"Recognizing and Treating Cyanide Exposure"

Case Report/Simulation Scenario

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Authors

Brenda S Bray, BPharm, MPH
Clinical Assistant Professor
Washington State University College of Pharmacy
Department of Pharmacotherapy

Colleen M Terriff, PharmD, BCPS
Clinical Associate Professor
Washington State University College of Pharmacy
Department of Pharmacotherapy
Deaconess Medical Center
Pharmacy Department

Reprint requests

Brenda S. Bray, BPharm, MPH
Clinical Assistant Professor
Washington State University Spokane
Department of Pharmacotherapy
PO Box 1495
Spokane, WA 99210-1495
bbray@wsu.edu

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Brief Summary/Abstract:

Healthcare providers and emergency responders involved in acute care require training and practice in recognizing and treating rare, but potentially devastating, exposures to toxic agents, such as cyanide. This scenario gives participants the opportunity to recognize cyanide exposure and differentiate it from other biological or chemical exposures. Additionally, the scenario allows participants to design and deliver the appropriate therapy to effectively treat cyanide toxicity – both pharmacologic and non-pharmacologic for treatment and support of the patient.

Case Information

Section 1: Demographics

Case Title: High School Musical: Unknown Chemical Exposure

Patient Name: Mr. Wallace Lincoln

Scenario Name: Recognizing and treating cyanide exposure

Simulation Developer(s): Brenda Bray, Colleen Terriff

Date(s) of Development: October 2007

Learner groups: Critical Care, Emergency Medicine residents, medical, nursing and pharmacy students; emergency responders from the community.

Section 2: Curricular Information

Educational Rationale

Effective emergency preparedness and response planning equips emergency responders to be ready for any type of incident, emergency, or catastrophe, including natural or man-made situations. Intentional acts (terrorism) are commonly categorized by the agent or weapon used such as chemical, biological, radiological, nuclear or explosive devices. This case was originally

designed for doctor of pharmacy students enrolled in an elective Emergency Preparedness and Response course, but it has application for a broader audience, such as emergency responders, medical residents and nursing students, and for interdisciplinary team training.

Learning Objectives

Learners will be assessed on the following core competencies, using the Accreditation Council for Graduate Medical Education Competences (ACGME Core Competencies),

1) Medical Knowledge:
    a) Recognize and describe signs and symptoms consistent with inhalation of a chemical or biological agent.
    b) Once the exposure agent is tentatively identified or confirmed, do the following:
        i. Identify feasible pharmacotherapeutic alternatives to treat the poisoning, including possible antidotes with suggested dosing regimen
        ii. Identify non-pharmacologic measures available to treat the biological or chemical poisoning
        iii. Indicate measures for supportive care
2) Patient Care:
    a) design and implement the optimal therapeutic plan
    b) administer appropriate antidote and supportive care
    c) anticipate and monitor potential side effects of antidotes
3) Interpersonal and Communication Skills
    a) Demonstrate ability to successfully communicate with a critically ill patient

b) Demonstrate ability to interact with a multidisciplinary group of health care providers.

Guided Study Questions

1) What is cyanide and how is it absorbed?
2) What are the signs, symptoms and sequelae of cyanide exposure?
3) What are the goals of pharmacotherapy?
4) What are the therapeutic alternatives (pharmacologic and non-pharmacologic) for cyanide exposure/poisoning?
5) What are the potential side effects of the antidotes for treating cyanide poisoning?

References used during case design

- Baud FJ. Cyanide: Critical issues in Diagnosis and Treatment. Hum & Exp Tox. 2007;26:191-201.
- Bond WF et al. The Use of Simulation in Emergency Medicine: A Research Agenda. Academic Emergency Medicine. 2007;14:353-364.
- Colley J, Baker DE. Hydroxocobalamin. In: Cada DJ, Baker DE, Levien TL, eds. Formulary Monograph Service. St. Louis: Wolters Kluwer Health, Inc. Jan. 2007.
- Cyanide Antidote Kit [package insert]. Decatur, IL: Taylor Pharmaceuticals; February 2006.
- Cyanokit [package insert]. Napa, CA: Dey/L.P.; December 2006.
- Emergency Preparedness and Response [Internet]. Atlanta (GA): Centers for Disease Control and Prevention; [updated 2004 Jan 27; cited 2007 Sept]. Facts about cyanide. Available at: www.bt.cdc.gov/agent/cyanide/basics/facts.asp.

- Gracia R, Shephard G. Cyanide poisoning and its treatment. Pharmacotherapy. 2004;24(10):1358-1365.
- Mutlu GM, Keikin JB, Oh K and Factor P. An unresponsive biochemistry professor in the bathtub. Chest. 2002;122:1073-1076.
- Terriff CM. Cyanide exposure. In: Schwinghammer TL, Koehler JM, ed. Pharmacotherapy Casebook: A Patient-Focused Approach. New York: McGraw-Hill. 7th edition, 2008.

Didactics

Prior to participating in this simulation scenario, students were presented with overview lectures on Chemical and Biological Terrorism. Baseline knowledge of recognition and treatment of cyanide toxicity is recommended.

Assessment Instruments

- Refer to debriefing points below, which were utilized as a clinical checklist.

Section 3: Preparation

Supplies and Equipment

Laerdal® SimMan® (or other comparable simulator)

Non-invasive blood pressure cuff

Pulse oximetry

Electrocardiogram

Gloves – small, medium, large, XL

Medications:

- Normal saline large volume IV bag, IV tubing
- pralixodime 600 mg , atropine 2 mg (MARK-1 or DuoDote Auto-injectors®)

- diazepam 10 mg autoinjectors
- hydroxocobalamin (Cyanokit: two 2.5 gram vials)
- levofloxacin 750 mg IV piggyback, doxycycline 100 mg IV vial

Cotton ball with almond extract placed near patient's head

IV pole

IV Pump

Oxygen tubing

Ambu bag

Syringes

Code Cart with medication tray

Hospital gown/scrubs for patient (following decontamination)

Personal protective equipment

Supporting Files

Simulated Patient chart: Physician order sheets, Physician progress notes, Nursing notes, emergency department flow sheet, lab results for blood gas, lactate level, cyanide levels, CBC< electrolytes, blood culture, sputum culture, chest x-ray, acetylcholinesterase level.

Duration (varies depending on needs of learners):

Set Up: 15-20 minutes

Simulation: 15-30 minutes

Debriefing: 20-30 minutes

Case Stem

Hundreds of patients have been exposed to an unknown agent during the intermission of the high school musical. Patients are presenting to area emergency departments with a wide spectrum of symptoms ranging from confusion to seizures. Your hospital emergency department is just starting to admit patients. The team (i.e. group of four) is asked to do the following for patients as they are admitted:

♦ Determine likely exposure

♦ Order appropriate lab work

♦ Initiate therapy

Patient Data Background and Baseline State

History of Present Illness:

Mr. Wallace Lincoln, admitted to bed #2 following a decontamination procedure which included clothing removal and an on-scene water rinse, is a 53 year old white male, the orchestra conductor at the high school. Mr. Lincoln is complaining of headache, dizziness, weakness, abdominal pain, chest pain, shortness of breath. Mr. Lincoln is acting confused, intoxicated and has slurred speech. Lab work is pending.

Medical and Surgical History: non-contributory

Social History: difficult to obtain; patient denies recent alcohol consumption or illicit drug use.

Family History: non-contributory

Review of Systems: patient unable to provide answers to questions

SimMan® settings:

Initial State:

HR = 52

BP = 155/98

RR = 28

O2 saturation = 97% on room air

Eyes – mydriasis (excessive dilation)

Bitter almond breath odor (almond extract)

Progressive State (after 5 minutes):

HR = 118

BP = 91/52

RR = 36

O2 saturation = 97% on room air

Eyes – mydriasis (excessive dilation)

Mr. Lincoln complaining of: headache, dizziness, weakness, abdominal pain, chest pain, shortness of breath

Mr. Lincoln acting: increasingly confused, intoxicated, slurred speech

Questions for patient assessment (within first 10 minutes)	**Mr. Lincoln's responses**
Standard responses	Yes
	No
	I don't know
	Okay
	A little
	A lot
	Not so good
	Incoherent mumble
Do you have any allergies to medications?	I'm allergic to penicillin
Are you currently on any medications?	Lipitor® for my high cholesterol

Do you have any medical conditions?	Just high cholesterol.
How are you feeling Mr. Lincoln? What symptoms do you have?	I'm so nauseated, I think I might vomit. My chest hurts and I can't breathe. I can't catch my breath. My stomach hurts so bad. I feel so dizzy – everything is spinning. My head hurts! I'm scared! My legs are so weak – I couldn't walk. Now my hands won't work either. Please help me.
Tell me what happened	Suddenly during the musical everyone started feeling sick.
Indications of confusion (slurred speech, sound confused)	Where is the orchestra? I need to get back to the school! Let me out of here! What are you going to do? What's going on?

Current Medications and Allergies:

Allergy status: penicillin allergy (unknown reaction)

Current drug therapy: atorvastatin (Lipitor®) for hyperlipidemia

Physical Examination:

General: patient is confused with slurred speech

Weight, Height: 5'11", 210 lbs

Vital Signs: HR 52, BP 155/98, RR 28, O2 sat- 97%, temp = 98° F

Lungs: clear to auscultation, rapid, shallow breaths

Heart: sinus rhythm, bradycardia initially, progressing to tachycardia

Abdomen: normal bowel sounds present; no masses

Extremities: no edema noted; pedal pulses present

Neurologic examination: deferred

Laboratory, Radiology, and other relevant studies (results provided when requested by students):

Basic Metabolic Panel:

Na: 142 (135-146)

K: 3.7 (3.5-5.1)

Cl: 105 (98-108)

CO2: 16 (23-30)

BUN: 16

Cr: 0.8

Glucose: 122

Complete Blood Count

HgB: 12 (12-16)

Hct: 38 (36-45)

RBC: 4 (4-5.1)

WBC: 6 (4.5-11)

Lactate: 6 (0.5-1.6)

Blood gases (arterial):

pH: 7.21 (7.35-7.45)

$P0_2$ 100 (80-100)

pCO_2 22 (35-45 mm Hg)

0_2 sat 95 (85-100)

HCO_3 14 (22-26)

Anion gap: 22

Miscellaneous:

Tox screen: pending

Cholinesterase: pending

Cyanide level: pending

Spinal tap: under consideration

Progressive State following administration of appropriate antidote (after 10-15 minutes):

HR = 102

BP = 105/72

RR = 24

O2 saturation = 97% on 2-4 liters oxygen

Improved cognition

Background Information for Facilitators

Cyanide Exposure Background: [1-3] Cyanide exposures can occur with smoke inhalation from industrial or residential fires and with poisonings, either accidental or intentional, via a suicide attempt or act of terrorism. Substances of concern are gaseous hydrogen cyanide, water-

soluble (i.e. potassium cyanide) and poorly water-soluble (i.e. silver cyanide) cyanide salts and cyanide-containing compounds, cyanogens, that release cyanide during metabolism, as with sodium nitroprusside. Through a variety of routes (inhalation, injection, ingestion) cyanide can cause cellular metabolism to shift from aerobic to anaerobic conditions, which then increases lactic acid production and leads to a potentially severe metabolic acidosis. Onset of signs and symptoms depends on form of cyanide, with gaseous hydrocyanide causing immediate symptoms and mortality in a matter of minutes, contrasting with cyanogens that may take a few hours. Patients can present with dizziness, confusion, giddiness, loss of consciousness, seizures and coma. GI symptoms include abdominal pain, nausea and vomiting. Palpitations, shortness of breath, hyperventilation and subsequent cardiac arrest may occur. Physical findings may include either bradycardia and hypertension (earlier) or subsequent hypotension with reflex tachycardia. Tachypnea, giving way to apnea, with a normal pulse oximetry, is also concerning. If patients were extracted from a fire, soot around mouth and nose may be present. Eyes might show mydriasis. Finally, patients may have smell of bitter almonds on breath (but not everyone in population can detect this odor.)

While the lengthy differential diagnosis list includes concerns such as anxiety attack, acute coronary syndrome, myocardial infarction and acute drug intoxication, this mass casualty event is most likely a terrorist act. Learners need to differentiate the causative agent, based on information from the scene and signs and symptoms of presenting patients. Potential exposure may include a riot control agent, vesicant or blistering agent, nerve agent or one of a variety of industrial chemicals, including chlorine, ammonia and cyanide.

Because quick triage and appropriate selection and administration of treatment, including supportive care, are crucial to minimize mortality with cyanide exposure, learners need to react in a timely fashion.

Healthcare workers need to verify that appropriate decontamination has occurred prior to admission into the facility. Decontamination involves clothing removal and skin washing (water or soap and water) which can be conducted at the scene or outside the facility.

Simulation Background: The room is situated like an emergency department patient triage room. Patient is in scrubs (has been decontaminated through clothing removal and skin washing), has pulse oximetry, blood pressure cuff, heart rate monitor and peripheral IV access. Cotton ball with almond extract is hidden under his head to simulate cyanide metabolite odor on breath.

Students enter the room and perform initial assessment and interview which reveals information as described above in patient background. Students must request the following: blood gas, lactate level, cyanide levels, CBC, electrolytes, blood culture, sputum culture, chest x-ray, acetylcholinesterase level. Once assessment is complete, students must identify the potential exposure, recommend an appropriate treatment plan, administer antidote and state monitoring plan for safety and efficacy for exposure and antidote.

De-Briefing Points:

1) General: teamwork/communication with patient and team members (learning obj 3)

- Self assess individual and group interactions during stressful simulation scenario

- Consider appropriate agencies to notify of the incident (i.e. CDC, Poison Control, local emergency management, public health)
- Consider personal safety and the importance of verifying that appropriate patient decontamination has occurred.

2) Patient Assessment and Treatment:[1-3] The following points should be reviewed during the de-briefing to review patient specific findings relevant to cyanide toxicity. (learn obj 1)

a) Assure appropriate decontamination procedure has occurred.

b) Immediate Care (learning obj 2a): If required, implement immediate life-saving maneuvers including resuscitation measures such as CPR, intubation and ventilator support

c) Supportive Care should include the following (learning obj 2a)

- Oxygen delivery 100%
- Intravenous and intra-arterial lines (for blood gas and hemoximetry)
- Establish IV access for administration of drugs and fluids
- Treatment of acidosis with sodium bicarbonate titrated according to arterial blood gas and bicarbonate levels
- Cardiovascular monitoring

d) Information from the patient/or observations about the patient should include the following

- Determine allergy status
- Current medications & disease states
- General weakness, confusion

- Dizziness, lightheadedness, headache
- Acting intoxicated
- Abdominal pain, nausea, vomiting
- Seizures and loss of consciousness
- Tachypnea, hypotension, bradycardia
- Bitter almond breath odor

e) Physical exam

- Mydriasis
- Bitter almond breath odor (discussion point: not everyone can detect this odor)
- Chest pain with shortness of breath
- Apnea
- Vital signs variable: initial bradycardia and hypertension, then hypotension with reflex tachycardia, followed by bradycardia and hypotension
- Pulmonary edema

f) Lab work

- Basic metabolic panel and CBC helps rule out infection, anemia, electrolyte abnormalities and renal dysfunction.
- Blood gas (metabolic acidosis) – consider anion gap
- Lactate level (elevated due to hypoxic intracellular damage and tissue death)
- Cyanide levels (whole blood): expect to be elevated; delay in report; should not delay treatment
- Normal O_2 pulse oximetry reading (This may be falsely re-assuring since the oxyhemoglobin cannot be utilized for cellular oxidative phosphorylation.)
- Carboxyhemoglobin (expected to be elevated): delay in report

g) Design optimal therapeutic plan and administration of appropriate antidote (learning objectives 1b & 2b)

- If cyanide toxicity is strongly suspected, administer antidote in the absence of laboratory confirmation.

- Two therapeutic options exist: cyanide antidote kit and hydroxocobalamin. For this case, taking into consideration patient's hypotension and unknown chemical exposure (unsure if carbon monoxide involved) hydroxocobalamin is preferred antidote.

- Preferred: Cyanokit® (hydroxocobalamin):[1,4] an active form of vitamin B_{12}, is capable of binding cyanide, forming cyanocobalamin, an inert compound that is subsequently excreted in the urine. Adult dose is 5 g (2 x 2.5 g vials) diluted in normal saline, and administered intravenously over 15 minutes. This dose can be repeated as needed (15 minutes or up to 2 hours later.)

- Alternate: Cyanide Antidote Kit:[1,5] The cyanide antidote kit containing amyl nitrite, sodium nitrite, and sodium thiosulfate is traditionally used to treat cyanide poisoning. Amyl nitrite and sodium nitrite induce methemoglobinemia, which preferentially binds cyanide. Sodium thiosulfate acts a sulfur donor, converting cyanide to thiocyanate, which is excreted renally as a nontoxic metabolite. First, amyl nitrite ampule is crushed in gauze and held under patient's nose for inhalation (15 seconds, then 15 seconds of rest, repeat; use new ampule every 3 minutes if necessary as IV access is being established.) Intravenous administration of sodium nitrite (10 mL of 3% solution) should begin as soon as possible at a rate of 2.5-5 mL/min in adults. This is followed by sodium thiosulfate (12.5 g in 50 mL) infused

intravenously at rate of 3-5 mL/min, which may be repeated at one-half dose if symptoms are persisting after 60 minutes.

h) Monitoring Parameters to evaluate therapeutic plan:[1] (learning objectives 2b)

- Signs and symptoms of toxicity for patient improvement or deterioration.
- Monitoring for a decrease in lactate levels daily may be useful to gauge improvement in tissue damage.
- Monitor blood gases (to see improvement in acidosis and oxygenation) as needed.
- other laboratory tests, such as co-oximetry (for carboxyhemoglobin or methemoglobin levels) may be useful if results can be made available within hours.
- Cyanide levels may be determined, but are not required for patient management.
- Hydroxocobalamin may interfere with certain laboratory parameters (performed by colorimetrics) due to this drug's deep red color. For example, serum creatinine, glucose, and hemoglobin may be artificially increased.
- Monitor heart rate, blood pressure and pulse oximetry continuously.
- Airway/breathing, cardiovascular system and CNS changes (i.e., mental status deterioration and seizures).
- Potential antidote side effects and monitoring:
    - Hydroxocobalamin:[4] red-colored skin (flushing; may last up to 2 weeks) and urine (may last up to 5 weeks)- common; increase in blood pressure, nausea, headache and infusion site reaction; monitor for allergic reaction (i.e. rash, edema, anaphylaxis). Patient's blood pressure increased after hydroxocobalamin administration.

- Cyanide antidote kit:[1,5] amyl or sodium nitrite may also cause an allergic reaction, hypotension and worsen carbon monoxide poisoning (if co-present). In addition, if sodium thiosulfate is infused too rapidly, transient hypotension may result. Methylene blue solution (1%) should be administered (1-2 mg/kg over 5-10 minutes) if vomiting, severe hypotension and blue skin is observed.

References

1) Leybell I, Borron SW and Roldan CJ. Emedicine [Internet]. New York: Web MD, Inc.; c1996-2006 [updated 2009 Dec 14, cited 2010 Mar 10]. Toxicity, cyanide. Available at: www.emedicine.com/emerg/topic118.htm.
2) Emergency Preparedness and Response [Internet]. Atlanta (GA): Centers for Disease Control and Prevention; [updated 2004 Jan 27; cited 2010 Feb 28]. Facts about cyanide. www.bt.cdc.gov/agent/cyanide/basics/facts.asp.
3) Baskin SI, Kelly JB, Maliner BI, Rockwood GA and Zoltani CK. Chapter 11: Cyanide Poisoning. [Intranet] In: Medical Aspects of Chemical Warfare. U.S. Army Medical Department Borden Institute. [2008, cited 2010 Mar]. Available at: http://www.bordeninstitute.army.mil/published_volumes/chemwarfare/Ch11_Pg_371-410.pdf
4) Cyanokit [package insert]. Columbia, MD: Meridian Technologies, Inc.; September, 2009.
5) Cyanide Antidote Kit [package insert]. Decatur, IL: Taylor Pharmaceuticals; February 2006.