Mass Casualty Chemical Exposure and Implications for Respiratory Failure

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Exposure to chemical agents, both deliberate and accidental, over the past 100 years has resulted in the deaths of thousands and a significant number of casualties requiring hospitalization. The respiratory system is an important portal of entry into the human body for many of these agents, and pulmonary symptoms are a hallmark of many chemical exposures. The 4 major chemical warfare agents are: lung-damaging, blood, blister, and nerve compounds. The review will cover historical exposures, signs and symptoms, treatment, and long-term consequences. There are numerous examples of deliberate (as well as accidental) exposure to harmful chemicals, and each incident requires the provider to understand the signs and symptoms of the particular chemical so that the correct treatment is provided. The respiratory implications of these agents appear to be dose and timing dependent, with full recovery often seen if supportive measures and appropriate antidotes are administered in a timely fashion. *Key words: chemical warfare agents, lung-damaging agents, blood agents, blister agents, nerve agents, antidotes, respiratory effects of chemical agents.*
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Introduction

The industrial age brought a number of new processes into our civilization, including the mass-production of chemicals. With the increasing use of these chemicals it was only inevitable that they were adapted for warfare. World War I marked the first mass casualty event from an intentional chemical exposure. On April 22, 1915, Germany sprayed chlorine gas onto the battlefield at Ypres, Belgium, against the French and Canadian military forces. Approximately 168 tons along a 7,000-m front were released into the atmosphere over the battlefield. It is important to note that the wind direction changed and subsequently both sides of the battlefield were exposed to the chemicals. There were reportedly 5,000 casualties. The continued use of chlorine and mustard gas throughout the

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war has been attributed to over half a million deaths. Most of the gas exposure casualties were due to mustard gas; however, chlorine and phosgene produced 80% of the fatalities from chemical agent exposure in World War I. A number of international treaties banning the use of chemical agents in war were successfully introduced following World War I; however, war-time use of chemical weapons continued throughout the 20th century. The most recent episodes were in 1963 in Yemen and in the 1980s, with the use of mustard gas against the Iranian military and Kurdish civilians.[1] Nerve agents were used as genocide materials in World War II by the Nazis. In 1994 and 1995 a terrorist group in Tokyo used nerve gas in an apartment building and a subway train.[2] Despite these well-publicized incidents, the most likely exposure of a health care provider to a chemically injured patient is due to industrial accident. The greatest example of this was the 3 tons of methyl isocyonate accidentally released over Bhopal, India, from a chemical plant mishap, which exposed a population of over 200,000. Deaths attributed to the exposure now number over 6,000. The number of hospitalized was in the tens of thousands, and the number of ventilator patients is unknown.[3] Today's health care provider must be comfortable with and knowledgeable about the signs and symptoms of exposure to various chemical agents, and their treatment.

Classification of Chemical Warfare Agents

Chemical agents that are damaging to humans are classified according to their war-time use and physiologic action, into 4 primary categories: (1) lung-damaging agents, which are exemplified by chlorine and phosgene, (2) blood agents such as cyanide, (3) blister agents, which include mustard and lewisite, and (4) nerve agents. A fifth group of incapacitating agents, such as tear gas, is considered to be a subcategory.[4] Lung-damaging agents primarily cause pulmonary injury and edema, and may also irritate the eyes and other mucous membranes. Blood agents interfere with cellular oxidative phosphorylation, causing direct cell death. Blister agents directly attack exposed tissue, including skin, mucous membranes, and airways, causing direct toxic damage. Nerve agents act by interfering with acetylcholinesterase and the subsequent transmission of nerve impulses throughout the nervous system. Nerve agents as a group include the warfare agents that were developed during and after World War II, but also include organic insecticides.

Lung-Damaging Agents

The primary chemical agents that attack the lung tissue and cause pulmonary edema are ammonia, chlorine, and phosgene. The toxicity of the compound is related to the water-solubility of the chemical. Compounds like ammonia are highly water soluble and cause damage in the nasal, ocular, and upper airways. Limited water-soluble compounds such as phosgene damage the alveolar capillary membrane, resulting in pulmonary edema and acute respiratory distress. Chlorine has intermediate water-solubility and can damage both upper and lower airways. There is often a latent period following exposure, with symptom onset delayed several hours to days. When symptoms do develop, however, the patient may develop sudden death due to laryngeal obstruction from edema or bronchospasm.[5] All of these agents are commonly found in industrial use and are responsible for a substantial number of our potential respiratory casualties in the event of exposure. Chlorine is widely used in the manufacturing of paper, metal, textiles, and pharmaceuticals, and the chemical is routinely transported via interstate truck and rail lines. Since 1916 there have been over 500 documented serious industrial accidents involving chlorine.[6] The majority of these exposures were acute, and levels reported were often above 300 ppm. Exposure to chlorine results in immediate symptoms, including nasal irritation, burning sensation of the mucous membranes, and lacrimation. The patient will develop copious oral, pharyngeal, and pulmonary secretions and a choking sensation, along with chest pain and dyspnea. The patient may develop fulminant pulmonary edema, leading to acute respiratory distress and sudden death if not treated immediately. However, it appears that following the successful treatment of an acute chlorine exposure there appear to be no long-term pulmonary effects, in symptoms or lung function. Long-term exposure to chlorine can lead to the development of reactive airway disease that requires treatment similar to that for asthma.[7]

Chlorine is a greenish yellow gas that is heavier than air; therefore it tends to settle in low-lying areas. The first move to be taken following exposure to chlorine is to remove the patient from that environment. The clothing should be removed from the patient, and the skin copiously flushed with soap and water. If the patient has contact lenses, they need to be removed. Following exposure, the patient requires supportive care, to include use of intubation and ventilator care, with no specific antidote available for chlorine. Rest is recommended for toxic inhalation injuries, because exertion worsens the symptoms.[8] Aggressive use of bronchodilators and humidified air has been shown to be useful. In addition to supportive airway management with mechanical ventilation and positive end-expiratory pressure, additional therapies have been investigated, including the use of inhaled sodium bicarbonate. Sodium bicarbonate has been used to neutralize the hydrochloric acid generated from the chlorine inhalation.[9] Steroids have been evaluated, but with limited human studies at this point.[10] It is important to monitor patients closely for the development of secondary infections, including

bronchitis and pneumonitis, which are very common in these particular chemically injured patients.[11] They usually occur within 3–5 days after exposure, with development of a fever and chest infiltrates. However, it is important that prophylactic antibiotics not be used and that they are given to the patient only when proven systemic pulmonary infection is documented.

Ammonia is a highly water-soluble agent used in a number of industrial processes, including fertilizer production. It appears to be absorbed in the upper airway, leading to obstructive symptoms of cough, stridor, and laryngospasm. It is critical that the patient exposed to ammonia be considered for early intubation, prior to the development of a complete blockage of the airway. Treatment is symptomatic, and once the effects have worn off, the edema usually resolves and the patient recovers fully, with no permanent effects.[12]

Phosgene was used as a weapon in World War I and is also currently used in a number of manufacturing processes, including the development of dyes, pharmaceuticals, and pesticides. It was implicated as one of the chemicals in the Bhopal tragedy in India in 1985. Phosgene is a colorless gas with a smell characteristic of freshly mown hay. It is also heavier than air and remains a gas above 8.3°C. Phosgene combines with water in the mucous membranes and lung tissue to produce hydrochloric acid and carbon dioxide. The clinical syndrome is initially a slight irritation to the nasal passages and the lungs; however, there is a symptom-free period of approximately 2–10 hours. Severe exposure leads to a second onset of symptoms less than 6 hours following exposure, whereas a mild exposure can lead to an onset of symptoms more than 6 hours following exposure. Any exertion in this period of time markedly increases toxicity. The alveolar membranes are attacked during this time by the carbonyl group, which is produced by the chemical action, leading to noncardiogenic pulmonary edema, subsequent hypotension, and volume depletion. A chest radiograph at the time of early onset (2 h) will often be negative; however, a radiograph at 7 hours will be markedly changed, with substantial bilateral pulmonary infiltrates seen.

In patients who have been exposed to phosgene it is critical that the airway be managed with early consideration of intubation and positive end-expiratory pressure. Bronchodilators combined with corticosteroids have been recommended for severe phosgene inhalation. It is imperative that diuretics be avoided, as they will contribute to further hypotension and eventual cardiac failure. Volume replacement is the mainstay of therapy, along with ventilator support. There appears to be minimal lasting damage to the lung tissue, and the patient will improve within 4–5 days unless they develop a secondary infection.[13,14]

Blood Agents

Blood agents are characterized by hydrogen cyanide and cyanogen chloride. They affect metabolism by shutting it down at the cellular level. These cyanides are encountered commonly in manufacturing as well as being a by-product of combustion. They are a colorless, highly volatile liquid that acts by combining with cytochrome A to block oxidative phosphorylation and adenosine triphosphate production. The heart still pumps oxygenated blood, and the patient is characteristically pink, but despite the well-oxygenated blood, tissue hypoxia rapidly ensues, and the brain is particularly vulnerable to tissue hypoxia. Death comes rapidly after severe exposure to cyanogens.[15] Low-intensity exposure can produce headache, vertigo, and nausea, and moderate exposure can lead to severe central-nervous-system dysfunction, including weakness and confusion. The patient may develop seizures and go into a coma. Exposure to cyanogens can lead to death within minutes, and therefore it is critical that if the patient has been exposed the antidote be administered as rapidly as possible.

Clinical manifestations are classically bright red venous blood, skin, and fundal vessels. Patients often report the odor of bitter almonds. The patient develops tachypnea, hypertension, respiratory depression, and bradycardia. An arterial blood gas analysis would show a profound metabolic acidosis with a high anion gap. All patients should be immediately removed from further exposure and decontaminated, including the removal of all clothing and cleaning the exposed skin with soap and water. For low exposures there may be no important symptoms noted by the medical team. Supportive care and observation may be all that is necessary for 24–48 hours. With moderate exposures there should be airway and circulation support.[16]

Severe exposure does require specific antidotes for cyanide, along with administration of oxygen, hyperventilation, sodium bicarbonate, and intravenous fluids. The current Food and Drug Administration approved antidote kit (Taylor Pharmaceutical/Akorn, Decatur, Illinois) consists of amyl nitrite, sodium nitrite, and sodium thiosulfate, and should be administered as follows. Sodium nitrite is given to the patient, which displaces the cyanide moiety from the cytochrome oxidase molecule and forms cyanomethemoglobin. The current dose of sodium nitrite is 10 mL of 3% solution administered intravenously over 5–15 min. Amyl nitrite can be administered to an awake breathing patient by crushing the glass ampoule and holding it under the patient's nose. Two to three breaths per glass ampoule is the usual dose. The blood pressure must be carefully monitored to avoid hypotension. Once a clinical response has been seen, sodium thiosulfate should be administered to the patient. Sodium thiosulfate reacts with cyanide to form thiocyonate, which is then excreted by the kidney. Sodium thiosulfate is administered as 50 mL of 25% solution intravenously over a 10-min period.[17] Since 1970, hydroxo-

cobalamin, a cobalt-containing cyanide chelator, has been successfully used in combination with thiosulfate and is an alternative to the regimen outlined above.[18] Following a successful treatment after cyanide exposure the patient should recover fully, with no long-term effects noted.

Blister Agents

Vesicants or blister-producing agents cause severe eye, mucous membrane, and skin irritation. Sulfur mustard was first used in July 1917, as previously mentioned, and was responsible for 80% of the chemical casualties in World War I. The vesicants also include lewisite and phosgene oxime; the primary difference is the onset of action. Mustard exposure symptoms and signs often present 24 hours after exposure. Phosgene oxime causes immediate irritation upon exposure. Mustard agents are absorbed rapidly by the tissue and irreversibly alkylate deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) and cellular proteins, causing cell death. Skin exposure symptoms range from erythema to bulbous lesions to full-thickness damage. Gastrointestinal symptoms include nausea, vomiting, and necrosis of the gastrointestinal mucosa. However, it is the primary pulmonary symptoms that we are interested in. Mustard inhalation injury leads to substantial inflammatory reaction, and severe exposure can cause hemorrhagic bronchitis and/or necrosis.[19] Secondary infections, including bronchial pneumonia, are common, and in fact are the major cause of mortality if untreated. Unlike the previous agents, mustard gas does have long-term effects on the respiratory tract, including recurrent infections, narrowing of the airways, bronchiectasis, and respiratory cancers. The onset of pulmonary symptoms is marked primarily by upper-airway complaints such as hoarseness, cough, and wheezing, often within 4–6 hours of exposure. Pseudomembranous casts of the bronchial tree have been found.[20] Treatment of mustard injury is primarily supportive, because there is no specific antidote for mustard exposure. Decontamination is critical but must occur with 1–2 min of exposure if you are attempting to minimize tissue damage. The treatment of mild pulmonary exposure is limited to the use of humidified air and cough suppressants. Oxygen, ventilation, and positive pressure can all be used for moderate-exposure inhalation injuries. For severe exposure, consider early intubation. Bronchodilators have been used if wheezing is present. Antibiotics should be reserved for patients who have infections and the organism is identified.[21]

Nerve Agents

Nerve agents are highly lethal organophosphate compounds first developed in Germany before World War II as a potential pesticide. Germans used tabun, sarin, and soman as weapons of genocide in concentration camps during World War II. An additional nerve agent was developed after World War II, which is titled VX. All of these agents are highly lethal and capable of killing large numbers of people with a small dose. Each of them acts in a similar fashion, by inhibiting the breakdown of the neurotransmitter acetylcholine. This results in excess stimulation of muscarinic and nicotinic receptors.[22]

Signs and Symptoms of Nerve-Agent Exposure. The nerve agent droplets are absorbed through the upper respiratory tract and large airways during vapor exposure. Liquid drops are absorbed directly through the skin and any other exposed tissue. Respiratory exposure can yield an onset of symptoms within seconds to minutes. However, skin exposure can be delayed by 15–20 min to several hours. Excessive stimulation of the nerve receptors yields a substantial increase in the production of bodily fluids, which is marked by watery eyes, salivation, profuse sweating, and increased airway secretions. In addition, the muscarinic effects include bronchoconstriction. Nicotinic receptors cause twitching of the skeletal muscle, followed by fatigue and paralysis. Severe exposure to a nerve agent often results in respiratory failure from neuromuscular weakness. Cardiac toxicity is classically biphasic, with an initial period of sinus tachycardia and hypertension, followed by a vagally mediated bradycardia. Hypertension occurs at the end stage. Most cases of patient death are due to respiratory failure, which precedes cardiac failure. There are gastrointestinal symptoms such as nausea, vomiting, and diarrhea, which are commonly seen. Central-nervous-system effects include loss of consciousness, seizures, and flaccid paralysis.[23]

In 1994 the terrorist group Aum Shinrikyo initially used sarin gas in an apartment building, which resulted in approximately 600 exposures, 58 hospital admissions, and 7 deaths.[24] In 1995 a similar diluted form of sarin gas was released into 5 subway cars in Tokyo, Japan, resulting in 5,000 patient evaluations, 45 patients who required respiratory support, and 11 deaths. The 45 patients were evaluated for respiratory symptoms with arterial blood gas analyses; however, only 4 of the patients required intubation, 3 were extubated within 24 hours, and one died from severe anoxic brain injury following cardiopulmonary arrest.[2]

Treatment of Nerve-Agent Exposure. The management of a nerve-agent exposure should include immediate decontamination and removal from the environment. Airway breathing and circulation support should always be administered, along with the appropriate antidotes. The first successful decontamination of a nerve agent relies heavily on copious amounts of water and a 0.5% sodium or calcium hypochlorite solution. The United States mili-

tary uses a charcoal and absorptive resin mixture to decontaminate droplets on exposed surfaces. If the patient requires intubation prior to effective decontamination or removal from the environment, it is critical that the airway be controlled with a definitive airway, and not by using an esophageal combi-tube, because of the excessive secretions often noted in these patients. Once the airway is secure, an appropriate charcoal filter device should be used, with a closed-circuit transport ventilator or self-inflating bag-valve device, along with a secure source of oxygen.[25] During the intubation it is important to avoid the use of succinylcholine, because the nerve agent's inhibition of acetylcholinesterase activity will severely prolong the paralytic effect. Respiratory secretions following an exposure may be substantial, and mucus plugging will be a problem. Humidified air, along with aggressive use of nebulized ipratropium and β agonist, will be necessary.[26] During this process, after the airway is secure and decontamination is completed, the antidote should be administered as rapidly as possible. The treatment of nerve-agent poisoning is done using atropine and pyridine-2-aldoxime chloride (2-PAM-Cl). Atropine is administered in 1–2-mg increments every 5–10 min, looking for a response in dyspnea and reduction in airway resistance. Atropine serves as a useful agent because it blocks the effects of excess acetylcholine. Following administration of atropine, 2-PAM-Cl, an oxime acting to remove the organophosphoryl molecule, which is bound to the acetylcholinesterase, is given. A 600–800-mg intramuscular dose or 1–2 g intravenously over 30 min is used.[27] If the patient develops any seizure activity, valium or lorazepam has been used with high success. With stabilization of the symptoms (bronchorrhea and bronchoconstriction) following the administration of the antidote and with supportive measures the patient should be conscious and breathing within 3–4 hours of exposure and go on to recover with full function. However, with exposure to a persistent chronic low level of an organophosphate compound, and/or complications following mechanical ventilation, such as secondary infections, mechanical ventilation may be required for days or weeks.[28] All of the mechanically ventilated patients who were treated after an acute exposure to an organophosphate nerve agent required ventilator support for less than 48 hours. Only patients who had long-term low-dose exposures developed complications that required longer ventilation. These patient numbers are very small.

Management of a Chemical Incident

In the event of a large number of human casualties following a nerve-agent exposure it will be critical to set up an outdoor decontamination center with access to large amounts of water. Additionally, litters for all of the moderately injured patients, a large number of support personnel for decontamination, patient transport and security, and a large amount of protective clothing for those working outside the hospital will be needed. For those patients exposed to large amounts of nerve agent, 15 mg of atropine may be required per victim, which would deplete the hospital's entire supply very quickly. In addition, such medications as diazepam and 2-PAM-Cl would have to be stockpiled. Each patient will also require an intravenous line and appropriate personnel to place them.[29] Up to this point in history it appears that the number of chemical casualties that require ventilator support is very small, usually less that 5% of the total number of casualties. However, in a large mass casualty experience, even a small number of ventilator requirements may exceed the capacity of the hospital.

Summary

Despite the highly sensationalistic nature of a terrorist nerve-agent attack, the most likely cause for human exposure to a chemical agent will be following an industrial accident. Chlorine, ammonia, and phosgene appear to be the most likely, predominantly from factory accidents and/or railcar spills. Terrorist attacks have been rare thus far, with nerve agents being the most lethal. One should note that the largest number of casualties following a chemical incident will often be hysterical patients who think they have been exposed. Nevertheless, in the early minutes after an attack it will be very difficult for the health care worker to separate out the hysterical patient from the exposed patient. This will need to be prepared for in the hospital disaster plan. In addition, it appears that the number of chemically injured patients who require ventilator support will be small compared to the number of potentially exposed patients. If the patient does develop respiratory symptoms, prompt intervention with supportive measures in most cases with prompt administration of potential antidotes will often yield a successful outcome. Any delay in treatment can result in anoxic brain injury and death. Most patients will require ventilator support for only 2–3 days, but secondary infection might prolong that course. It will be incumbent on hospitals that are near chemical plants and railways to consider increasing their supplies of appropriate medications and ventilators. Annual education to providers and hospital staff on the signs and symptoms of chemical injuries is mandatory, and a regular mass casualty exercise should include the possibility of chemical scenarios.

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Discussion

O'Laughlin: Just a couple of comments. There was a recent FDA [Food and Drug Administration] approval for a new cyanide treatment option, hydroxocobalamin, which has been used in Europe for I don't know how many years, but a couple of recent articles on that were recently published on its use.[1–3]

The other comment that I wanted to make is in regard to chemical events, even for smaller or medium-size hospitals—one or two patients with a chemical exposure, especially to a pesticide or nerve agent—you are going to have enormous resource utilization required just to manage a couple of patients. A colleague of mine had to deal with a patient who had a pesticide exposure when he was working outside the United States at a medium-sized hospital, and they used every bit of atropine that they had in the facility. It is just one thing to consider with planning—not just large numbers, but resource issues as well.

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Muskat: I would second that. I think clearly from the use of atropine, in particular to nerve agents, the data clearly suggest that every patient who is exposed and you decide to treat, you're looking at substantial amounts of atropine and you *will* exhaust your hospital supply in no time. If you have more than a few patients, there's no question. That's why I threw in the caveat that if you are in a hospital that is even at a moderate risk of getting those patients, look to your supplies and make sure that you are prepared.

O'Laughlin: In regard to the ideal world and reality, just because I've seen it happen a couple of times—the mass-care event when people are first arriving at your facility before you know that you're dealing with a chem-

ical issue—the idea of respiratory therapists and other doctors usually not working the ED [emergency department] coming down and not necessarily needing to know about the decontamination process, it's going to be problematic for the first few patients who come through often times. Unless the event is known, we will have to backtrack and find the potential secondary exposures. There have been a few cases where things have been tracked around hospitals and then people get in trouble.

Muskat: I think that the Tokyo data clearly show that problem. Patients arriving at 2 hospitals, an MD [medical doctor] eventually making the diagnosis, but the number of health care providers that were exposed and indeed became symptomatic was substantial. I think that the more intelligence that we get from our EMS [emergency medical services] system, the better. We tend to think of ourselves living in a bubble in a hospital, and we are. We are very dependent on our EMS folks telling us what's coming and so forth. So I think as providers that if there is any hint that you've got a lot of patients coming with similar types of symptoms, the first question that we should be asking is "Are we at risk? Is there something out there that you haven't told us?"

Rubinson: Your point about needing to get therapeutics to patients quickly and maybe that'll reduce the event's impact—there really is in my mind 2 major agents that have antidotes—cyanide agents and nerve agents. With nerve agents we have Chempacks to be able to augment our regional supply. With cyanides we do have the new treatment, but it's 600 to 800 bucks a pop. They also have a relatively short time to expiration.

Do you see us as being any further along 6 years later from 2001 than before, or are we at risk of reverting back to that level of preparedness pre-9/11, despite going through a lot of money? Is there anything that we can learn from the military to apply to the civilian side?

Muskat: I've read recently that large amounts of the money that were allocated for hospital preparations and EMS systems and so forth have still not been spent. Perhaps the question we ought to be looking at regards the issue of stockpiling particular agents in certain predetermined areas such as the ED. With cyanide exposure, realistically, the people who need to have it are the EMS personnel in the field if we're going to make a difference on those moderate exposures. So, yes, I think that's something that we definitely need to look at as a society, and as we plan these mass casualty type scenarios everybody's worried about, but unfortunately, unless someone's willing to pay the dollars to put aside a stockpile of something, that rarely will happen.

Malatino: I am not sure how many members of the audience realize that we do have the Chempack; you mentioned it, Lewis [Rubinson]. The Chempack is forward-deployed supplies; they're not maintained in Push Packages or Managed Inventory in the Strategic National Stockpile. They are forward-deployed to the states and they are given to—they're divided among hospitals and EMS folks. Again, they're only nerve agents. So it's just your, like, Mark-1 kits, which is your atropine and your 2-PAM [pralidoxine] and then also your diazepam. So that is just about it, but at least it's forward-deployed. And it's not an unlimited supply, but it's there in case they need it.

Rubinson: Yeah, Eileen, I think the Chempack's a great resource for the country. One of the problems, though, you had mentioned about spending HRSA [Health Resource and Services Administration] money, which is now under the ASPR [Assistant Secretary for Preparedness and Response] is that you can't spend on building out storage areas for the Chempacks. So what's the most limited resource at an institution? It's storage. So it's all on us to actually find storage or build appropriate storage sites, and you need the communications link and 24-hour security available for the Chempacks. The security and communication are to consider it still a piece of the federal Stockpile because the idea is to extend the expiration date as long as they know that it's always been under particular control.

Hence, while many would want the stockpile, not all can afford the storage space. It may come across as local hospitals' not taking a piece of shared responsibility, but its hard to get the majority of facilities to invest capital for a low-frequency, albeit possibly high-impact event when they have so many demands for their capital expenditures. I know in Seattle we couldn't afford to have certain hospitals build out Chempack space, and the other source of money that we were chasing turned out to say no. So we ended up having it in a place that's slower to deploy to EDs.

Also, for EMS, if you take the Chempack antidotes out into the field on an unknown but possible hazmat [hazardous materials] event, my understanding is that the materials are no longer considered to be under the SNS [Strategic National Stockpile]. So it's a great resource, but unfortunately you get caught up in the regulatory issues.

Sandrock: Lewis, we have the same problem in our county, where I'm unfortunately in charge of the Chempacks. Our hospitals don't want to take them for that exact reason.

I have a quick question about the pulmonary irritants. If you have inhalational burn injuries in a house fire, for example, sometimes we do early intubation aggressively in some of these patients, in case they lose their

airway. With some of the water-soluble ones such as chlorine and ammonia, if you see these patients, is it better to intubate these patients early versus watching them? Is there data behind that? We're used to waiting for symptoms, but sometimes by then you're behind the 8-ball.

Muskat: If you are at all suspicious that your patient has been exposed to a moderate exposure of chlorine and they are beginning to have symptoms, don't wait for these to develop further and have subsequent difficulty intubating. The good news is that it appears if you've guessed wrong and it's mild exposure they appear to be extubatable relatively shortly after that. I agree; like a burn inhalation, there are all kinds of toxic compounds in the fumes/smoke. I would view chlorine and some of the other respiratory agents as the same type of exposure. It's an irritant that tends to be upper-airway, causing spasm and edema. Therefore it is necessary to be aggressive and take appropriate precautions.

Sandrock: One other follow-up to what you guys mentioned about the Chempacks. We had a debate in some of our hospitals in California. If these patients are exposed to a nerve agent, not decontaminated, and not in respiratory failure, the numbers that will progress to respiratory failure are relatively low. We had a debate whether we should stock powdered bulk atropine or whether we should get Mark-1 kits, which have a shorter shelf life and expire. The argument is in favor of the Mark-1 kits, if you get exposed to a contaminated patient and you're a health care worker because you want to rapidly be able to deploy them. But, the flip side is that if you do your decontamination right and you have very few patients progressing, pharmacy can draw up the atropine in the time that you need. I wanted to hear your thoughts or anybody else's on this battle, because it still seems to be one that has been lessened a lot by the Chempacks, but it certainly is a battle as well.

Muskat: Interestingly enough, in Japan one year before the Tokyo incident there was another attack in a building where the gas was released into the building by the same terrorist group. 200 patients were exposed and only 5 of them ended up on ventilators. These were identified early. If you have not developed symptoms within the first hour or so, it is highly unlikely that you will. So the triaging of chemical or nerve-agent exposure patients is a relatively straightforward one, again. as I outlined before. Given the rarity of these exposures to date, I would recommend stocking items with longer shelf lives.

Rubinson: I'm a little hesitant to adopt the thinking that no one will progress if they do not have severe symptoms at hospital arrival. I know there are anticipated situations where this is likely to be true. There also, though, seem to be possibilities of dermal exposure to a persistent agent such as VX, where there is ongoing exposure pre-decontamination, and symptoms may not peak until hospital arrival if folks present rapidly enough. On the other hand, if it is an inhalational exposure, then I would agree that almost all serious exposures will have declared themselves, as Christian [Sandrock] suggests.

Hanley: I have a question about the Chempacks. Are they are forward-deployed everywhere or are they only in places that would be considered high-risk targets?

Malatino: They're in the process of being forward-deployed to all of the states, and the states get to decide how much they put in their EMS packs, their kits, and how much they put in the hospitals, and what that mix is, whether you want more multi-dose vials, or the powder, or you want the auto-injectors, and so they get to decide that, but they're in all states eventually.

Wilgis: Just a real quick question, Dr Muskat. Of the patients who do get intubated and ventilated, what are the long-term outcomes for these patients? Do they survive? If I'm planning for a ventilator stockpile, what's my turnaround on that vent [ventilator] when I can use it on another victim, and 10% of 900,000 is a lot of victims, if we had something like Bhopal.

Muskat: For the pulmonary agents chlorine and phosgene there appears to be a relatively short duration requirement. These patients usually clear the chlorine and recover relatively quickly, in a matter of several days. Some do develop a more severe form, along with a potential superinfection; a very few may develop an ARDS [acute respiratory distress syndrome] picture. Mustard gas tends to cause a more damaging lung problem, so these patients may take a long time to recover. Nerve agents, again, also relatively short limited lung injuries. So if I had to summarize: most chemical-exposure injuries are of relatively short duration. Your ventilator requirements should not be tremendous unless we get into a Bhopal type incident.

Wilgis: Less than a week?

Sandrock: Yes, less than a week.

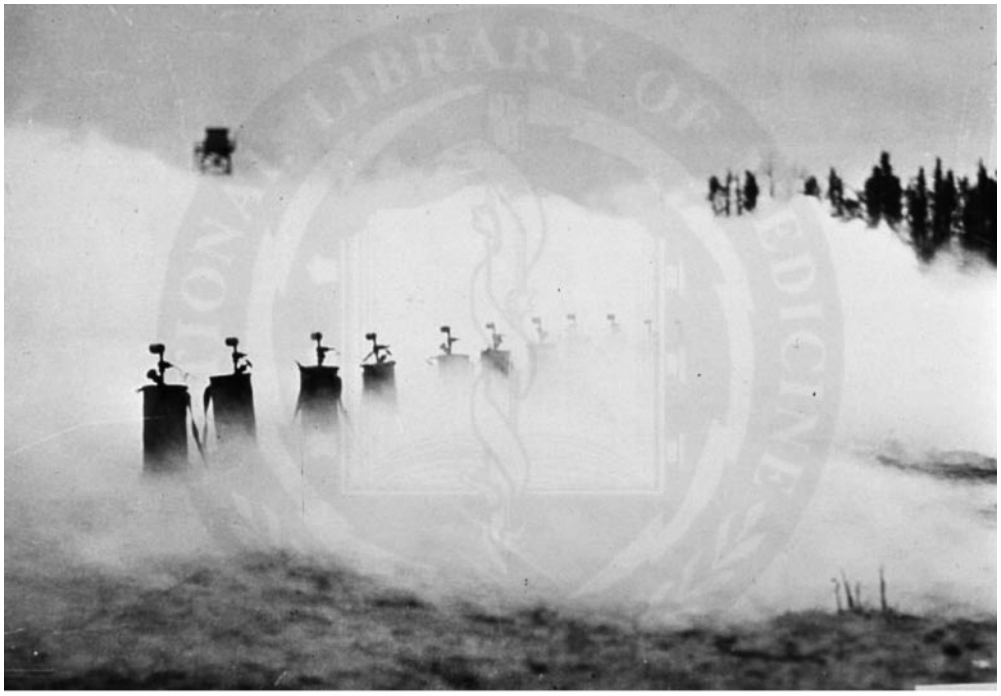
Branson: Just a comment to John's question. The patients from Japan who ended up getting ventilated were all basically off in less than a day, unless they had an anoxic brain injury and had CPR [cardiopulmonary resuscitation] in the field and then came in; but if they just had exposure enough to require intubation, they were off in less than a day. So it is kind of antidote-dependent.

Again, trying to bring back to my topic and for respiratory therapists, I see all of these advertisements for mechanical ventilators in the journals, and they've all got this big biochemical filter on the side of it, as if that's some critical component that we all must have. And I actually think that you mentioned that the first thing you do when somebody is exposed, you eliminate them from the exposure. So I would like to hear what the rest of you have to say. I don't find much value in that whatsoever, because I don't see myself sitting in the room where the exposure is ongoing, ventilating the patients.

Muskat: No question. If they are properly decontaminated, they're not going to "off-gas" chemicals from their lungs. Supporting a ventilated patient in an environment where you and the patient are still exposed to active chemical is challenging. However, once the patient is intubated, further lung exposure to the chemical is significantly limited. Nevertheless, rapid movement of the patient to and through a decontamination station is vital. The decontamination of nerve agent requires copious amounts of water and the removal of all contaminated clothing.

Rubinson: I think Rich [Branson] brings up a great point. I think this is where military or national security applications do not necessarily translate to widespread civilian need. Having a filter for people who are on chronic vent units in a place in the Middle East when there were identified missile attacks that may have been loaded with chemical agents could make sense. There is a defined threat, and the time delay from notification to placement of the filter (since leaving them on indefinitely will be costly to keep replacing filters) can happen quite quickly. Stopping external air from being drawn into the air-handling unit of the facility might lessen the need for the filter.

Branson: If you're selling the ventilator that they're using in the field or with the military, I think the expense of that filter is obviously worth it, but I don't think it is necessary. I guess my point is, don't buy a biochemical filter for all of your stockpile ventilators, because you're not going to use ventilators in an environment where you will be drawing in the agent into the ventilator. I think it's a waste of money, and we need to be careful not to waste our money.



Old print showing a cloud of (poisonous?) gas produced by mobile cylinders during World War I (undated)
Courtesy National Library of Medicine