maintenance, as well as antidotes to control bronchial secretions, and to reverse cardiovascular effects and muscle weakness.
- High doses of atropine and prolonged treatment with pralidoxime may be required in severe poisoning.