Chemical Attack: Airway and Anxiety Management

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INSTRUCTIONS

The questions that appear throughout this case are intended as a self-assessment tool. For each question, select or provide the answer that you think is most appropriate and compare your answers to the key at the back of this booklet. The correct answer and a discussion of the answer choices are included in the answer key.

Note: These self-assessment questions are not intended for CME credit. To apply for CME or CEU credit, you must complete the CME Test and the Evaluation Form at the back of this booklet and submit them according to the directions provided.

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INTENDED AUDIENCE

Internal medicine, family medicine, and emergency medicine clinicians, and mental health care professionals, including psychiatrists, psychologists, and social workers who will provide evaluation and care in the aftermath of a terrorist attack or other public health disaster

LEARNING OBJECTIVES

Upon successful completion of this case, participants will be able to:

- Describe the central and peripheral compartments of the respiratory tract and their importance in understanding the pathophysiology of pulmonary toxicants.
- Define the pathology and clinical hallmark of damage to each compartment of the respiratory tract.
- Summarize the management of patients with damage to each compartment of the respiratory tract.
- Recall the diagnostic criteria for Acute Stress Disorder and differentiate it from the diagnostic criteria for Post Traumatic Stress Disorder.
- Describe treatments for Acute Stress Disorder.
- Describe recommendations for interventions for individuals who develop symptoms after witnessing or experiencing a traumatic event.

CASE HISTORY

On a warm spring afternoon in downtown Chicago, you are riding a taxi to a medical convention, when a crowded city bus approaching an intersection crashes into the back of a garbage truck that is stopping at a red light. The three cars just behind the city bus end up in a pile-up. You rush out to help. As you enter the bus, you see that the bus driver is slumped to the floor, unconscious and bleeding from the head. Two of the passengers are lying motionless near the front of the bus. You smell a strong but hard-to-describe odor, and some passengers are screaming, "We've been sprayed!"

COMMENT: The understandable instinct to rush in and help victims needs to be tempered by the realization that your exposure to liquid, vapor, or gas from the bus or from the passengers could turn you into another casualty. In an emergency, wrapping the face with several layers of a handkerchief or clothing may provide some protection but is not a guarantee of full respiratory protection. You must always protect yourself first! Do not enter an area where an unknown substance has been released without the appropriate personal protective equipment.

Outside the bus, you talk with several victims and a bystander named Mary who was waiting at the bus stop and had witnessed the accident. You discover the following:

A man had boarded a full city bus at the last stop and had taken a seat near the front. After the bus had begun moving again, he donned a gas mask, pulled a one-gallon spray canister from his bag, and began spraying the driver and passengers with an unidentified liquid that caused some passengers' skin to burn and their eyes to water. The bus was moving at approximately 30 mph when the driver collapsed onto the steering wheel. The bus then slammed into the garbage truck at the red light. The force of the collision threw the driver forcefully into the windshield, causing him to slump to the floor, unconscious and bleeding from his head. Several passengers were also thrown against the backs of the seats just ahead of them, into bus windows, or onto the floor of the bus. The perpetrator shouted something unintelligible from behind his mask and ran from the bus. Many of the bus passengers were coughing and complaining of pain and nausea as they pushed their way off the bus, screaming. Some were weak and also salivating. Several were rubbing their eyes and exhibiting copious tear production. Two passengers lying near the front of the bus were apneic and pulseless despite no evidence of external injury. A few passengers from the middle and rear of the bus reported a pungent odor reminiscent of strong perfume or cologne. You consider what the sprayed agent could be.

COMMENT: The reported odor, irritation, weakness, salivation, and collapse suggest a chemical agent. However, the presence of a chemical agent does not exclude the simultaneous presence of a biological or radiological agent. In addition, these effects can all be psychological following exposure to a relatively nontoxic substance or to a psychologically stressful situation.

Types of chemical agents that may be used by terrorists or in warfare include:[1]

- Respiratory tract irritants (pulmonary agents)
- Asphyxiants (cyanides)
- Vesicants (blister agents)
- Cholinesterase inhibitors (nerve agents)

The reported effects, including sudden collapse and death, can occur with extremely high concentrations of any of these agents. A variety of widely available industrial chemicals could lead to skin and eye irritation as well as effects on the respiratory tract. These chemicals include pesticides, strong acids and bases, chlorine compounds, and various dusts and smokes. For a review of factors that differentiate chemical agents and their effects, refer to the Table on page 4.

Table. Features of Selected Major Chemical Exposures*

Feature	Asphyxiants	Cholinesterase Inhibitors	Respiratory Tract Irritants	Vesicants
Most likely agent in accidental release	Carbon monoxide	Organophosphorous pesticides	Chlorine and its derivatives, phosgene, ammonia, strong acids, other toxic industrial chemicals, smoke	Methyl bromide
Most likely agent in act of terrorism	Cyanide	Nerve agents (eg, sarin and VX)	Chlorine, phosgene	Sulfur mustard, Lewisite, phosgene oxime
Hallmark	Tissue hypoxia in cardiovascular system and central nervous system with weakness, collapse, apnea, and convulsions; usually, absence of respiratory tract irritation and miosis; no increase in secretions	Cholinergic syndrome with tremors, fasciculations, muscle weakness, and eventually paralysis with or without miosis and increased exocrine-gland secretions; increasing effects on central nervous system (including collapse, apnea, and seizures) with increasing exposure	Centrally acting pulmonary agents: respiratory-tract irritation with noise (eg, coughing, hoarseness, wheezing). Peripherally acting pulmonary agents: chest tightness or shortness of breath.	After several hours, eye injuries, skin burns with blister formation, respiratory irritation. Exposure to high concentrations may lead to systemic effects including possible bone-marrow suppression.
Typical presentations				
Mild symptoms	Headache, fatigue, anxiety, irritability, dizziness, nausea	Miosis, dim vision, eye pain, rhinorrhea, irritability, headache, chest tightness, sweating	Centrally acting agents: nose and throat irritation, sore throat, cough, chest tightness, eye irritation Peripherally acting agents: often none initially	Conjunctivitis, limited erythema, epistaxis, sore throat, cough, pain, late-onset blisters
Moderate–to–servere symptoms	Dyspnea, altered mental status, cardiac ischemia, syncope, coma, seizures	Salivation, lacrimation, urination, defecation, gastrointestinal cramping, and emesis (SLUDGE); wheezing, muscle weakness, fasciculations, cognitive impairment, incontinence, coma, seizures, apnea	Centrally acting agents: laryngitis, wheezing, stridor, laryngeal edema (with possible irritative laryngospasm), and partial or total airway obstruction (usually manifested by noise) Peripherally acting agents: mild to no initial irritation followed by a clinically asymptomatic latent period of hours and then chest tightness or shortness of breath heralding incipient pulmonary edema	Corneal damage, vesicles and bullae, nausea, wheezing, stridor, laryngeal edema, acute lung injury, skin blistering or sloughing
Hyperacute onset *sudden collapse*	High concentrations of cyanide or hydrogen sulfide and oxygen deficiency within a confined space	Exposures to VX or high-vapor concentrations of other nerve agents	Extremely high concentrations of chlorine or phosgene cause sudden collapse with clotting of blood in pulmonary vessels	Rare, even with high concentrations
Acute onset *typically within minutes to hours after exposure*	Most exposures to high concentrations of asphyxiant gases (carbon monoxide, cyanide) or oxygen deficiency	Vapor exposure, ingestion of liquid form, or moderate –to-large dermal exposure to liquid	Riot-control agents, centrally acting pulmonary agents such as ammonia, hydrochloric acid, and chlorine	Phosgene oxime, Lewisite, high concentrations of sulfur mustard
Delayed onset *typically 4 to 6 hrs after exposure*	Low-to-moderate concentrations of substances that metabolize to primary asphyxiant: methylene chloride (producing carbon monoxide); acrylonitrile and propionitrile (producing cyanide)	Limited exposure of skin to droplets; prolonged exposure to low doses of vapor	Peripherally acting agents such as phosgene and nitrogen dioxide. Latent period for lower doses may be even longer.	Sulfur mustard

 Table adapted with permission from *N Engl J Med.*[1]

QUESTION 1

What is the significance of the strong perfume odor?

a. **Its similarity to perfume probably excludes the use of a dangerous agent.**
b. **The perfume-like smell indicates probable use of a nerve agent such as sarin.**
c. **The nature of the odor in this case is not a useful clue in identifying the agent.**
d. **The failure to detect the odor of newly mown hay excludes the use of phosgene.**

Reminder: You can find the Answer Key & Discussion on page 15.

QUESTION 2

While your colleagues and you are assessing the situation, police and emergency medical response personnel arrive on the scene. Which of the following actions regarding decontamination is correct?

a. **All passengers must be decontaminated by whole-body washing with soap and water before being transported.**
b. **None of the passengers need to be decontaminated.**
c. **All passengers should be first instructed to remove their outer clothing.**
d. **Passengers should be washed using diluted bleach.**

COMMENT: When the identity of the agent is in doubt, all liquid must be considered to have the potential to cause systemic toxicity via absorption and must be removed as quickly as possible. Prompt decontamination of liquid chemicals may be one of the simplest and yet most effective and important life-saving measures that can be taken at the scene of an exposure. Because many toxic liquid chemicals may quickly penetrate the eyes, skin, and wounds, decontamination must occur as soon as possible and should begin with removal of liquid-soaked clothing. Removal of outer clothing can eliminate 85% to 90% of contamination.[1] Ideally, decontamination should occur in the field, but the hospital must also be prepared to decontaminate, as many ambulatory patients may arrive on their own.

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Emergency personnel notify the receiving hospital to be prepared to receive casualties. The hospital activates its mass casualty plan, calling for additional staff to be available in the emergency department, wards, and intensive-care units.

At the hospital, several of the patients from the middle of the bus report full resolution of their initial eye and throat irritation and coughing within a half-hour. Miosis is not present in any of the patients, and the initially reported salivation resolves in all cases. Several patients complain that their eyes still hurt despite 15 minutes of irrigation with normal saline. Initial ocular examination reveals conjunctival injection bilaterally but no corneal abrasions. Two patients begin to wheeze. The medical history of one includes a childhood history of eczema, while the other has a history of hay fever and allergies. Two other patients develop facial erythema, but no blistering is present and most patients have normal-appearing skin.

Assessing Chemical Exposure

Agent(s):
Type and estimated doses

State(s):
Solid, liquid, vapor, gas, aerosol

Body sites:
Routes of entry, ie, exposure and absorption

Effects:
Local vs. systemic

Severity:
Of effects and exposure

Time course:
Sequence of events

Other diagnoses:
Differential diagnoses

Synergism:
Interaction among multiple co-existing diagnoses

COMMENT: If chemical, biological, and radiological detectors are available, they may help identify the agent or agents, although false positives and false negatives are possible. The effects of biological agents may not be apparent initially, and exposure to these agents may require laboratory diagnosis. Severe exposures to chemical agents may require that a quick presumptive diagnosis be made clinically without waiting for laboratory confirmation. The most useful tool in this regard is acquaintance with the limited number of basic toxidromes. For chemical agents, the cholinergic toxidrome and the classical presentation of cyanide casualties should be committed to memory. (For a description, please refer to another case in this series, *Sarin*, by Dr. James M. Madsen.) Response to empirical treatment, including administration of antidotes as indicated, can also have diagnostic utility. A quick but thorough assessment of any chemical exposure victim can be conducted by use of the mnemonic ASBESTOS (see Sidebar).

In the emergency department, several patients continue to exhibit tachypnea with mild tachycardia. They also report feeling "weak and trembly."

COMMENT: Weakness and trembling suggest exposure to a cholinesterase inhibitor such as a nerve agent, and thus the patient should be examined with particular attention to detecting other nicotinic signs, such as fasciculations, and muscarinic signs, such as miosis, bronchospasm, lacrimation, rhinorrhea, salivation, increased bowel sounds, and diarrhea. However, weakness and trembling can also reflect the following:

- cholinergic effects of exposure to pulmonary agents
- blister agents - look for pulmonary effects, eye effects, and late-onset skin and systemic effects
- cyanide - look for initial flushing and tachypnea followed by respiratory depression, a decreased arteriovenous oxygen gradient, and a high-anion-gap acidosis, classically without cyanosis
- hypoglycemia - unlikely as a sole cause following the circumstances of the attack
- psychological reactions either to a relatively nontoxic agent or superimposed upon the physiological effects from a toxic agent.

Laboratory and radiological examinations do not take the place of a quick presumptive clinical diagnosis for severely affected chemical agent casualties. However, blood specimens should be obtained for electrolytes, a CBC with differential, and standard toxicology at a minimum and for blood-gas analysis if respiration is compromised. Urine for toxicology may also be useful. Pulse oximetry and electrocardiography should be initiated, and chest radiographs should be obtained when coughing or when other pulmonary effects are noted or suspected. Slit-lamp examination of the eye after fluorescein instillation should also be performed for all victims in which corneal damage (ie, corneal abrasions or chemical erosions) is suspected.

QUESTION 3

Between 2 and 4 hours after exposure, 5 patients from the front third of the bus, begin to report chest tightness and shortness of breath. What is the significance of these symptoms?

a. Respiratory effects from nerve agents and pulmonary agents would not be expected to present this late after exposure, effectively ruling out these kinds of agents and suggesting psychological effects.
b. These findings are typical of a respiratory tract agent affecting the lower or peripheral airways.
c. These findings strongly suggest that bronchodilators and early intubation should be considered.
d. These findings imply denudation of respiratory epithelium from large to medium-sized bronchi.

COMMENT: There are two major types of pulmonary effects from toxic agents, which are best understood in reference to the two major physiological divisions of the respiratory tract:

1) The central or conducting compartment (tracheobronchial region) is the portion of the respiratory tract from the larynx to about the 17th dichotomous branching of bronchioles. This is at the level of terminal bronchioles that are approximately 2 mm in diameter. This compartment is the region in which bulk air movement occurs with each breath. Physiologically, the airways in the head and throat (nose, nasopharynx, and oropharynx) can also be added to this division.

2) The peripheral or gas-exchange (respiratory) compartment is the region of the respiratory tract including the distal terminal bronchioles, the respiratory bronchioles, the alveolar ducts, and the alveolar sacs, or alveoli. The peripheral compartment represents the region in which air movement occurs only by diffusion (Brownian motion). This is because of the enormous increase in the total cross-sectional area of the airways by the time that this region is reached and the concomitant decrease in air velocity that is imposed by the constraints of a closed conduit.

QUESTION 4

Which of the following chemical agents is the most likely cause of the chest tightness and shortness of breath?

a. **A strong mineral acid or base such as hydrochloric acid or ammonia**
b. **A riot-control agent or tear gas**
c. **Phosgene**
d. **Chlorine**

COMMENT: Phosgene and chlorine were devastatingly effective chemical warfare agents in World War I but are now considered obsolete for military use.[2] Nevertheless, both chlorine and phosgene, each with an annual industrial production of millions of tons, are easily obtainable by governments and individuals, can still be effective on the battlefield, and pose a particular terrorist threat in enclosed spaces such as buildings, buses, subways, and trains.[3]

Both chlorine and phosgene are usually classified as "choking," "irritating," "lung," or "pulmonary" agents.[1] It is crucial to understand the following:

- most pulmonary toxicants exert a preference for one compartment (central or peripheral) over the other
- in high concentrations any pulmonary toxicant can affect both compartments of the respiratory system
- the pathology and clinical presentation of damage to each compartment are distinct
- diagnosis and treatment should focus primarily on the site of the damage within the respiratory tract and should only focus on the agent insofar as knowledge of the type and dose of agent can help predict the compartment(s) affected.

The sites at which inhaled particles (such as smoke and dust particles) act in the respiratory tract are determined by the sizes and shapes of the particles. However, for vapors and true gases, site of action is determined by a combination of 3 separate factors:

- Solubility in aqueous solutions: Highly soluble gases and vapors tend to dissolve in fluids in the central compartment. Less water-soluble compounds can penetrate all the way to the peripheral compartment.[1]
- Chemical reactivity: Highly chemical reactive vapors and gases tend to react with the first tissue that they encounter, in this case the central compartment. Less reactive chemicals have the opportunity to reach the peripheral compartment.
- Dose: High doses of inspired vapors and gases represent such an excess that they will have effects in both the central and peripheral compartments of the respiratory tree.[1] Doses of vapors or gases are expressed as a concentration-time (or Ct) product. Ct product is determined by multiplying the concentration of the agent by the duration of exposure.

QUESTION 5

What is the most likely pathological process occurring in the patients with chest tightness and shortness of breath?

a. Reflex bronchoconstriction from airway irritation

b. Necrosis and denudation of respiratory epithelium

c. Pseudomembrane formation eventually leading to partial or total airway obstruction

d. Damage to alveolar-capillary membranes eventually leading to pulmonary edema

COMMENT: The pathophysiology of damage to the central compartment or upper airways of the respiratory tract involves:

- irritation of mucous-membranes, usually by acidic moieties released after the agent has dissolved or reacted in aqueous solution;
- irritative laryngospasm in some cases;
- necrosis and denudation of respiratory epithelium of conducting airways.

The irritation is usually prompt and is a function of concentration rather than dose,[4] although recent studies suggest that the issue may be more complicated.[5] The epithelial damage may require additional time. Airways can be obstructed either by amorphous necrotic debris or by membrane-like sheets (pseudomembranes) of stripped respiratory epithelium. Necrotic debris is also an excellent culture medium for bacteria, so secondary bacterial infection is a common complication of damage to central airways.

The function of the central airways is to conduct air to the peripheral airways. Disruption of smooth laminar flow in a conduit leads to turbulence, which creates noise. **Thus, the clinical hallmark of central compartment damage is noise, and victims may cough, sneeze, become hoarse, or exhibit rales, rhonchi (wheezing), or inspiratory or expiratory stridor.** Laryngospasm may also occur as a reflex reaction to irritation.

There is no specific antidote for central pulmonary effects, and management consists of the following:

- provision of warm, moist, oxygenated air;
- bronchoscopic identification and removal of pseudomembranes as appropriate; administration of bronchodilators for irritative bronchoconstriction (either from the agent or from underlying lung disease);
- infection surveillance;
- prophylactic administration of antibiotics is discouraged.

The pathophysiology of damage to the peripheral compartment or lower airways of the respiratory tract is noncardiogenic pulmonary edema, which is slightly different from the noncardiogenic pulmonary edema induced by high altitude. Damage to capillary endothelium in alveolar septa occurs almost immediately after tissue contact. Damage results in leakage of fluid into the airway lining which ultimately leads to hydrostatic pressure increasing to the point that fluid spills into the alveoli and then tracks up the airways, a condition called "dry land drowning."

Physical examination of the dyspneic patients reveals lung fields clear to auscultation, no dullness to percussion, and a regular cardiac rate and rhythm. Chest radiography is normal, as is blood-gas analysis. The dyspnea, however, persists.

COMMENT: Noise is not a predominant characteristic of damage to the lower airways. Rather, delayed-onset **dyspnea (specifically, chest tightness or shortness of breath) is the hallmark of damage to the lower airways.**[1] Dyspnea from expansion of alveolar septa with fluid occurs after a clinically asymptomatic, or latent, period. The length of the latent period is inversely correlated with dose (eg, onset of dyspnea within four hours of exposure is an especially grave prognostic indicator). Although early opacification on chest radiographs may occur near the end of the latent period, **the earliest clinical indicator of incipient pulmonary edema is chest tightness or shortness of breath without accompanying signs.**

Hallmarks of Respiratory Tract Injury

Central Compartment = noise (sneeze, cough, stridor, wheezing)

Peripheral Compartment = dyspnea (chest tightness, shortness of breath)

Less common or minor effects from exposure to phosgene and other peripherally acting pulmonary agents include the following:

- hypoxic sequelae to the heart
- hypoxic sequelae to the vasculature (Raynaud's phenomenon has been documented)
- liver toxicity (transaminases may be elevated)
- kidney effects (with elevated blood urea nitrogen and numerous red and white blood cells in the urine)
- metabolic acidosis (superimposed upon respiratory acidosis)
- hematological effects including increased erythrocyte fragility, leukocytosis, and intravascular coagulopathy (including immediate collapse from widespread clotting in pulmonary vessels after massive exposure)[4]
- possible neurological and neurobehavioral changes

As you are examining patients already in the emergency department, two physically fit sisters in their mid-twenties check into the emergency department. They explain that they were on the bus that was attacked, they smelled something odd, and that they knew the area so they decided to jog the two blocks to the emergency department. They are slightly out of breath but do not seem particularly winded given their having just jogged the two blocks.

COMMENT: Physical exertion after exposure to a peripherally acting pulmonary agent shortens the latent period and worsens the prognosis. Even healthy and physically fit individuals are at high risk for impending collapse and fulminant pulmonary edema. All suspected victims of this type of exposure should be kept at mandatory bed rest during observation and management.

Several hours later, some of the patients from the middle of the bus report full resolution of their initial eye and throat irritation and coughing. Their physical examination, laboratory studies, and chest radiographs are unremarkable and remain so after two hours of observation. They are anxious to return home to be with their families.

QUESTION 6

What is the most appropriate next step regarding disposition of these patients?

a. **They should be discharged with instructions to return to the hospital if their condition worsens.**

b. **They should be held for an additional two hours and then given a trial of exertion to see whether they become short of breath.**

c. **They should be observed in the hospital for at least 8 to 24 hours.**

d. **They should be kept at strict bed rest for one week.**

COMMENT: Medical management for peripheral pulmonary effects should ideally begin in the latent period, before the onset of dyspnea. Suggestions for medical intervention during the latent period include the use of ibuprofen, N-acetylcysteine (NAC), theophylline (but not pentoxifylline, which is ineffective), and steroids even though none of these medications has been specifically approved by the Food and Drug Administration (FDA) for this indication.[1]

Positive-pressure ventilation (eg, the use of continuous-positive-airway-pressure masks, or CPAP masks) during the latent period may be of use but may be poorly tolerated by asymptomatic patients. Secondary bacterial pneumonia may occur following exposure to pulmonary agents. Antibiotics should be used when signs and symptoms of pneumonia develop, not as prophylaxis.. Exertion has been shown to shorten the onset of the latent period and to increase the severity of pulmonary edema. Patients should be kept at strict bed rest during observation, which should continue with serial vital-signs and chest auscultation performed at least every half-hour and with chest radiographs every 2 hours, for at least 8 hours. In the absence of serial chest radiography, asymptomatic individuals should be observed for 24 hours.

Pulmonary edema requires treatment in a pulmonary intensive-care unit (ICU). If indications from the clinical presentation of the patient or the presentations of other patients from the attack suggest that pulmonary edema is likely to develop, the patient should be monitored in an ICU. In the ICU a central line can be inserted and pressures in the pulmonary and systemic vasculature can be used to gauge the balance between removing sufficient fluid from the pulmonary circulation and removing too much fluid from the systemic circulation. Positive end-expiratory pressure (PEEP) should also be used to retard fluid leakage into alveoli.

A total of 24 casualties resulted from the phosgene attack on the bus. The bus driver suffered a scalp laceration, a concussion with a penetrating skull injury, and blunt trauma to the chest. While he was in surgery, he became hypotensive and difficult to ventilate. Chest radiography showed chest infiltrates consistent with early-onset pulmonary edema. He survived surgery but expired in the surgical intensive care unit four days later. Autopsy showed a secondary bacterial pneumonitis arising in a setting of pulmonary edema. The two passengers who were found collapsed and apneic at the front of the bus were pronounced dead in the emergency room. Both of the two sisters who had jogged to the hospital developed pulmonary edema, and one succumbed to infectious complications five days after admission. Fourteen patients, including all of the five who reported chest tightness within four hours of the incident, developed florid pulmonary edema, and eight eventually died, for a total death toll of eleven. Four weeks after the incident, all of the survivors underwent repeat pulmonary function testing and exhibited normal findings. There were no residual pulmonary effects in any of the survivors. However, three patients reported symptoms of posttraumatic stress disorder four weeks after the event.

COMMENT: Medical professionals need to be prepared to manage both the medical and psychological sequelae of a terrorist attack with pulmonary toxicants. Psychological sequelae may be seen in victims exposed to the agent, those who fear exposure, those with loved ones hurt by the attack, and those affected in other ways. Below is a description of the psychological effects of a victim who witnessed the phosgene attack on the city bus.

Two weeks after the chemical attack, Mary, a witness to the bus disaster, is still experiencing recurrent and intrusive thoughts about the event. "This is silly," she thought as she walked toward her bus stop, "It happened over two weeks ago. I know I can do this!"

She recollected how terrified she was that day. Although she was a block away and on the opposite side of the street, she witnessed the accident: a bus collided with a garbage truck. She recalled thinking how horrible it was, and how worried she was for the injured and how many people might be dead. After the initial impact, she realized that it was not a typical accident. Passengers from the bus were screaming, climbing over one another, and breaking windows in order get out of the bus. Of the passengers who initially escaped, many were gasping for air, rubbing their eyes, and mumbling something about "being sprayed." A couple of the passengers passed out on the grassy knoll and appeared to be dead.

The scene was chaotic. Ambulances, police, news reporters, and "important looking people" arrived at the scene. They were doing their best to direct the bystanders away from the scene, but many just stayed as close as they were permitted looking at all the damage and casualties. Mary could still see from her vantage point and watched with curiosity and horror as the scene unfolded. She saw passengers and others near the area continue to call out in distress; some were even frantically removing their clothes. The ambulance personnel worked on those who were passed out on the knoll, as other injured people seemed to have difficulty breathing and seeing. Eventually, emergency personnel in "space suits" arrived at the accident site.

Investigators and reporters quickly swarmed the area. Mary was reluctantly interviewed a number of times, first by police and other investigators as she had witnessed the collision, and then multiple times by the media.

Mary eventually made it to work later that day. Along with her coworkers, she watched the events unfold on the local and national news stations. The authorities described the accident as an "unfolding mystery." Some of the channels even had terrorism experts commenting on the scene. They mentioned, based on the interviews and witnessed accounts, that, "it could be cyanide, it could be sarin ... we can't rule out the possibility that agents such as anthrax were released at the same time. There have already been casualties and there are likely to be more." There were several reports of accidents in other states that were initially reported as possible terrorist attacks. The experts discussed possible "infection and contamination" from a variety of different biological and chemical agents along with the symptoms that could indicate exposure.

Already a nervous person, Mary perseverated on the images and commentary over the workday. She thought, "I was definitely in the range of what they were talking about." Mary became scared, weak, felt fatigued and flu-like. She recalled that she had coughed a couple of times after leaving the scene while on the way to work. Also, her shoulders were sore, she felt exhausted, and thought she might throw up. "Could this be anthrax?" she thought. "Didn't the experts say there was a gastrointestinal form of anthrax?"

QUESTION 7

If you were consulted in the above case and received the above history, one appropriate and simple intervention to help minimize Mary's stress might be to:

a. Excuse Mary from work for several weeks to recover.

b. Suggest that she turn off or limit television viewing of the incident.

c. Refer her for an immediate psychiatric intake in order to start anxiolytic medication.

d. Report to the nearest emergency room to ensure she was not infected.

No longer able to control her worry, Mary abruptly left work and proceeded to a nearby emergency room. When she got there, she was surprised to find the emergency room filled with people. To her, it felt as if there were "hundreds" of people there, most of them were standing around and waiting to see a doctor because they thought, like her, they might have been exposed. Waiting in the triage area made things worse, as she heard rumors regarding the attack and the different agents that were discovered. Many of her symptoms were similar to those waiting in triage; she started to feel more nauseous and weak. Her face looked flushed in the restroom mirror and she was sure she was "burning up with fever."

When she was eventually seen, it was only for a few minutes. She was asked about her symptoms and present difficulties. She was not even seen by a doctor. She looked at the nurse in disbelief when she was told, "You look pretty good. You're probably frightened like everyone else but your vital signs are basically normal. No fever. Nothing to worry about. If you experience shortness of breath, chest pain, a bad cough, confusion, rash, or worsening dizziness, you should see your doctor or return to the emergency department." She thought to herself, "Maybe they don't know how sick I could be. How do they know?"

Mary left the emergency room reluctantly, thinking that her concerns had been dismissed by the medical establishment. She felt scared, helpless, and a little angry. She would just have to "wait it out and hope for the best." For the first time that day, she remembered she had to go home and take care of her dog. The distraction seemed to help a bit. Mary began to feel a little better when she reminded herself of her role taking care of her beloved pet at home. She felt less alone and helpless, as she focused on something other than the horror of the day and her vulnerability.

A brief interview accompanied by a focused physical exam is medically indicated and is an essential component of psychological first aid.

COMMENT: The effective identification and triage of patients with psychological concerns from those with illness due to exposure, is a critical first task of emergency management. A brief interview accompanied by a focused physical exam is medically indicated and is an essential component of psychological first aid. Physicians should treat anxiety with calm reassurance, explaining that it is a normal reaction and likely self-limited, and that given the level of concern, seeking help was an appropriate response. In Mary's case, the fact that she had witnessed the attack and was in the immediate area could prompt an intervention, such as a follow-up registry so she would know that she will be contacted regardless of continuing symptoms. Terms such as "worried well" should not be used, as this conveys that people's concerns are not serious and their symptoms are "made up" or "all in their head." A term such as "low risk" may be more appropriate.

Individuals who do not respond to reassurance may require a period of monitoring before they feel safe to leave. These individuals, who remain fearful and not reassured by negative findings, may be best

cared for and monitored in a separate holding area in close proximity to the emergency department. This holding area would allow for continued evaluation and reassurance, and easy return to the emergency department if required.

Over the next few days following the accident, Mary continued to experience difficulties. She began having problems getting to sleep and regularly thought about the bus accident, specifically the mayhem, the anguish on people's faces and her own possible exposure. Some of the thoughts running through her mind included, "What is this going to do to me? Was I exposed? Is this going to happen again?" These thoughts made her anxious and were almost always accompanied by fatigue, stomach pains, and muscle aches.

Compounding all of this, she was late to work two times because of the new circuitous route she began following in order to avoid taking the usual bus. On more than one occasion, her coworkers commented to her that she seemed "not as sharp," as she was making simple mistakes in her paperwork. They also referred to her as being "in a daze" some of the time. Her coworkers often had to call her name multiple times in order get her attention. Mary also noticed that she started to forego her regular activities and social obligations, in part because she thought about her safety, and because it just felt better to stay home. She was aware that she felt "detached and removed." In the face of such a "real tragedy," her former interests and activities just seemed "insignificant and pointless."

COMMENT: Mary exhibits many of the symptoms of Acute Stress Disorder (ASD).[7] For the diagnosis of ASD, the symptoms must begin within 4 weeks of the trauma, continue for at least 2 days and resolve within 4 weeks. If the symptoms do not abate within the 4 weeks, the diagnosis of Posttraumatic Stress Disorder (PTSD) should be considered.[7]

Acute Stress Disorder symptoms produce significant occupational, interpersonal, or social impairment. The ASD diagnostic symptom clusters include: [7]

1) re-experiencing of the traumatic event – which may occur through recurrent dreams, flashbacks, thoughts, a sense of reliving the experience, or distress on exposure to reminders of the event.

2) avoidance behavior – manifested by avoidance of stimuli such as thoughts, places, feelings, conversations, activities, people, and conversations, reminding one of the events.

3) symptoms of hyperarousal – including symptoms of increased anxiety, usually in the form of difficulty sleeping, irritability, problems concentrating, restlessness, and exaggerated startle response.

4) dissociative symptoms – experienced either during or after the event and include derealization, depersonalization, dissociative amnesia (ie, the inability to recall important aspects of the event), reduction in awareness of surroundings, and a subjective sense of numbing, detachment, or absence of emotional responsiveness. This additional cluster of dissociative symptoms differs from the symptom clusters defined by PTSD.

Acute Stress Disorder appears to be a reliable predictor of PTSD. Several studies have shown a large majority of survivors of traumatic experiences (up to 80%) meeting criteria for ASD met criteria for PTSD at a 6 month follow-up.[9-10] Risk factors for ASD have not been studied as rigorously as those for PTSD. Exposure to prior trauma, premorbid psychiatric conditions, and prior PTSD have been implicated as risk factors for the development of PTSD, as well as experiencing dissociation during the actual event. Dissociation during the event is often described as a sense of time slowing or being outside oneself watching the scene as one would watch a movie.[11-12]

QUESTION 8

Which of the following interventions, as studied in randomized controlled trials, has shown efficacy treating ASD, as well as possibly preventing the progression to PTSD?

a. Benzodiazepines

b. Selective serotonin reuptake inhibitors

c. Cognitive behavioral therapy

d. Hypnosis

Mary knew there was something wrong, because she did not feel like herself. She understood she was changing her habits as a result of her experiences over the past 2 weeks. Although government officials had confirmed, almost immediately, that the agent was indeed phosgene, Mary continued to fear that this was not the whole story. She felt that the press was minimizing possible longer-term dangers of chemical exposure. It occurred to her that she could investigate the risks herself rather than depending on news stories. A superb researcher, she meticulously combed online libraries for articles on phosgene, terrorist attacks and the public's reaction, reading as many resources as she could obtain. She felt relieved that many of her symptoms were not typical for phosgene exposure and was able to reassure herself again that she had not been close enough to the accident to be exposed.

From her readings, she also started to gain some understanding about the psychological and behavioral effects of terrorism, and how her response was not really unusual at all. She found that following the 1995 Aum Shinrikyo sarin attack at major subway stations in Tokyo, over 4,000 people presented for care who had no history or evidence of exposure. The attack killed 11 people and 1,046 people were admitted to hospitals because of visual symptoms, nausea, headache, cough, dyspnea, cardiac symptoms and neuropathy.[14] Based on this event, Mary reasoned that the rate of psychological casualties to medical casualties was about 4:1.[14,15] She also learned that arousal and intense anxiety were often experienced as physical symptoms much as she had felt, such as palpitations, shortness of breath, flushing, and nausea.

In another study of emergency room visits during scud missile attacks on Israel during the 1991 Gulf War, almost 80% of patients seen were suffering from anxiety or accident injuries in response to the threat, such as improper use of gas masks or running and falling.[16] As distressing as these scenarios were, Mary felt better by understanding that other people had similar experiences to hers.

Over the subsequent days, Mary began to think about her reactions and was able to quietly laugh about it. She felt ashamed about the circuitous route she created to avoid using the bus, which added over an hour and three transfers to her usual commute. Putting these events into perspective with her new found knowledge helped her a great deal, and her sleep, physical symptoms, and anxiety improved. She also began socializing again. The last step for her, she thought, is to ride that bus once again.

As the bus approached, she felt nervous but assured. This would be her first ride on the bus since the phosgene attack. She entered the bus, paid the fare, and sat in her regular seat. She felt relieved to see some familiar faces on the bus as well. She felt the strength of others who were not going to let the attacks alter their routine.

COMMENT: In response to acts of terrorism, most individuals will experience some level of distress. The range of response is quite varied and can include sadness, depression, anger, insomnia, diminished concentration, fear, and hypervigilance. Other responses include altering behavior-changing routines, traveling less, staying at home, or increasing use of alcohol or tobacco. Most people recover. However, some will develop more chronic symptoms and illness such as depression, substance abuse, generalized anxiety, panic, and unexplained physical symptoms. Patients suffering from these conditions are most likely to be seen in primary care settings. PTSD may also develop, although other problems are more common. Risk factors for developing PTSD include: premorbid psychiatric illness, female gender, having a family history of psychiatric illness (such as depression, anxiety, PTSD), previous exposure to trauma, being directly exposed to the trauma or event, acute losses and negative life events after the trauma.

It is important to remember that human beings are resilient, adapt to stressful situations, and often develop new strengths in the face of adversity. (For additional information regarding resiliency and post-traumatic growth, see another case in this series, *Psychiatric Sequelae in a Survivor of 9/11* by Drs. Derrick Hamaoka and Molly Hall.) Mary sets an example of "active coping," which can be thought of as recognizing and accepting the impact of traumatic experiences and then implementing concrete, obtainable actions to improve things.[17]

ANSWER KEY & DISCUSSION

QUESTION 1

What is the significance of the strong perfume odor?

a. Its similarity to perfume probably excludes the use of a dangerous agent.
b. The perfume-like smell indicates probable use of a nerve agent such as sarin.
c. The nature of the odor in this case is not a useful clue in identifying the agent.
d. The failure to detect the odor of newly mown hay excludes the use of phosgene.

ANSWER: The correct answer is c. Although characteristic odors have been associated with certain military and industrial chemicals, odor by itself is misleading for several reasons. First, odors are notoriously subjective, so that interpretations of the odor of a given chemical are often different. Significant damage can occur below the olfactory threshold for several agents. The ability to detect the characteristic odor of hydrogen cyanide is conferred by a single gene that half the population lacks. Olfaction is the sense most susceptible to accommodation, and some chemicals, such as hydrogen sulfide, may damage the olfactory pathway so that the odor rapidly becomes unnoticeable. Finally, odor is a well-recognized precipitating factor for a variety of psychological reactions.

QUESTION 2

While your colleagues and you are assessing the situation, police and emergency medical response personnel arrive on the scene. Which of the following actions regarding decontamination is correct?

a. All passengers must be decontaminated by whole-body washing with soap and water before being transported.
b. None of the passengers needs to be decontaminated.
c. All passengers should be first instructed to remove their outer clothing.
d. All passengers should be washed using diluted bleach.

ANSWER: The correct answer is c. Prompt decontamination of liquid chemicals may be one of the simplest and yet most effective and important life-saving measures that can be taken at the scene of an exposure. Because many toxic liquid chemicals may quickly penetrate the eyes, skin, and wounds,

decontamination of liquid must occur as soon as possible and should begin with removal of liquid-soaked clothing and with immediate local, or "spot," decontamination of affected skin, eyes, and wounds. Washing with water, with or without soap, will suffice for most cases. Bleach is usually contraindicated because of its relative slowness of action and its propensity to cause the kind of tissue damage that may lead to increased penetration of agent into tissues. Some chemicals, such as pulmonary toxicants, may cause local skin and eye irritation without posing a major risk for systemic distribution via percutaneous or intraocular absorption. Nevertheless, when the identity of the agent is in doubt, all liquid must be considered to have the potential to cause systemic toxicity via absorption and must be removed as quickly as possible.

QUESTION 3

Between 2 and 4 hours after exposure, 5 patients from the front third of the bus, begin to report chest tightness and shortness of breath. What is the significance of these symptoms?

a. **Respiratory effects from nerve agents and pulmonary agents would not be expected to present this late after exposure, effectively ruling out these kinds of agents and suggesting psychological effects.**
b. **These findings are typical of a respiratory tract agent affecting the lower or peripheral airways.**
c. **These findings strongly suggest that bronchodilators and early intubation should be considered.**
d. **These findings imply denudation of respiratory epithelium from large to medium-sized bronchi.**

ANSWER: The correct answer is b. Dyspnea refers to the subjective sensation of difficulty breathing. It may be expressed as a tightness in the chest or shortness of breath, and can arise in a variety of situations, including high altitudes, physical exertion, and emotional stress. In the context of chemical agents, delayed-onset dyspnea is the hallmark of exposure to a pulmonary toxicant, or respiratory irritant affecting the lower, or peripheral airways.

QUESTION 4

Which of the following chemical agents is the most likely cause of the chest tightness and shortness of breath?

a. **A strong mineral acid or base such as hydrochloric acid or ammonia**
b. **A riot-control agent or tear gas**
c. **Phosgene**
d. **Chlorine**

ANSWER: The correct answer is c. Phosgene is a major industrial chemical used to make plastics and pesticides. At room temperature it is a poisonous gas, but with cooling and pressure, it can be converted into a liquid. When liquid phosgene is released, it quickly turns into a gas that stays close to the ground and spreads rapidly.[2] Phosgene affects the lower, or peripheral, portion of the respiratory tract. Strong mineral acids and bases primarily affect the upper, or central, airways, as do riot-control agents ie, tear gas, sulfur mustard, and smoke or dust particles. Chlorine tends to affect the upper and the lower airways to approximately the same degree. *Please review the Appendix for a discussion of other chemical agents and their effects on the pulmonary compartments.*

QUESTION 5

What is the most likely pathological process occurring in the patients with chest tightness and shortness of breath?

a. **Reflex bronchoconstriction from airway irritation**
b. **Necrosis and denudation of respiratory epithelium**
c. **Pseudomembrane formation eventually leading to partial or total airway obstruction**
d. **Damage to alveolar-capillary membranes eventually leading to pulmonary edema**

ANSWER: The correct answer is d. "Irritation" is a process largely affecting the supraglottic airways, the larynx, and the upper airways. Damage to the upper (central) airways can lead to necrosis and sloughing of respiratory epithelium, sometimes as membrane-like sheets, or pseudomembranes. This process can lead to partial or total airway obstruction. The pathological process occurring with lower-airway damage is damage to capillary endothelium in alveolar septa. Fluid leaks from the capillaries first into the alveolar walls and then into the alveoli and results, usually after a delay of several hours, in acute respiratory distress syndrome (ARDS), or noncardiogenic pulmonary edema.

QUESTION 6

What is the most appropriate next step regarding disposition of these patients?

a. **They can be discharged with instructions to return to the hospital if their condition worsens.**
b. **They should be held for an additional two hours and then given a trial of exertion to see whether they become short of breath.**
c. **They should be observed in the hospital for at least 8 to 24 hours.**
d. **They should be kept at strict bed rest for one week.**

ANSWER: The correct answer is c. Resolution of initial central-compartment effects such as mucosal irritation and coughing does not exclude exposure to a peripheral-compartment agent such as phosgene (the actual culprit in this case). In fact, the transient presence of such signs indicates exposure to a relatively high concentration. If the duration of exposure translates to a sufficiently high concentration-time product, or Ct (a rough indicator of dose), peripheral-compartment damage will already have occurred but may not manifest itself for several hours.

A high index of suspicion must be maintained, and the patient must be kept at rest and monitored for dyspnea, which apart from nonspecific changes on chest radiographs will be the first clinical indicator of incipient pulmonary edema. At the very least, vital signs and lung sounds should be monitored every 30 minutes, and initial chest radiography should be repeated every two hours. Oxygen should be administered, and other therapies that might be effective during the latent period should also be considered. Patients should be kept under observation for at least eight hours. After that, if their chest radiographs are normal and they exhibit no dyspnea, they may be discharged with strict instructions to be driven back to the hospital at the first onset of dyspnea. Preferably, patients with a history of initial central respiratory effects should be monitored for 24 hours. This 24-hour monitoring period should be considered mandatory for patients for whom chest radiographs are unavailable.

QUESTION 7

If you were consulted in the above case and received the above history, one appropriate and simple intervention to help minimize Mary's stress might be to:

a. **Excuse Mary from work for several weeks to recover**
b. **Suggest that she turn off or limit television viewing of the incident**
c. **Refer her for an immediate psychiatric intake in order to start anxiolytic medication**
d. **Report to the nearest emergency room to ensure she was not infected**

ANSWER: The correct answer is b. After reviewing that she had witnessed a very frightening event and that her increased anxiety and distress could account for her physical symptoms, suggest that she turn off or limit television viewing of the incident. This intervention may prove to be an appropriate and simple way to minimize stress. Repeated viewing of a horrific event on television can be distressing and is an indirect exposure to trauma. This is one component of psychological first aid or early interventions employed after a disaster including attending to basic needs, normalizing sleep-work cycles, providing sufficient rest, facilitating reunions of families, and providing information and education. (For additional information regarding psychological first aid, see another case in this series, *Emergency Mental Health After a Suicide Bombing* by Dr. David Benedek.)

Keeping her from work and other regular activities would be detrimental. This would reinforce avoidance behavior. Getting people back to their homes and jobs as soon as possible helps individuals and communities recover more quickly.[6]

Judicious use of benzodiazepines or sedative-hypnotics may be warranted if the anxiety and/or sleep difficulties are resistant to reassurance. Since reassurance and other simple measures have not been used at this point, these should be attempted first. Therefore, referral would not be the most appropriate effective intervention at this time.

Mary is well and does not report concerning symptoms. While reporting to the emergency room would be a prudent course of action if she were experiencing disabling physical symptoms and appeared acutely ill, this would not be the simplest and most appropriate action based on the above scenario.

QUESTION 8

Which of the following interventions, as studied in randomized controlled trials, has shown efficacy treating ASD, as well as possibly preventing the progression to PTSD?

a. **Benzodiazepines**
b. **Selective serotonin reuptake inhibitors**
c. **Cognitive behavioral therapy**
d. **Hypnosis**

ANSWER: The correct answer is c. Studies have demonstrated efficacy of cognitive behavioral therapy (CBT) for ASD.[13] This intervention has also shown promise limiting the progression to PTSD. Principle tools of CBT employed for ASD are normalization of feelings/affect, relaxation techniques (such as deep breathing, and deep muscle relaxation), and prolonged imaginal exposure (which involves repeated and detailed imaging of the experience in a safe setting).

Benzodiazepines might be helpful in decreasing some of the initial hyperarousal symptom but do not treat the symptoms of ASD or PTSD. Although certain selective serotonin reuptake inhibitors have the FDA indication for the treatment of PTSD (ie, sertraline and paroxetine), these have not yet been shown through randomized controlled studies to be effective for treating ASD. Lastly, hypnosis may serve as an adjunctive treatment, but it is not well studied by randomized controlled trials in patients with PTSD and ASD. Therefore, it is not considered the first-line treatment for either disorder.

APPENDIX:
DESCRIPTION OF CHEMICAL AGENTS WITH CENTRAL AND PERIPHERAL COMPARTMENT EFFECTS

CENTRAL COMPARTMENT

Chemical Warfare Agents

- Sulfur mustard, which is relatively insoluble in water, but its incredibly high chemical reactivity once dissolved tips the scales in favor of action in the central compartment. Sulfur mustard is officially classified as a blister agent, or vesicant, but it also acts as a central compartment pulmonary agent when inhaled.

Industrial Chemicals

- Acids, such as hydrogen chloride, acetic acid, hydrogen fluoride, and sulfur dioxide
- Bases, such as ammonia
- Low-molecular-weight aldehydes, such as formaldehyde and acetaldehyde
- Acrolein, which also has peripheral compartment effects
- Chloramines, which also have peripheral compartment effects
- Smoke particles, although not industrial chemicals, also lodge in the central compartment of the respiratory tract and have central effects

PERIPHERAL COMPARTMENT

Chemical Warfare Agents

- Diphosgene
- Chloropicrin
- Chlorine is also grouped with these agents, but chlorine is intermediate both in water solubility and in chemical reactivity and exerts mixed central and peripheral compartment effects in almost equal proportions
- Lewisite, a blister agent or vesicant, acts both as a central agent and, because of its effects on capillary permeability throughout the body, as a peripheral compartment agent in the lungs when inhaled
- HC smoke, which is standard white military obscurant smoke, also has prominent peripheral compartment effects

Industrial Chemicals

- Carbon tetrachloride
- Methyl isocyanate (the chemical released in Bhopal, India in 1984)
- Phosgene, which is a dual-purpose chemical used extensively in industry
- Acrolein, which also has Type I effects
- Oxides of nitrogen, which are present in low concentrations in photochemical smog but in much large concentrations in munitions fires
- Perfluoroisobutylene (PFIB), a combustion product of polytetrafluoroethylene (Teflon®)
- Chloramines, which have both central and peripheral compartment effects
- Arsine, which has peripheral compartment effects in addition to its systemic effects

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