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Clinical Research and Practical Application of Mass Casualty Medicine

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Original Articles

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ORIGINAL ARTICLE

A benchmark system to optimize our defense against an attack on the US food supply using the Risk Reduction Effectiveness and Capabilities Assessment Program

Ofia Hodoh, MS, BS; Cham E. Dallas, PhD; Paul Williams, DVM; Andrew M. Jaine, PhD; Curt Harris, PhD

Abstract

Objective: *A predictive system was developed and tested in a series of exercises with the objective of evaluating the preparedness and effectiveness of the multiagency response to food terrorism attacks.*

Design: *A computerized simulation model, Risk Reduction Effectiveness and Capabilities Assessment Program (RRECAP), was developed to identify the key factors that influence the outcomes of an attack and quantify the relative reduction of such outcomes caused by each factor.*

Setting: *The model was evaluated in a set of Tabletop and Full-Scale Exercises that simulate biological and chemical attacks on the food system.*

Participants: *More than 300 participants representing more than 60 federal, state, local, and private sector agencies and organizations.*

Results: *The exercises showed that agencies could use RRECAP to identify and prioritize their advance preparation to mitigate such attacks with minimal expense. RRECAP also demonstrated the relative utility and limitations of the ability of medical resources to treat patients if responders do not recognize and mitigate the attack rapidly, and the exercise results showed that proper advance preparation would reduce these deficiencies.*

Conclusions: *Using computer simulation prediction of the medical outcomes of food supply attacks to identify optimal remediation activities and quantify the benefits of various measures provides a significant tool to agencies in both the public and private sector as they seek to prepare for such an attack.*

Key Words: emergency response, food terrorism, simulation, public health preparedness, intervention, food defense

Introduction

Food processing, distribution, and supply systems are essential elements of the US economy and these systems present significant vulnerability to attack.[1,2] Biological and chemical contamination of the food supply poses an enormous threat to human life and public health. Deliberate biological or chemical contamination of the food supply bears the risk of significant social disruption and diminished confidence in the food supply, widespread panic, economic collapse, and massive fatalities.[3] The impact of H5N1 on the poultry industry,[4] bovine spongiform encephalopathy on the beef industry,[5] and the 2008 melamine poisoning incident on the milk industry[6] suggests the scope of the risk.

Studies using predictive simulation modeling have suggested that prompt detection of food terrorism events will result in significant reductions in morbidity and mortality without fully quantifying the likely consequences of food terrorism.[7,8] Jaine[9] has developed the Risk Reduction Effectiveness and Capabilities Assessment Program (RRECAP)* as a computer simulation model to address this gap and provide greater detail as to how public health agencies, first responders, and private sector organizations might minimize these consequences. It does this by

*Patent pending.

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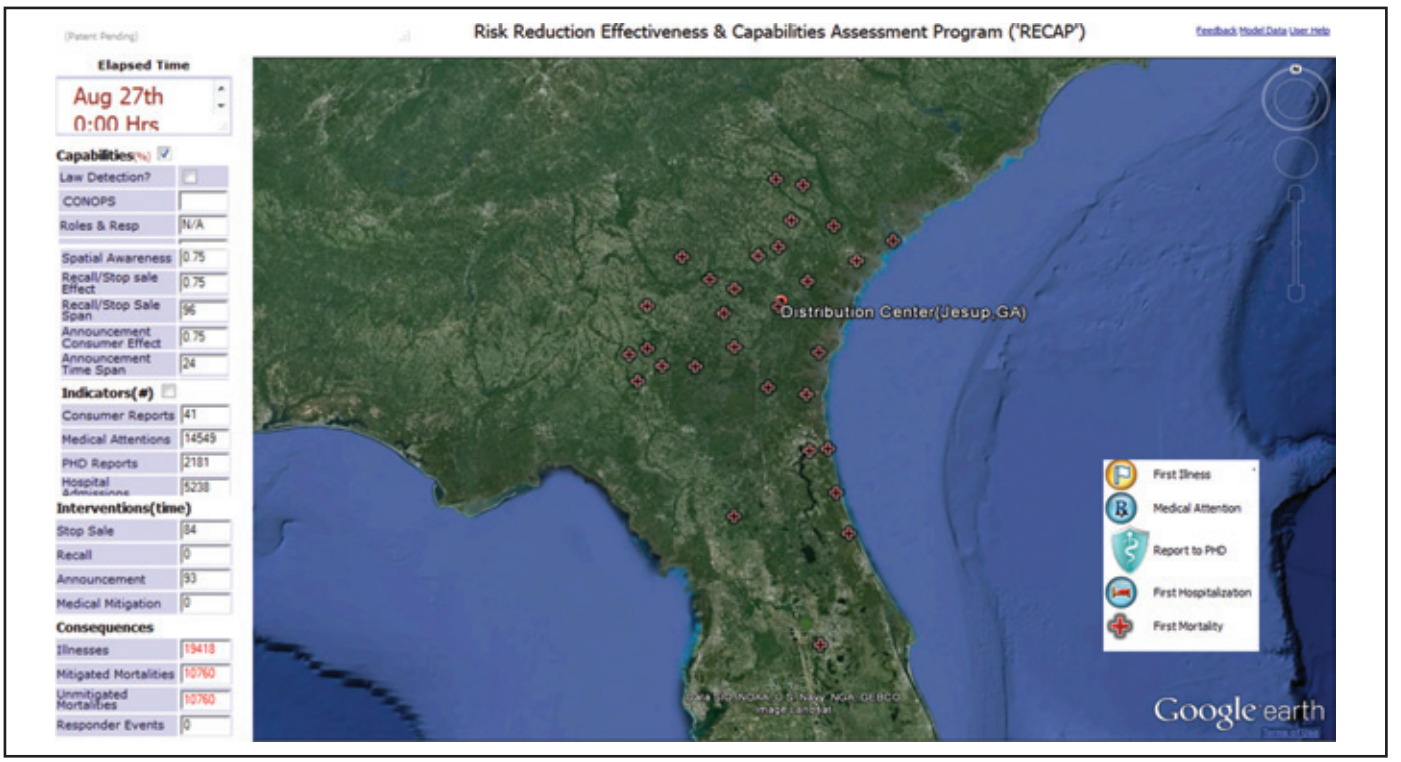

Figure 1. RRECAP key performance capabilities GIS map and indicators table.

evaluating the operational and organizational characteristics that exist for federal, state, and private sectors responding to potential cases of food terrorism in light of superior quantification of consequences.

This article describes the evaluation of the RRECAP model in a large, multiagency training operation named Georgia FoodEx 2009,[10] which comprised a Tabletop Exercise (TTX) and Full-Scale Exercise (FSE). The TTX simulated deliberate contamination of seafood with ricin and rapid consumption in the United States. The FSE simulated terrorists intentionally contaminating chicken nuggets with lethal doses of methyl parathion (MP) at a food processing plant. To our knowledge, this is the first operation-based exercise that used the actual chemical agent during the operation. The research complies with the Homeland Security Exercise and Evaluation Program (HSEEP), which uses discussion and operation-based exercises to measure and assess public health preparedness to respond to terrorist acts and human-caused or natural disasters.[11,12]

Among the objectives of the exercises were to use RRECAP to identify the key factors that determine the effectiveness of the response to each attack (the Key Performance Capabilities [KPCs]), evaluate the degree to which changes in capabilities affect the outcome of an attack (the Key Impact Metrics), and make recommendations of ways to optimize prioritization of KPCs to minimize the negative impact of the attack.

Methods

Model description

RRECAP is an innovation that can measure the effectiveness of federal, state, and private sectors in preventing and responding to attacks on various complex systems such as food, communication, and transportation. RRECAP is a predictive model designed to help government and industry improve their ability to respond to all forms of attacks through improving prevention and response. The program works by showing the geographic and temporal evolution of a simulated deliberate food contamination event using a geographic information system (GIS) map (see Figure 1). This map overlays distribution and consumption

information with profiles of morbidity and mortality outcomes and displays the results in an animated map that depicts the temporal evolution of the consequences of the quantities and locations of morbidities and mortalities that result from the attack as they spread throughout the affected areas.

To improve prevention, the model addresses two components:

1. applying principals of Organizational Performance Management as a means to identify partnerships between various levels of government and the private sector and

2. helping the private sector identify methods to reduce food vulnerabilities.

To improve response, it assesses five components:

1. benchmarking preparedness via discussion and operation-based exercises;

2. performing sensitivity analyses to determine which KPCs are influential in minimizing outcomes of an attack;

3. quantifying the benefits of improving preparedness by rendering values for the key indicators (eg, morbidities and mortalities) under different sets of values of the KPCs;

4. prioritizing the relative benefit of investments in improving different capabilities; and

5. assisting organizations in developing Risk Management Plans to enhance response effectiveness to all forms of attack.

In addition to showing the consequences of an event, the model demonstrates the effects of implementing interventions and changes in timing of interventions to minimize impacts of catastrophic incidents.

RRECAP evaluation in Georgia 2007/2008 TTX

In the first of two exercises to test the effectiveness of RRECAP, a TTX was used to look at issues in prevention, protection, response, and recovery during an attack on the US food supply. The HSEEP compliant exercise was held in May 2008 in Atlanta, GA, with 16 state and federal agencies participating. The exercise simulated an intentional contamination of seafood with ricin introduced at the point of production in an overseas country and entering the United States through Hartsfield-Jackson Atlanta International Airport, a key entrance point for seafood imported into the country. The scenario assumed that people in several states rapidly consume the highly perishable seafood. The scenario incorporated an early notification that an Al-Qaeda affiliated terrorist group published a warning on the Internet of a planned attack on the food system.

The focus of the exercise was on decision making before it became a massive international effort. The capabilities analyzed included: roles and responsibilities, conduct of operations, communications, and spatial awareness. Once the basic capabilities were understood in the TTX, they were used as the foundation for building the FSE.

RRECAP evaluation in Georgia FoodEx 2009 FSE

The second and by far the larger exercise using the RRECAP simulation evaluation included many of Homeland Security's 37 nationally identified Target Capabilities and quantified the effectiveness of key capabilities in reducing attack consequences. The attack scenario involved chicken nuggets intentionally contaminated with a concentrated lethal pesticide distributed throughout the southeastern United States. The MP-scenario was validated by the Department of Homeland Security's Chemical, Biological or Radiological Threat Risk Analysis Center as a plausible scenario.

Scenario profile and model assumptions

The design of the FSE placed a priority on assessing emergency management capabilities under a scenario that has rapid escalation of morbidities and mortalities. The scenario involved contamination of

approximately 9,071 kg of chicken nuggets with liquid MP (77 percent technical form) when terrorists sprayed it into open boxes at a distribution center in Jesup, GA. MP is a highly toxic organophosphorus pesticide used to kill insects on agricultural crops.[13] According to the World Health Organization, 200,000-250,000 deaths each year occur globally from MP poisoning, most of them suicides.[14] Technical material is 80 percent pure and MP is colorless, odorless, and tasteless. To determine the likely time it would take to validate contamination with field measurements, we injected a controlled small sample of chicken with the pesticide so that a lethal dose actually was present. The chicken was divided into 0.113 kg servings and contaminated with the chemical at a level where 90 percent of people who consumed a serving would become ill (Infectious $Dose_{90}$ [ID_{90}]) and 50 percent of them would die (Lethal $Dose_{50}$ [LD_{50}]). The sample was taken under strict control to the exercise site for sampling in the field. The model outcomes include realistic time course data based on this exercise. Table 1 describes key parameters of this scenario.

Scenario summary

The FSE took place from August 7 to August 12, 2009. The FoodEx 2009 exercise was embedded within a cluster of parallel exercises taking place at two field locations on August 10, 2009, as well as in a number of agency offices and labs across Georgia between August 7 and August 10, 2009. The two field locations included a simulated terrorism lab in a private residence located in a training facility at the Federal Law Enforcement Training Center (FLETC) in Brunswick, GA, and a simulated food distribution warehouse located in a farmer's market facility in Jesup, GA, approximately 50 miles from the terrorism lab. Table 2 presents the scenario timeline.

RRECAP was used to model the outcomes under a range of different scenarios. The first simulation depicts the outcomes that would have presented without any intervention. The subsequent simulations depicted the likely outcomes with response parameters set at the values that were observed during the exercise and the different interventions that the exercise participants invoked.

One of the activities of this exercise was to assess the levels to which responders were able to perform the identified key capabilities. When this assessment is made, the value (length of time that it takes to identify the correct vector with sufficient accuracy to enable an appropriate intervention to be invoked) is entered in the "Interventions" section of the model (see Figure 1). The "Indicators" table is generated as a part of the RRECAP scenario and shows various observable outcomes of the attack. Four indicators most influential in helping identify and mitigate a foodborne attack are as follows:

1. consumer reports (including those to the food producer);

2. medical attentions;

3. reports to the Public Health Departments; and

4. hospital admissions.

Sensitivity analysis

A sensitivity analysis was performed after the results were determined from the FSEs to determine which KPCs were most influential in minimizing the outcomes of the attack.

Results

RRECAP evaluation in Georgia 2007/2008 TTX

This exercise used RRECAP to evaluate the profiles of morbidity and mortality presentation due to consumption of ricin-contaminated seafood. In the simulation, tens of thousands of servings of contaminated seafood were consumed in the United States resulting in thousands of morbidities and mortalities. Following the completion of the exercise, an Improvement Plan was developed that identified several key areas in need of enhancement. This exercise revealed that the computerized simulation provides both evaluation of the effectiveness of various response activities and improves the focus and involvement of exercise participants. Other recommendations included the following:

Table 1. RRECAP model parameters	
Data item	**Value**
Product sourcing	
Contaminated quantity	36,287 kg servings; 25,000 servings per million population in the state
Shipped per day	226,796 kg/d
Product distribution	N(10 d, 2.9 d)
Shipping rate	1,900 servings/h
Shipping days/week	5 d/wk
Shipping hours/day	10 h/d
Contaminated locations	100 individual locations per million population in state
Geographic spread of consumption	100 percent to homes within 200-250 mile radius of Jessup, GA
Consumer handling and consumption	
Serving size	One 1/4 breast
Consumption amount	Uniformly consumed by all subpopulations
Consumption delay	1-3 d following arrival at consumption point
Consumption profile	N(36 h, 9 h); terminates at 72 h
Agent information	
Agent name	Methyl parathion (77 percent technical material)
Patient response information	
Attack rate	90 percent (LD_{50} approximately 3-20 mg/kg)
Consumer reporting	$\bar{X}$ = 0.515 percent (average level in severe illnesses)
Time from consumption to symptom onset	N(4.5 h, 1.8 h); min time symptom onset of 1 h
Time from symptom onset to seeking medical care	$\bar{X}$ = 5 h
Proportion seeking medical care	75 percent
Hospitalization	$\bar{X}$ = 8 h following illness presentation
Proportion of hospitalizations	36 percent of ill will be admitted
Mortality level	50 percent of affected will die after consuming a single serving
Time-to-mortality	ln N ($\bar{X}$ = 72 h, max = 204 h)
Public health response	
Rate reporting to public health	Minimum = 48 h; $\bar{X}$ = 96 h; max = 120 h
Volume reporting to public health	15 percent

Table 1. RRECAP model parameters (continued)	
Data item	**Value**
Surge capability	504 beds within 50 miles; 7,646/100 miles; 14,606/150 miles; 30,473/200 miles; 53,895/250 miles
Agency response information	
Outbreak consequence accuracy	Range of 0-100 percent
Outbreak consequence sensitivity	Range of 0-2; 0.25 (default)
Intervention information	
Recall time span	6 h (default)
Recall effectiveness	6 h (default)
Recall time span for nonidentified companies	240 h/5 d (default)
Public announcement time span	48 h (default)
Effectiveness of public announcement	50 percent (default)
Effectiveness of medical mitigation	50 percent (default)

1. development of a Risk Management Plan with comprehensive public/ private training;

2. development of an exercise program to nurture a public/private partnership;

3. expand the modeling to measure the effectiveness of the Target Capabilities to mitigate the consequences of a variety of scenarios; and

4. evaluate medical surge and other resource management and spatial awareness capabilities.

RRECAP evaluation in Georgia FoodEx 2009 FSE

No intervention. This RRECAP simulation investigated morbidity and mortality without any interventions. As the attack progressed, RRECAP illustrated the number of morbidities and mortalities expected to occur based on agent-specific parameters to a final endpoint.

In the absence of any interventions, by 11:00 am on the sixteenth day (371 hours) following the start of the exercise, just under 72,000 morbidities and 40,000 mortalities occurred (Figure 2). Just under 54,000 hospital beds existed in a 250-mile radius of the contamination area, but more than 66 percent of those beds are in constant use (based on the national average).[15] The enormous number of casualties would cause an overwhelming demand on local and regional hospitals.

Stop Movement/Stop Sale intervention. In the first simulation, RRECAP identified how event consequences grow over time under a worst-case scenario (ie, when the event goes undetected). The primary goals of RRECAP are to identify the KPCs that are most effective in reducing event consequences. The scenario data used by RRECAP identify the set of capabilities required for effective response of the modeled scenario known as "Key Capabilities." The Stop Movement/Stop Sale Intervention simulation models the extent to which interventions precipitated by exercise participants would reduce these consequences.

Table 2. Timeline of events Georgia FoodEx 2009 Full-Scale Exercise	
Day	**Event**
Prior to Day 1	36,287 kg of chicken nuggets are shipped by truck to the Distribution Center in Jesup, GA. Terrorists contaminate nuggets on the truck with liquid methyl parathion.
Day 1	The product is shipped to 42 towns and cities from the distribution center in Jesup.
Days 2 and 3	2,000 servings are sold per day as "Dock Sales."
Day 3	Georgia Department of Community Health's epidemiology group reports thousands of patients admitted to local area hospitals with seasonal influenza symptoms, similar to one another yet uncharacteristic for late summer.
Day 4 (5:00 AM)	The terrorist (plant employee), acting suspiciously, is transported to local emergency room with botulism-like symptoms. Symptoms of organophosphate poisoning (eg, excessive salivation, lacrimation, nausea and vomiting, and diarrhea) are comparable to foodborne botulism symptoms (eg, dizziness, dry mouth, and diarrhea).
Day 4 (5:50 AM)	Public Health Department goes to home of suspicious patient, is refused entry and call police. Police enter home, see a laboratory and notify the local Emergency Management Agency (EMA).
Day 4 (6:00 AM)	Incident Command System (ICS) is established and EMA alerts the Georgia Emergency Management Agency. The Georgia Bureau of Investigation, Special Weapons and Tactics (SWAT)-CBRNE team arrive and begin pursuing investigation. The fourth CST alerts forty-fourth and forty-sixth.
Day 4 (8:00 AM)	Shipments of contaminated product restart.
Day 4 (1:00 PM)	Stop Movement/Stop Sale issued by the Georgia Department of Agriculture (GDA) and the Incident Commander (IC) on the contaminated product.
Day 4 (2:55 PM)	Forty-fourth CST detects lethal doses of methyl parathion in chicken.
Day 4 (8:00 PM)	Methyl parathion contamination confirmed by USDA laboratory.
Day 4 (9:00 PM)	Public announcement issued IC and GDA on contaminated product.
Day 4 (11:00 PM)	Exercise ends.

The initiation of the exercise was that one of the terrorists had displayed signs of illness while at work and transported to the hospital, where he exhibited flaccid paralysis before becoming nonresponsive. Simultaneously, local hospitals reported high numbers of ill individuals seeking medical attention, which triggered an immediate public health response led by local public health officials to suspect criminal activity. As the hospital had no family contacts for the patient, the local epidemiologist went to the home, knocked on door, observed lab materials when the door opened, was refused entry, and immediately called the police. The police entered the home, saw a laboratory, and called the local Special Weapons and Tactics (SWAT) team. The SWAT team saw the laboratory producing suspicious materials and called Georgia Emergency Management Agency (GEMA). GEMA alerted the State Operations Center and the fourth Civil Support Team (CST) in Georgia was activated to help identify the suspicious materials. While awaiting arrival of the CST the on-site Incident Command (IC) together with the Georgia Department of Agriculture (GDA) contacted the local staff of the food production company and found that some of their employees were reporting illness. This triggered the IC/GDA to order a Stop Movement of all product shipped from that location. During this part of the exercise, the GDA invoked two specific interventions: the identification of the product

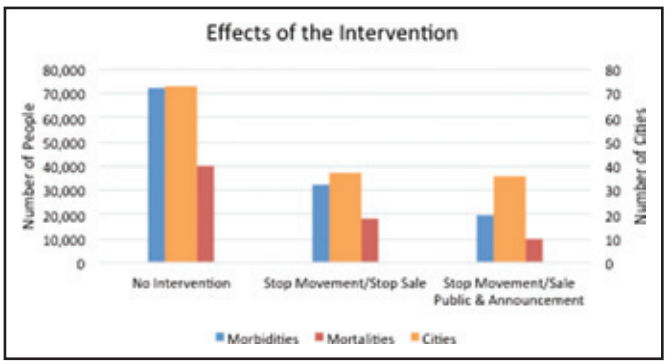

Figure 2. Combined effects of the intervention on the number of morbidities and mortalities.

suspected of contamination at "Hour 84" following the start of the exercise, and at that time, he ordered the cessation of all movement and sale of that product, "Stop Movement."

The time of the intervention, "84 Hours," was entered in the Interventions table (Figure 1) and the simulation proceeded to run. During the first hours of the event, there were no interventions, so the evolution of consequences was identical to those generated in the previous scenario. The intervention occurs at "84 Hours," and RRECAP continues to run the simulation modeling the effects of that "Stop Movement" intervention. When the evolution stopped, the consequences of the intervention were recorded showing the number of morbidities and mortalities.

The Stop Movement/Stop Sale Intervention reduced the number of morbidities to under 32,000 and the number of mortalities to 18,000, respectively (Figure 2). However, even at these levels, surrounding hospitals would still be unable to respond adequately to the affected victims, which would worsen considerably the extent and severity of morbidity.

Stop Movement/Stop Sale and public announcement intervention. At "Hour 93," the fourth CST, which was on site with its mobile laboratory, confirmed the identity of the contamination agent from the samples brought under control, and the Assistant Commissioner ordered a Public Service Announcement of product contamination. The time of announcement, "93 Hours," was entered into the Interventions table (Figure 1) and the model proceeded to run. Displays showed when the intervention occurred, and recorded the number of morbidities and mortalities; RRECAP continued to run the simulation of the effects of the "public announcement" intervention. At the conclusion of the evolution, the number of morbidities and mortalities that resulted from the combined effects of both the Stop Movement/Stop Sale and the public announcement was recorded as just over 19,000 morbidities and under 10,000 mortalities, respectively (Figure 2). While these numbers of patients resulting from the attack would still overwhelm surrounding hospitals, the overall impact on public health would be significantly diminished relative to the 84-hour intervention data.

Table 3. Changes in key indicators (observations) because of the interventions

	Interventions		
	No intervention*	**Stop Movement/Stop Sale***	**Stop Movement/Stop Sale and public announcement***
Observations			
Consumer reports	196	87	38
Medical attentions	53,962	24,331	14,491
Public Health Department reports	8,048	3,650	2,173
Hospital admissions	19,424	8,760	5,216

*The total number of people affected.

Table 4.Comparison of capabilities modeled at 25, 50, and 75 percent				
% Efficiency	Effect	Intervention		
		No intervention	Stop Movement	Stop Movement and announcement
25	Illnesses	71,995	47,131	46,361
50	Illnesses	71,995	32,461	18,162
75	Illnesses	71,995	19,829	19,418
25	Mortalities	39,980	26,201	25,542
50	Mortalities	39,980	18,162	17,430
75	Mortalities	39,980	11,036	10,760

Analysis of key indicators

RRECAP displays the various observable outcomes of the attack in the "Indicators" section of the output (Figure 1). The consequences of the *No Interventions* scenario were approximately 200 consumer reports, 54,000 people seeking medical attention, 8,100 reports by Public Health Departments, and 20,000 people admitted to hospitals (Table 3). The consequences of the *Stop Movement/Stop Sale Intervention* reduced all these parameters by 55 percent, and the consequences of the *public announcement* further reduced consumer reports by an additional 25 percent, and the remaining indicators by 18 percent.

Sensitivity analysis

RRECAP has the ability to monitor any number of capabilities. For this study, it was determined after the FSE that five KPCs were influential in identifying and mitigating a foodborne attack:

1. *Spatial awareness*. The percentage of businesses that handled the product. This was captured by using the Food and Agriculture System Criticality Assessment Tool (FAS-CAT) to identify critical nodes within the system.

2. *Recall effectiveness*. If a recall was invoked, then the percentage of product that was returned due to that recall.

3. *Recall/Stop Sale time span*. If a Stop Sale or recall was invoked, then the amount of product that was stopped/recovered due to that action.

4. *Announcement effectiveness*. If a public announcement was invoked, then the percentage of the product that was not yet consumed and was prevented from consumption by the public announcement.

5. *Announcement time span*. If a public announcement was invoked, then the length of time that it took for that announcement to be effective.

The scenario was based on a default response effectiveness at 50 percent. For the sensitivity analysis, three different percentages (25, 50, and 75 percent) were entered in the capabilities section of the model (Figure 1). Table 4 shows the results of the sensitivity analysis for the number of morbidities and mortalities. The combined effectiveness of the response strategies for the existing capabilities at increasing efficiencies reduced morbidities and mortalities by approximately 34, 55, and 73 percent, respectively. Responding at lower efficiencies would negatively affect more people. Figures 3 and 4 show the results of the sensitivity analysis for the total number of people affected by the attack.

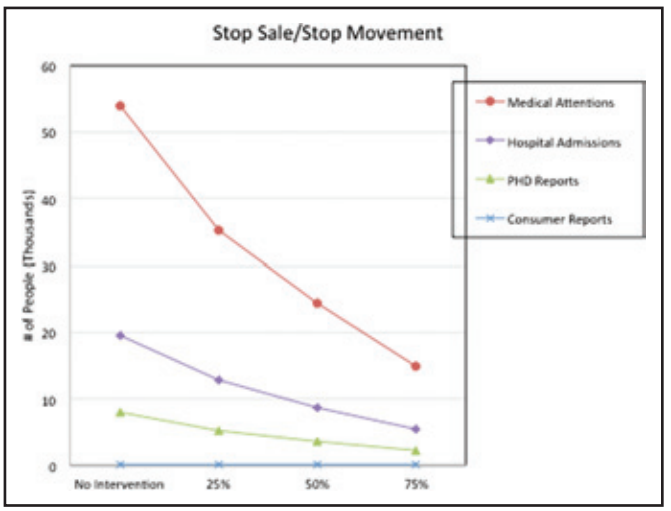

Figure 3. Comparison of indicators (observations) modeled at 25, 50, and 75 percent for Stop Sale/Stop Movement intervention.

Discussion

Incidents of intentional contamination of the food supply worldwide in the past 50 years suggest that terrorist groups understand the potential of such attacks to create social disruption, panic, and death.[16,17] In 1984, the Rajneeshee cult attempted to reduce voter turnout in a local election in Oregon by deliberately contaminating restaurant salad bars with *S. typhi*. While the group did not achieve its aim, 751 people were treated for salmonellosis, the local health department closed down all 10 restaurant salad bars,

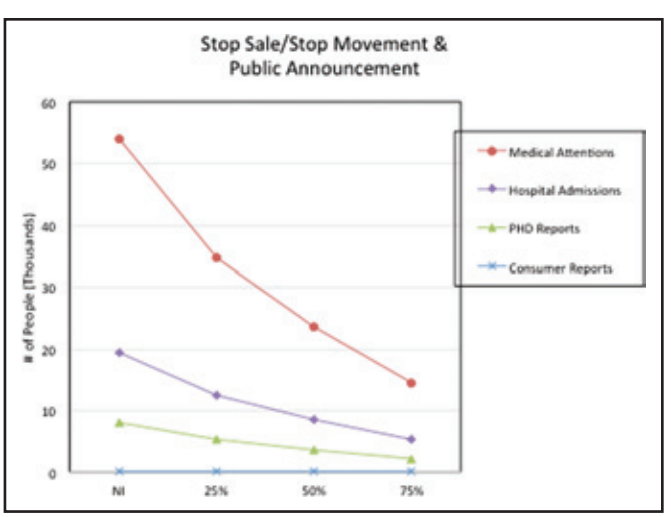

Figure 4. Comparison of indicators (observations) modeled at 25, 50, and 75 percent for the Stop Sale/Stop Movement and public announcement intervention.

and policy changes were implemented nationwide to prevent future attacks. Other examples include a plot, detailed in the notebook of a high-level Al-Qaeda operative detained in Afghanistan, to compromise the world's largest producer of Meals Ready to Eat (MREs) the food rations US soldiers use during field operations, with poison.[18] In 2003, a church member in rural Maine poisoned 13 individuals by contaminating coffee at a church gathering with arsenic,[19] and 92 people reported illnesses after consuming ground beef contaminated with an insecticide containing nicotine sulfate in Michigan.[20]

In 2004, President George W. Bush signed Homeland Security Presidential Directive 9, establishing a national policy concerning the protection of the food system from terrorists.[21] A report by the US Department of Homeland Security and the Federal Bureau of Investigation revealed that the "Mujahidin Poisons Handbook" appears on the Web sites of many radical Islamist groups describing techniques for attacks on the food supply.[22] In a bulletin to the nations law enforcement officials, the FBI warned that Al-Qaeda might use poisons to contaminate the US food and water supplies.[23]

The current study addresses the results of such an attack by simulating a scenario that involved a food product both simulated and actually contaminated with a lethal pesticide distributed in the southeastern United States, and involving a live response including deployment of the fourth, forty-fourth, and forty-sixth CSTs and over 60 state, federal, and private agencies. The RRECAP tool was used to measure the effectiveness of current capabilities and showed that if the attack had not been mitigated the consequences would have been more than 70,000 morbidities and 40,000 mortalities in Georgia, Florida, and South Carolina (Figure 2). RRECAP showed the combined effects of the high levels of performance of key capabilities combined with the swiftness of high-level officials making key decisions would reduce morbidities by 30 percent. The Stop Movement/Stop Sale action reduced the number of morbidities and mortalities in half and the additional effect of the public announcement further reduced these by an additional 45 percent, as evaluated by the RRECAP tool. Additionally,

RRECAP yielded a plan for improvement by identifying a set of capabilities that, if improved by a specified and achievable amount (50 percent), could reduce consequences from baseline by approximately 73 percent. RRECAP also showed that existing capabilities reduced the total number of cities that the incident would have affected from 73 to 36 (Figure 4), reducing the urban human health impact to a range much more manageable with immediately available healthcare resources, which are located in these metropolitan settings.

The RRECAP tool has certain essential data that are required to compute the levels of morbidity and mortality resulting from a catastrophic foodborne attack. Most measures are related to the time to perform specific response activities. The list (in the Methods section) could be extended almost indefinitely, but the objective of RRECAP is to assess the activities required to improve consequences of an attack. Thus, activities are only important to the extent that they can be reasonably expected to improve the consequences, the principal mechanism for which is often the time it takes to accomplish the activities. Therefore, the quality/quantity of performance is only significant if the timing of the performance is appropriate.

Limitations

The capability benchmarks RRECAP generates depend on implementation of a specific scenario and set of accompanying assumptions. Of course, in real-life events many other factors outside the control of responding agencies would play a significant mitigating or exacerbating role. Outbreaks may continue for longer than expected because key events fail to be recognized, while some are acknowledged quickly because of an incidental reason. For example, if the epidemiologist had delayed or failed to visit the terrorist's home, notification to law enforcement would have never occurred resulting in increased morbidity and mortality. The results RRECAP generates cannot be extrapolated to make specific projections of the consequences of different scenarios, or to real-life scenarios, and may only be used for relative comparisons.

Neither RRECAP nor any other currently known process can be expected to predict the actual outcomes of various scenarios in advance of the actual occurrence nor determine the extent and effectiveness of the responses, the precise effects of having specific levels of capability, or the exact success of interventions. These factors do not implicitly create uncertainty in RRECAP, as the objective is to determine the relative changes in outcome caused by differing values of various Target Capabilities. If the scenario values are maintained consistently across different exercises, the relative comparisons of results of those exercises are preserved, regardless of the absolute values.

Conclusions

RRECAP is a science-based predictive software system that enables users to quantify current levels of effectiveness of response to catastrophic attacks, provides focused guidance on optimal ways to achieve consequence reduction, and relatively quantifies benefits achieved through remediation activities. It provides a powerful tool to assess the effectiveness of preparedness projects currently implemented and under development and to focus them to achieve various strategic plans for effective prevention, mitigation, and response. It demonstrates the utility of computer simulation prediction to measure the relative benefit of policies and procedures that agencies might implement to prepare for deliberate attacks on the US food supply.

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Ofia Hodoh, MS, BS, Institute for Disaster Management, College of Public Health, The University of Georgia, Barrow Hall, Athens, Georgia.

Cham E. Dallas, PhD, Professor, Director, Institute for Disaster Management, College of Public Health, The University of Georgia, Athens, Georgia.

Paul Williams, DVM, Director of Agriculture, Food and Veterinary Programs, Georgia Emergency Management Agency/Homeland Security, Atlanta, Georgia.

Andrew M. Jaine, PhD, Director, Mediabase Inc., Incline Village, Nevada.

Curt Harris, PhD, Assistant Professor, Associate Director, Institute for Disaster Management, College of Public Health, The University of Georgia, Athens, Georgia.

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DM

ORIGINAL ARTICLE

An assessment of Chemical, Biological, Radiologic, Nuclear, and Explosive preparedness among emergency department healthcare providers in an inner city emergency department

Joseph G. Kotora, DO, MPH

Abstract

Introduction: *Emergency healthcare providers are required to care for victims of Chemical, Biological, Radiologic, Nuclear, and Explosive (CBRNE) agents. However, US emergency departments are often ill prepared to manage CBRNE casualties. Most providers lack adequate knowledge or experience in the areas of patient decontamination, hospital-specific disaster protocols, interagency familiarization, and available supply of necessary medical equipment and medications. This study evaluated the CBRNE preparedness of physicians, nurses, and midlevel providers in an urban tertiary care emergency department.*

Methods: *This retrospective observational survey study used a previously constructed questionnaire instrument. A total of 205 e-mail invitations were sent to 191 eligible providers through an online survey distribution tool (Survey Monkey®). Respondents were enrolled from February 1, 2014 to March 15, 2014. Simple frequencies of correct answers were used to determine the level of preparedness of each group. Cronbach's coefficient α was used to validate the precision of the study instrument. Finally, validity coefficients and analysis of variance ANOVA were used to determine the strength of correlation between demographic variables, as well as the variation between individual responses.*

Results: *Fifty-nine providers responded to the questionnaire (31.14 percent response rate). The overall frequency of correct answers was 66.26 percent, indicating a relatively poor level of CBRNE preparedness. The study instrument lacked precision and reliability (coefficient α 0.4050). Significant correlations were found between the frequency of correct answers and the respondents' gender, practice experience, and previous experience with a CBRNE incident. Significant variance exists between how providers believe casualties should be decontaminated, which drugs should be administered, and the interpretation of facility-specific protocols.*

Conclusions: *Emergency care providers are inadequately prepared to manage CBRNE incidents. Furthermore, a valid and precise instrument capable of measuring preparedness needs to be developed. Standardized educational curriculums that consider healthcare providers' genders, occupations, and experience levels may assist in closing the knowledge gaps between providers and reinforce emergency departments' CBRNE preparedness.*

Key words: disaster management, CBRNE, terrorism, decontamination

Introduction

The ability of the United States' emergency departments (EDs) to respond to a large-scale Chemical, Biological, Radiologic, Nuclear, and Explosive (CBRNE) incident is critically important to public health. Terrorist attacks and industrial accidents involving these agents have the potential to inflict a large number of casualties within a very short time. EDs lacking an effective disaster plan will be rapidly inundated with patients, rendering them incapable of continued full-scale operations. The 1995 sarin gas attacks in a Tokyo subway[1,2] exemplified this scenario.

For an Emergency Operations Plan (EOP) to be effective, all personnel must possess an acceptable working knowledge and familiarity with the policies

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and procedures outlined in the EOP. Hospital emergency preparedness coordinators are intimately familiar with the plan, because they are usually involved in its production and implementation. However, physicians, nurses, midlevel providers, and clinical ancillary staff may not be as knowledgeable or comfortable. Despite their potential unfamiliarity, clinical personnel working in the ED are expected to recognize a potential CBRNE agent, provide the casualty with proven antidotes and supportive care, manage the agent via effective decontamination and containment, and notify the appropriate agencies tasked with definitive investigation and management of the incident. This said, EDs and emergency healthcare providers rarely demonstrate an acceptable level of CBRNE preparedness.

Hospital preparedness for CBRNE incidents

Previously collected data from European hospitals describe a poor level of education and preparedness for CBRNE incidents. England reported less than half of the EDs in the northwest region were capable of producing a facility's disaster plan for employee reference with little or no advanced notice. EDs lacked a sufficient water supply for patient decontamination and many of the directors of the EDs did not have the appropriate level of knowledge regarding mandatory reporting of incidents to various agencies. Healthcare providers' training, drills and preparatory exercises, and the accessibility of personal protective equipment (PPE) were also noted to be deficient.[3]

A Belgian survey of 100 EDs had similar findings. Despite being rich in petrochemical and nuclear power installations, only half of the EDs had incorporated CBRNE incidents into their formal disaster plans. Decontamination and PPE were major issues as well, with only 42 percent of EDs reporting the presence of decontamination facilities and only 5 percent having PPE capable of combating chemical agents. Regarding treatment, less than half (47 percent) possessed an effective antidote to cyanide, and only 19 percent could effectively treat casualties of nerve agents such as Sarin, Soman, Tabun, or VX.[4]

Canadian EDs also struggle with CBRNE preparedness. In 2006, only 63 percent of EDs reported possessing a protocol for reporting suspicious biological agents to authorities. Regarding isolation and decontamination, 60 percent of facilities did not have a formal decontamination area, 85 percent had no means for external decontamination outside the facility, 97 percent had no positive pressure ventilation (PPV), and a mere 19 percent reported access to gas masks or chemical-resistant suits.[5]

Results from US hospitals' CBRNE preparedness have been mixed. ED disaster preparedness earned a C– by the American College of Emergency Physicians.[6] With a previous grade of C+ just 5 years prior, disaster preparedness saw the largest decline in success among all metrics included in the report. A 31.12 percent per capita reduction in federal disaster preparedness funding, no increase bed capacity in available burn centers, and a reduction in the number of available intensive care unit beds accounted for a large portion of the poor assessment.[7]

However, Mississippi previously reported 90 percent of its facilities actively maintained a detailed disaster plan and provided staff education pertaining to chemical or biological disasters. Seventy-five percent of the hospitals had decontamination facilities available, and approximately half possessed enough pharmaceuticals to effectively treat multiple casualties.[8] In Kentucky, nearly 99 percent of participating hospitals had a functional disaster plan and 96 percent could reproduce the plan with little-to-no advanced notice. Despite the presence of a disaster plan and a strong emergency response infrastructure, numerous gaps were found in Kentucky's CBRNE preparedness. Only 73 percent of the disaster plans specifically addressed CBRNE-related incidents. Many Kentucky hospitals did not have plans and systems with sufficient detail to effectively manage CBRNE patients. Staff education and training were also subpar, with nearly half of surveyed hospitals reporting the desire for additional training and education if external funds were available.[9] An analysis of metropolitan Philadelphia highlighted multiple areas for improvement regarding chemical and biological agent preparedness. Specifically, increased collaboration with external agencies, staff familiarity with the disaster protocol, and emergency physician knowledge and training were cited as requiring further development and refinement.[10,11]

Hospital administrators

Many administrators and ED directors report an overall weak level of preparedness among the United States' EDs. Madsen and Greenberg studied 89 ED directors from the nation's 12 largest cities. Their findings strongly coincide with the previously presented trend, a general lack of confidence and overall poor level of CBRNE preparedness. Significant variation in the content, depth, and breadth of disaster plans exists, with some plans completely omitting nerve agents such as Sarin and VX. Only 50 percent are familiar with the Hospital Incident Command System (HICS) system, and a mere 7.3 percent conduct regular annual drills focused on nerve agent victims.[12]

Individual practitioner preparedness for CBRNE incidents

Healthcare providers continue to express concern regarding their level of preparedness for CBRNE incidents, citing a lack of familiarity with the hospital incident command structure or knowledge deficits in caring for CBRNE-exposed patients. In a recent study published in the *American Journal of Disaster Medicine*, the vast majority of respondents agreed they had an overall poor knowledge of disaster preparedness and required additional training.[13]

According to the 2003-2004 National Hospital Ambulatory Medical Care Survey, nurses reported the highest percentage of previous training in terrorism response, followed by staff attending physicians. Resident physicians had the least amount of terrorism training, with only 39.3 percent. The best predictor of a well-equipped, well-trained, and adequately prepared hospital lies with certification from The Joint Commission (TJC).[14] TJC, previously known as the Joint Commission on Accreditation of Healthcare Organizations (JCHAO), is an organization that evaluates hospitals and awards accreditation for optimal performance. Possession of this accreditation influences a healthcare facility's ability to obtain licensure or receive federal monies through the Medicare program.[15]

Nurses

Nurses from all areas of medical care have advocated for increased awareness and training pertaining to weapons of mass effect (WME) as well as CBRNE. Nursing students are seldom offered courses that focus on clinical skills or practice-based learning applicable to CBRNE incidents and medical disasters.[16] Only one third of Australian nurses reported receiving training pertaining to chemical incidents, less than half had previous education regarding nuclear and radiological incidents, and only two thirds felt they were physically capable of wearing the proper PPE required of a healthcare professional during the care of CBRNE patients.[17]

Physicians

Physicians report similar levels of unfamiliarity and lack of preparedness for CBRNE incidents. In a study of 841 Texas physicians, a large percentage of doctors had little-to-no experience or training targeted toward CBRNE-related incidents.[18] Only 53.9 percent of trauma surgeons are aware of the symptoms related to a nerve agent and less than one third are aware of the prescribed treatments for injuries due to chemical WME. With respect to biological weapons, 61 percent of trauma surgeons are not confident they could recognize signs and symptoms consistent with a biological agent.[19] The most prepared physicians appear to be those with prior military service or training.[18,19]

Three thousand nine hundred sixty-eight office-based physicians from 15 different specialties were queried about their self-reported knowledge regarding the six most dangerous biological toxins (anthrax, tularemia, bubonic plague, smallpox, viral hemorrhagic fever, and botulism). The average physician had prior training with only 2.3 biological agents, and less than one fifth had prior training pertaining to all eight agents. Those in surgical specialties had the least amount of training and awareness related to CBRNE exposures.[20]

It is obvious that CBRNE preparedness and knowledge among healthcare providers is lacking and requires improvement. That said, the author sought to evaluate the level of preparedness regarding CBRNE incidents among the licensed healthcare professionals employed in the ED of a tertiary care academic medical center. Specifically, the author focused on the knowledge levels of attending

physicians, resident physicians, midlevel providers (nurse practitioners and physician assistants), and nurses (registered nurses and licensed practical nurses) regarding the diagnosis and management of CBRNE patients. Additionally, the author evaluated each provider's familiarity with basic decontamination and agent containment principles, the facility's disaster plan, the HICS system, and individual PPE. The author hypothesized that most participants would have minimal knowledge of CBRNE incidents, would be unfamiliar with the hospital disaster plan, and would have little or no experience with the proper wearing of PPE.

Methods

Study design and participants

This was an exploratory, retrospective observational study designed to evaluate the ED providers' CBRNE-specific knowledge, as well as their familiarity with the facility's disaster plan. The study population represented the entire employee census of physicians, midlevel providers, and nurses employed in the ED (N = 191). The survey was available online through Survey Monkey®, and was accessible to the study's subjects via e-mail invitation. A total of three e-mail invitations were sent to the address listed in their personnel recall roster profile. Participants were eligible for inclusion if they were currently employed as a registered nurse, licensed nurse practitioner or physician assistant, resident physician, or licensed attending emergency physician in the ED.

Ancillary staff (technicians, clerks, unit secretaries, security guards, transport personnel, non-emergency-trained physicians or nurses, and students) were excluded from the study. These subjects were excluded for the following three primary reasons: 1) personnel lacked detailed knowledge or familiarity with the EDs disaster plan, 2) an individual's job description did not include diagnosis and management of patients exposed to CBRNE agents, and 3) the individual would be unlikely to participate in the care of an actual CBRNE patient inside the study facility, due to legal, moral, ethical, or statutory limitations.

Subject protection and informed consent

Prior to implementation, the study was approved by the institutional review board of both the host location, as well as the primary investigator's affiliate institution (Rutgers' University, New Brunswick, NJ). Subjects who met the inclusion criteria and agreed to participate in the study were asked to provide electronic informed consent. Informed consent was obtained by asking each participant to read a paragraph on the first page of the survey, and chose the "I consent" button. Those who did not wish to consent to the study were asked to click the "I do not consent" button to opt out. To protect the anonymity of the respondents, the primary investigator was blinded to the IP addresses as well as e-mail addresses of both respondents and nonrespondents.

Study instrument

The study instrument was obtained from an online web search, using the keywords "preparedness," "healthcare provider," and "CBRNE." The chosen instrument was initially designed by the State of California-Disaster Medical Services Division, and was used to evaluate the state's physicians' and nurses' knowledge of CBRNE agents and incidents. Prior to distribution and utilization, the questionnaire was checked for face validity by three experts in disaster medicine to ensure all items coincided with protocols and principles of the study location and population. The instrument was composed of 32 multiple choice-single best answer or true/false questions, followed by eight demographic and practice-related questions.

The instrument was dissected into six general content areas, to permit comparisons among professions and demographic variables. The six content areas included chemical agents, biological agents, radiation/nuclear agents, explosive agents, general principles and practices common to all CBRNE agents, and facility-specific questions. The breakdown and representation of the major content areas is further depicted in Figure 1. The study questionnaire is available for review in Appendix A. Please note that each questionnaire item is coded both alphabetically and numerically. The numerical codes correspond to the recoded variables in Table 1 and are provided to

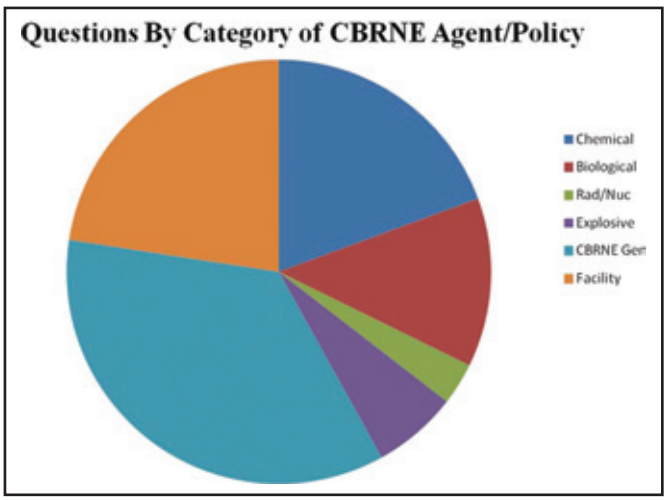

Figure 1. Composition of survey instrument.

facilitate reader comprehension regarding data interpretation.

Instrument precision and reliability

Using Cronbach's coefficient α, the test was evaluated to determine the internal consistency and reliability, to determine if the instrument sufficiently measured a respondent's knowledge and competency. Classically, coefficient α values of 0.7 or greater are considered sufficiently high to allow analyses.

Outcomes

The primary outcome variable of interest was defined as the percent of correct answers among all healthcare providers throughout the entire ED, regardless of discipline/occupation, years of experience, or previous experience with an actual CBRNE incident. The cohort and individual scores were determined by calculating the sum of correct responses chosen in the survey instrument. The raw score of correct answers was used as a metric to gauge the preparedness of the entire study cohort as well as individual healthcare provider disciplines (attending physicians, resident physicians, midlevel providers, and nurses). Preparedness was considered adequate if the total correct answer score was ≥75 percent.

Secondary outcomes included testing the reliability and precision of the study instrument to determine what significance the scores/results actually had on reported knowledge and competency of the providers. Additionally, the individual occupational disciplines, years of experience or practice, and prior exposure/experience with an actual CBRNE incident were analyzed using one-way analysis of variance (ANOVA) and a validity coefficient to determine if significant differences existed between background demographic variables and the reported preparedness score.

Instrument distribution

The survey was available for participation from February 1, 2014 to March 15, 2014. An e-mail distribution list was compiled for the entire census of the ED registered nurses, midlevel practitioners, resident physicians, pediatric EM fellows, and attending physicians from the ED administration (N = 191). The instrument questionnaire was uploaded into a commercial survey distribution tool (Survey Monkey, Palo Alto, CA) and sent to the recipients on February 1, 2014. Two follow-up reminder e-mails were sent on February 14 and February 28, to offer nonresponders additional opportunities to participate. A final reminder was sent on March 10, 2014. The study officially closed to respondents on March 15, 2014.

Statistical methods and analysis

Cronbach's coefficient α was used to determine the internal precision and reliability of the questionnaire. A coefficient α of ≥0.7 is considered precise/valid. Validity coefficients were used to determine what effect background or demographic variables had on the overall score of each group. Significance regarding validity coefficients is reported as r point biserial (r_{bp}). Of note, the r_{bp} test statistic is equivalent to the standard *t* test when reporting significance between two independent samples. The sign of the test statistic indicates the direction of the relationship. If there is a significant correlation between a true dichotomy and one of the instrument items, the r_{bp} will demonstrate which of the two groups has a higher mean.

Statistical significance is reported as $p < 0.05$ or $p < 0.01$. Because this was a pilot study and no reference data exist, variables with significance at the 0.10 ($p < 0.10$) were also reported. This was a retrospective observational study and no power calculation was required.

Results

Two hundred and seven individual e-mail invitations were sent to 191 potential participants (127 nurses, 10 midlevel providers, 31 resident physicians, and 39 attending physicians). The number of invitations exceeds the number of possible subjects because several providers had more than one e-mail address listed in the roster. Fifty-nine providers responded to the survey and completed it in its entirety. Five e-mail addresses were unfounded or unusable and four participants declined to participate. The overall participation rate was 31.4 percent of eligible subjects.

Respondent demographics

A table outlining the study subjects' demographics is provided in Table 1. Subjects who responded were most likely to be attending physicians or resident physicians, Caucasian, aged between 26 and 40 years, with 1-10 years experience in emergency healthcare. Midlevel providers (nurse practitioners and physicians' assistants) were underrepresented in the study, comprising only 6.77 percent of all respondents. Nurses accounted for 18.64 percent of the total number of respondents.

Instrument precision

The average intercorrelation of all possible pairs of items was 0.022. The Cronbach coefficient α for all items in the questionnaire was 0.4050, indicating a low level of precision and reliability. The chemical portion of the item had a negative coefficient α, suggesting a possible decrease in knowledge as the respondent's performance increased. Items pertaining to biological agents, general CBRNE casualty management policy, and facility-specific disaster management demonstrated similarly poor precision, with coefficient α of 0.2653, 0.2010, and 0.2110, respectively. The r-sums and coefficient α for individual classes of agents, as well as the entire questionnaire, are demonstrated in Table 2.

The precision and reliability of the instrument was not previously reported in the literature. Information pertaining to reliability could not have been obtained antecedent to the instrument's distribution.

Group performance/preparedness

Among the entire cohort, the total number of correct answers to the knowledge and competencies portion of the assessment was 66.27 percent. The overall score of all respondents to questions pertaining to chemical agents was 78.53 percent. The group answered 50.85 percent of the questions pertaining to biological agents correctly. Questions (77.40 percent) that focused on nuclear, radiation, or explosive incidents were correctly answered. The performance of the entire study population is demonstrated in Table 3. Figure 2 demonstrates the composite score of each healthcare provider group and reflects each group's CBRNE knowledge and competency.

After examination of the study instrument's precision and validity, it became apparent that further refinement of overall performance among individuals and groups was unlikely to accurately measure the level of CBRNE preparedness. However, significant information was obtained from individual question items in the survey instrument. Individual items with statistical significance provided insight, as they could assist with the production of a more reliable and more valid instrument in the future.

Validity coefficients

Females performed better in the areas of knowledge and clinical competency [$r_{bp} = 0.34369$ ($p < 0.01$)] and CBRNE policy-related questions [$r_{bp} = 0.3309$ ($p < 0.05$)]. Equally significant, providers who previously managed a CBRNE victim also demonstrated greater performance with respect to knowledge and clinical competency [$r_{bp} = 0.3817$ ($p < 0.01$)], external disaster policies [$r_{bp} = 0.3037$ ($p < 0.05$)], general CBRNE policy [$r_{bp} = 0.2803$ ($p < 0.05$)], chemical-specific agents, and facility-related disaster policies [$r_{bp} = 0.3190$ ($p < 0.05$)].

Analysis of individual respondent answers

One-way ANOVA was used to determine if statistically significant differences existed between how individual healthcare providers answered questions and their demographic variables. When the respondents were separated by occupation (attendings vs nonattendings, physicians vs nonphysicians, and attending only), a significant amount of variation was noted. The

Table 1. Survey respondents' demographics and practice experience				
	N	**Percentage of respondents, percent**	**Recoded variables**	
Occupation				
Attending physician	16	27.12	Physicians (10)	16 (27.12 percent)
Fellow	2	3.39	Trainee physicians (20 and 21)	28 (47.46 percent)
Resident physician	26	44.07		
Nurse practitioner	1	1.69	Midlevel providers (31 and 32)	4 (6.77 percent)
Physician assistant	3	5.08		
Nurse (RN or LPN)	11	18.64	Nurses (40)	11 (18.64 percent)
Total	59	100		59 (100 percent)
Race/ethnicity				
Caucasian	35	59.32	White (2)	35 (59.32 percent)
African American	9	15.25	Not White (1)	24 (40.68 percent)
Hispanic	0	0		
Asian	5	8.47		
Indian	7	11.86		
Arabic	0	0		
Native American	0	0		
Other	3	5.08		
Age demographic				
26-30	17	28.81	1	17 (28.81 percent)
31-35	16	27.12	2	16 (27.12 percent)
36-40	13	22.03	3	13 (22.03 percent)
41-45	7	11.86	4	7 (11.86 percent)
46-50	2	3.39	5	2 (3.39 percent)
51-55	2	3.39	6	2 (3.39 percent)
56-60	1	1.69	7	1 (1.69 percent)
>60	1	1.69	8	1 (1.69 percent)
Gender				
Male	29	49.15	2	49.15 percent
Female	30	50.85	1	50.85 percent

Table 1. Survey respondents' demographics and practice experience (continued)				
	N	**Percentage of respondents, percent**	**Recoded variables**	
Years of practice				
<1	7	11.86	1	7 (11.86 percent)
1-5	24	40.68	2	24 (40.68 percent)
6-10	14	23.73	3	14 (23.73 percent)
11-15	4	6.78	4	4 (6.78 percent)
16-20	5	8.47	5	5 (8.47 percent)
21-25	2	3.39	6	2 (3.39 percent)
26-30	0	*	*	*
>30	3	5.08	7	3 (5.08 percent)
Prior experience with CBRNE incident				
Yes	7	11.87	Yes (2)	7 (11.87 percent)
No	51	86.44	No (1)	52 (88.13 percent)
Unsure	1	1.69		
Prior HEICS course				
Never	32	54.24	Yes (2)	20 (33.90 percent)
Yes, <6 mo ago	0	0		
Yes, <12 mo ago	3	5.08		
Yes, ≥12 mo ago	17	28.81		
Unsure/do not know	7	11.86	No (1)	39 (66.10 percent)
*The lack of participants in that age demographic.				

greatest amount of variance existed between attending physicians and nonattending physicians [$F = 59.1485$, ($p < 0.01$)]. Separating physicians by residents versus nonresidents was also significant [$F = 72.3911$ ($p < 0.01$)]. Finally, practice duration or years of experience demonstrated significant variance [$F = 17.4724$ ($p < 0.01$)].

Prior management of a CBRNE casualty also demonstrated statistically significant variance. This was evident among physicians versus nonphysicians [$F = 4.2216$ ($p < 0.01$)], attending physicians versus residents [$F = 6.0935$ ($p < 0.01$)], and among individual attending physicians [$F = 10.3239$ ($p < 0.01$)]. These data suggest that individual attendings will likely have the most practice-based experience in CBRNE casualty assessment and management, when compared among all other healthcare providers.

The management of CBRNE casualties, specifically the administration of antidotes and medications, was significant as well. There was considerable variance observed among the treatment of nerve agents (question #13) (attendings vs nonattendings [$F = 3.6381$ ($p < 0.05$)] and attendings vs Residents [$F = 2.9626$ ($p < 0.01$)]). Overall, the greatest amount of variance between attending physicians and nonattending physicians occurred for questions pertaining

Table 2. Cronbach's coefficient for composite scores calculated from the CBRNE questionnaire			
Composite scores	**Number of questions**	**Average correlation**	**Cronbach's coefficient α**
Knowledge/clinical competency	24	0.0270	0.3998
External disaster plan/policy	6	0.1136	0.4347
Total of all items	30	0.0223	0.4063
CBRNE categories			
Chemical	6	–0.0235	–0.1598
Biological	4	0.0828	0.2653
Radiologic/nuclear	1	*	*
Explosive	2	–0.0150	–0.0305
CBRNE general/policy	10	0.0245	0.2007
Facacility disaster plan/policy	7	0.0368	0.2110
*Cronbach's coefficient α requires composite scores to include at least two questions.			

Table 3. Respondent performance to questionnaire items			
CBRNE agent class	**Total points attained**	**Total possible points**	**Percentage correct, percent**
Chemical	278	354	78.531
Biological	120	236	50.847
Rad/nuclear/explosive	137	177	77.401
CBRNE policy	459	649	70.724
Facility	228	413	55.206
Overall	1,212	1,829	66.266

to chemical agents [$F = 3.5447$ ($p < 0.10$)]. While individual practitioners may have differing opinions regarding treatment of individual agents or pathogens, prescribed treatment algorithms for chemical agents have been recommended by the Centers for Disease Control (CDC).

Policy questions regarding decontamination of casualties and managing the media were noteworthy. Among physicians and nonphysicians, as well as attending physicians versus nonattending physicians, there was statistically significant variation pertaining to how a hospital employee should react if he or she is exposed to an agent during the decontamination process (question #14) (physicians vs nonphysicians [$F = 4.944$ ($p < 0.01$)], attending physicians vs nonattending physicians [$F = 6.0895$, ($p < 0.01$)]). In addition, the appropriate water temperature required to decontaminate a casualty (question #27) was significant (physician vs nonphysician [$F = 3.2164$ ($p < 0.05$)] and attending vs nonattending [$F = 3.5696$ ($p < 0.01$)]). Equally, there was significance regarding whom should discuss the disclosure of information to the media (question #25) (physician vs nonphysician [$F = 3.0180$ ($p < 0.01$)] and attending vs nonattending [$F = 3.2125$ ($p < 0.01$)]).

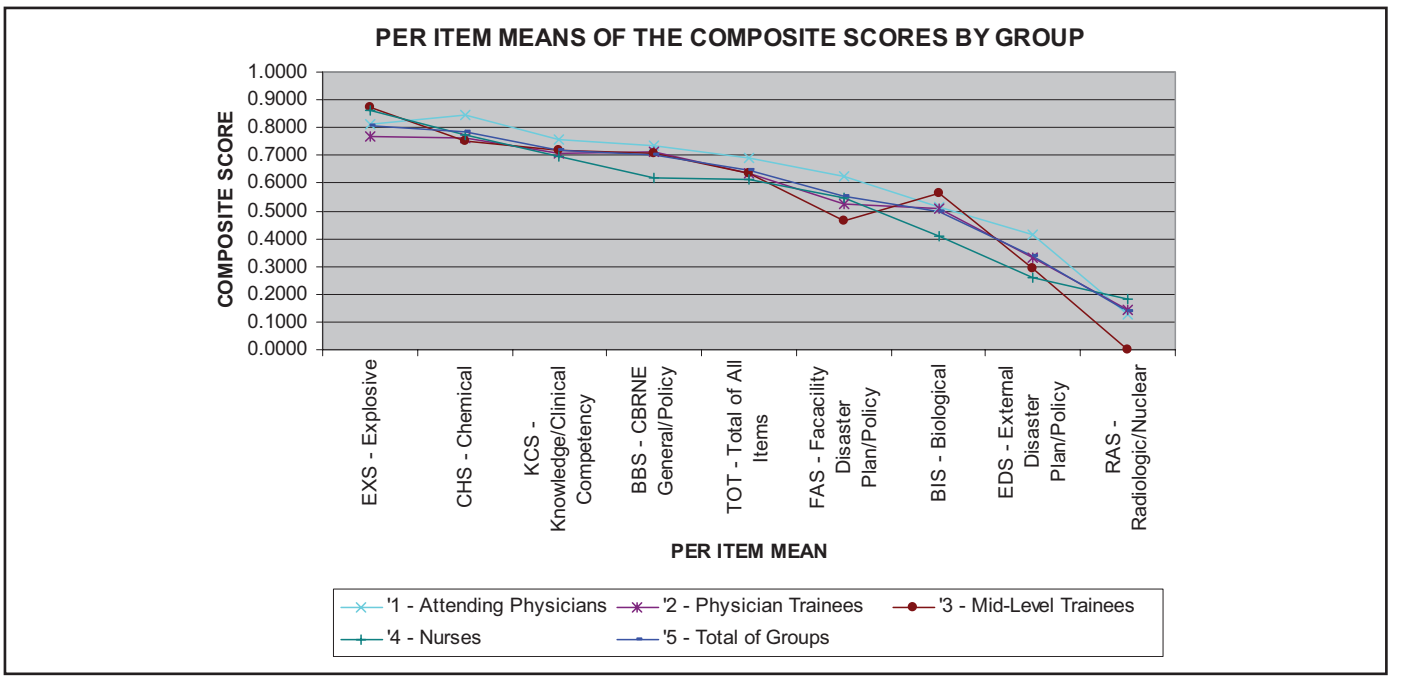

Figure 2. Comparison of group means to correct answers, by CBRNE category.

Personal protective equipment

Question #29 could not be analyzed for variance because there is no correct answer to this question. This question was designed to illicit feedback regarding the individual provider's comfort level and familiarity with the use and wear of PPE. Twenty-seven respondents or 45.76 percent of the study population either had no experience with PPE or did not know what PPE meant. Only 33.90 percent had been fitted, trained, and had the chance to don and doff PPE during a mock drill or actual incident.

Discussion

The results of the raw score of correct answers provided by the total cohort of healthcare providers in this study does not accurately assess their overall knowledge base or level of CBRNE preparedness. This is primarily limited by the study instrument's lack of reliability and precision.

Given this information, it is difficult to determine if the lack of precision is explainable by the actual instrument, or by confounding factors associated with the respondents' performance. Each respondent completed the study instrument at his or her leisure without investigator supervision. It is unknown when or where the respondent completed the questionnaire and these factors may have influenced the answer choices selected. For example, if the questionnaire was completed during a shift in the ED, it is likely that the provider was distracted or had to be interrupted numerous times. Equally significant, the primary investigator had no way of controlling the use of external resources (ie, textbooks, Web sites, and medical reference materials) the respondents may have used to complete the instrument. Finally, there was no way for the investigator to incentivize individual respondents to complete the questionnaire to the best of their ability, using only their knowledge base as their source of answering each item. If it were possible to control for the above confounders, the results of the study may have been significantly different.

The majority of this instrument was developed by a state-funded organization designed to evaluate and improve the knowledge base of individual healthcare providers in California. It is unknown what the results of the experiences in California are regarding the instrument, or how precise and reliable the instrument was among California's providers. However, if

this instrument behaved similarly among California providers, the instrument does not measure an individual or group's level of CBRNE knowledge. Hence, this instrument is a poor measure of CBRNE preparedness. Good performance on this questionnaire does not reflect an adequate knowledge base, and the same is true for poor performance. That said, policy and funding decisions should not be made based on this instrument.

However, it is possible to take the data obtained from this instrument and use it in the development of a more precise and more reliable instrument that accurately assesses an individual's CBRNE-specific knowledge and competency. The results from the one-way ANOVA provide some guidance as to how future assessments could be structured to produce a precise instrument.

The significant variance among provider occupation and experience level suggests that knowledge and competency surrounding CBRNE incidents varies according to a provider's occupation and how long they have been out of training. This is specifically true for chemical incidents. Regarding specific chemical agents, age and years in practice were strongly correlated with individuals who chose the correct response. CBRNE incidents are infrequent events and require regular periodic review. Providers who do not regularly review these agents are unlikely to perform well on any assessment. This may explain some of the variance observed in this study. It was clinically reassuring that most respondents were familiar with the signs and symptoms of nerve agent exposures and their corresponding treatments. However, only 33.90 percent could distinguish between chemical agents that caused immediate signs and symptoms and those with a delayed presentation.

The variance among required antidotes for nerve agents is especially alarming. Nerve agents (Sarin, Soman, Tabun, and VX) constitute some of the most dangerous CBRNE agents in existence. A casualty exposed to these agents will die without the administration of atropine in the proper dosage.[21] While this education is available to nurses in practice, it may not be given the same attention during their primary education.[22] This study suggests that integration of training from all healthcare disciplines is required to deliver the required information regarding casualty management to all providers. Rather than focusing on specific training curricula for individual disciplines, a novel curriculum designed for advanced healthcare providers may be beneficial and effective.

Regarding biological agents, only 54.24 percent of the respondents were aware that pneumonic plague (*Yersinia pestis*) is capable of horizontal transmission and requires prophylactic therapy for exposed healthcare providers. 6.78 percent believed no action is necessary when one is exposed to plague. 52.54 percent believed there is a vaccine against *Clostridium botulinum* available to the general public. While there are investigational vaccines currently in development, no vaccine currently exists for large scale distribution.[23] 71.19 percent of respondents knew the correct indications for administration of potassium iodide following a nuclear incident. For items pertaining to general practices and principles of CBRNE incident management, 70.72 percent of the questions were answered correctly. Regarding facility-specific questions unique to the population's ED, only 55.21 percent of questions were correctly answered.

Physicians receive a sizeable amount of education and training regarding the management and care of CBRNE patients. Since 2007, every emergency physician who has graduated from an ACGME-accredited residency has received training in the decontamination of patients, the use and wear of PPE, managing exposures from CBRNE incidents, and diagnosing and treating CBRNE victims.[24] Nurses, conversely, may not have the same level of education and training during their schooling.[16]

PPE and patient decontamination are additional areas that require assessment and further refinement. Based on the results from question 29 in this study, the majority of respondents have little-to-no experience with the wear and use of a PPE. That said the first time they would become familiar with PPE would likely be during an actual CBRNE incident. Furthermore, the validity coefficient for item #14 suggests that as individuals gain more experience and age, they become less familiar with the policies and procedures regarding decontamination. This is suboptimal

and counterproductive to establishing a well designed, functional CBRNE disaster response plan. The lack of familiarity with PPE and the decontamination process is further emphasized by the variance in the answers to questions 14 and 27. The significance of the variance in these variables indicates that very few providers are familiar with the established protocols and best practices regarding decontamination. There is consensus agreement among experts in the field of disaster management that workers at all levels need additional training, awareness, and familiarization with CBRNE-specific PPE.[25,26] Future policy decisions need to focus efforts on improving the integration of patient decontamination and the wear of PPE.

A longer, more detailed study instrument would likely produce a more reliable and precise measure of CBRNE preparedness. Specifically, if respondents were asked detailed questions regarding individual agents, individual antidotes and medications, and policy questions related to individual CBRNE-related incidents, a policy maker would have more objective data to make decisions regarding areas of strengths and weaknesses pertaining to CBRNE preparedness.

Limitations

This was a retrospective observational survey study and is therefore subject to the selection biases and information biases inherent in all retrospective study designs. In addition, data were obtained from a single institution and the study population was relatively small. However, this study did obtain information from every major provider discipline currently practicing inside an ED.

Additionally, as previously stated the survey instrument was suboptimal and lacked sufficient precision and reliability. However, provider engagement and initiative during the completion of the questionnaire could not be controlled or accounted for. An unmotivated respondent who did not seriously consider each answer choice may have skewed the results, erroneously making the instrument imprecise. Future studies wishing to evaluate provider preparedness should focus on administering the instrument under more controlled conditions with subjects who desire to perform at their peak level.

Responder bias and nonresponder bias should also be considered. Those who agreed to participate in the study likely had an interest in disaster preparedness or believed they would perform well on the analysis. On the contrary, those who believe they are weak in this field of public health or have little interest may have chosen not to respond.

Conclusion

CBRNE agents will continue to pose a threat to the safety of US citizens for decades to come. A sound disaster response plan and a well-educated, experienced healthcare workforce are required to provide effective medical care to victims injured during these incidents. Subjects who participated in this study demonstrated a mediocre level of knowledge pertaining to CBRNE agents and incidents. Females and providers with previous CBRNE incident experience performed statistically better than males and those who lacked experience. These data suggest that future CBRNE-related policy decisions should draw heavily on those with actual CBRNE clinical experience. Very few subjects had sufficient experience or knowledge regarding the wear and use of PPE, and additional training and familiarization with PPE are required for healthcare providers. A considerable amount of variance exists among healthcare providers with the administration of critical antidotes and casualty decontamination. Additionally, there is a large amount of variance between provider knowledge and their occupation or experience/years in practice. This may reflect differences in education among healthcare disciplines with some disciplines offering more education and training then others. Ideally, every emergency healthcare provider should demonstrate competence and comfort in CBRNE management. A standardized curriculum for all providers who care for CBRNE casualties in an emergency environment may be optimal.

This is the first study to evaluate the CBRNE preparedness of the entire workforce of a hospital ED. Previous studies have chosen to either evaluate individual occupational disciplines singularly or have focused on the hospital ED from a systems approach. However, the integration and summation of all providers' knowledge and experience to CBRNE agents is

likely to be heavily drawn upon during an actual incident. Future studies should look to evaluate all providers of the ED in a single population with an instrument possessing acceptable precision, validity, and accuracy.

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Joseph G. Kotora, DO, MPH, Primary Investigator, Fellow, EMS and Disaster Medicine, Newark Beth Israel Medical Center, Newark, New Jersey.

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Appendix A

CBRNE QUESTIONNAIRE

KNOWLEDGE/CLINICAL COMPETENCY QUESTIONS

1. Chemical weapon agents are classified by their clinical effects. Each of the following are an important class of chemical agents except one:

   A. (1)Choking agents
   B. (2)Blood agents
   C. (3)Liver agents
   D. (4)Nerve agents
   E. (5)Blister agents

2. An outbreak of botulism is occurring in a nearby community. The hospital in that community is unable to care for all the patients from the outbreak, and patients are to be transferred to your facility. Which of the following actions should your facility take?

   A. (1)Prepare an area where the botulism patients can be isolated so that they do not spread the disease to others
   B. (2)Ensure that your facility has an adequate stock of appropriate antibiotics to treat the botulism patients
   C. (3)Ensure that staffing is adequate to care for the expected number of patients
   D. (4)A and C
   E. (5)All of the above

3. Administration of potassium iodine is appropriate therapy following which radiation exposure events?

   A. (1)Exposure to radioactive fallout following a thermonuclear explosion
   B. (2)Exposure to high levels of gamma radiation
   C. (3)Exposure to a radioactive cesium release from a medical facility
   D. (4)Exposure to radioactive fallout from a nuclear power plant accident
   E. (5)All of the above

4. The 1995 Tokyo subway sarin attack taught us which of the following lessons about emergency response to CBRNE events:

   A. (1)Interagency coordination is crucial for an effective response to CBRNE events
   B. (2)Immediate decontamination is a priority for protecting victims' health and for preventing secondary contamination
   C. (3)Appropriate personal protective equipment (PPE) must be worn by all personnel who may be exposed to contaminated patients
   D. (4)Medical personnel must have access to management guidelines for common hazardous agents
   E. (5)All of the above

5. You are treating multiple victims of an explosion. A 23 year old male is experiencing chest pain and shortness of breath. He should have the following evaluation and treatment:

   A. (1)High flow oxygen should be administered
   B. (2)He should be intubated and mechanically ventilated to prevent hypoxia and to reduce the work of breathing
   C. (3)A chest radiograph should be taken as soon as possible to rule out a pneumothorax
   D. (4)A and C
   E. (5)All of the above

6. Another victim of the explosion has abdominal tenderness, but lacks visible signs of injury. An abdominal CT scan has been ordered. How should he be managed?

   A. (1)The CT scan should be performed. If it is negative the patient can be discharged
   B. (2)The CT scan should be cancelled and exploratory surgery performed at once
   C. (3)The patient should be closely inspected for abdominal puncture wounds from flying debris. If no puncture wounds are found, the abdominal CT scan should be cancelled, and the patient can be discharged
   D. (4)The CT scan should be performed. If it is negative the patient should be admitted for observation

7. The main effects of all of the following chemical agents occur within seconds to a few minutes except one:

   A. (1)Sarin (a nerve agent)
   B. (2)Cyanide (a blood agent)
   C. (3)Chlorine (a choking agent)
   D. (4)Sulfur mustard (a blister agent)
   E. (5)Mace (a tearing agent)

8. You are notified that a patient that you cared for yesterday has now been diagnosed as having pneumonic plague. The patient had a fever and a cough when you cared for her. What actions should you take?

   A. (1)No action is necessary since pneumonic plague cannot be spread person-to-person
   B. (2)Ensure that you get vaccinated with the plague vaccine at once so that you do not become ill
   C. (3)Begin a course of antibiotics at once so that you do not become ill
   D. (4)Notify your family that you must be quarantined until it becomes known if you will develop plague
   E. (5)None of the above

9. Vaccines are currently stockpiled in the United States to prevent which of the following CDC Category A Bioterrorism Agents of Concern:

   A. (1)Smallpox
   B. (2)Plague
   C. (3)Botulism
   D. (4)A and C
   E. (5)B and C

10. All of the following should raise the suspicion of a chemical or biological weapon attack except one:

    A. (1)Spraying activity in an inappropriate area
    B. (2)Smoke or detectable material in the air
    C. (3)Animals in the region are ill or dead, but humans are unaffected
    D. (4)An unexplained odor inappropriate for the context of its surroundings
    E. (5)An unexplained deposit of material in an area where casualties occurred (eg, liquid droplets in absence of watering or rain)

11. The victim of a chemical attack is noted to have very small pupils. Which class of chemical agents should be suspected?

    A. (1)Blister agents
    B. (2)Blood agents
    C. (3)Tearing agents
    D. (4)Nerve agents
    E. (5)Choking agents

12. An outbreak of smallpox has been reported in your county. Appropriate containment measures include:

    A. (1)Suspected and confirmed cases should be isolated
    B. (2)Everyone that may have had contact with a person ill with smallpox should be vaccinated at once

C. (3)Healthcare and law enforcement personnel, and all others involved in containing the outbreak should be vaccinated at once
D. (4)Transfer of smallpox patients to designated facilities equipped for their care
E. (5)All of the above

13. Atropine should be administered as soon as possible to victims suffering from which class of chemical agents:

A. (1)Vomiting agents
B. (2)Nerve agents
C. (3)Blood agents
D. (4)Blister agents
E. (5)Choking agents

14. If a medical care provider who does not have personal protective equipment is directly exposed to a high-level chemical or biological agent release all of the following actions are appropriate except one:

A. (1)Immediately leave the area of the exposure
B. (2)Go to the specified decontamination area at once if it is nearby and is ready to receive casualties
C. (3)If there is no available decontamination facility, remove all clothing and thoroughly wash yourself with mild soap and water
D. (4)Scrub hard to remove all contamination
E. (5)Do not touch or put back on contaminated clothing

15. Each of the following statements is true regarding identifying and reporting CBRNE events except one:

A. (1)Medical facilities play a key role in identifying threats to public health
B. (2)Biological agents may be used covertly so that medical facility personnel may be the first to recognize an event has occurred
C. (3)Law enforcement agencies should not be notified until a suspected chemical or biological attack is definitively confirmed
D. (4)The state of New Jersey requires that any occurrence that threatens the welfare, safety, or health of patients, visitors, or personnel must be reported to the local health officer and to the appropriate state or federal agencies
E. (5)When a CBRENE event is suspected by medical facility staff, immediate internal and external notification is required

16. Victims contaminated in a chemical or biological attack should be brought into patient care areas at once for treatment.

1-True 2-False

17. Waste water used in decontaminating patients is contaminated, and might make you sick if it gets on your skin or clothing.

1-True 2-False

18. Following any chemical, biological, or radiation attack, all victims will be decontaminated before arriving at medical care facilities.

1-True 2-False

19. Standard latex medical gloves provide adequate protection for disposing of waste contaminated by a chemical weapon agent.

1-True 2-False

20. Chemical, biological, and radiation attacks are crimes, and victims' clothing should be saved because it may be used as evidence.

1-True 2-False

21. Each medical care facility has a plan in place so that employees can work together effectively if there is a natural or man-made disaster.

1-True 2-False

22. Level D personal protective equipment (PPE) provides the highest level of protection and is appropriate for highly dangerous chemical agents.

1-True 2-False

23. The Hospital Emergency Incident Command System [HEICS] employs a logical management structure to assist medical facilities in staying operational during a disaster.

1-True 2-False

24. Following a CBRNE event, patients and their families will experience psychological effects, but medical care facility personnel are not at risk for these problems.

1-True 2-False

25. The doctor responsible for caring for the victims of a CBRNE event should be the one to communicate with the representatives of the news media.

1-True 2-False

POLICY/EXTERNAL DISASTER FAMILIARITY/KNOWLEDGE QUESTIONS

26. When the Emergency Department is the recipient of casualties from a mass casualty incident (MCI), who should the ED notify of the incident?

A. (1)Emergency Department Medical Director
B. (2)On-Call Nursing Supervisor
C. (3)Emergency Preparedness Coordinator/ Mass Casualty Coordinator
D. (4)Chief Executive Officer
E. (5)Newark Police Department
F. (6)The Federal Emergency Management Agency (FEMA)

27. Regarding decontamination of casualties of a Chemical, Biological, Radiological, Nuclear, or Explosive (CBRNE) incident, which of the following answers are true?

A. (1)Casualties decontaminated at the scene do not need further decontamination, and should be brought directly into the main Emergency Department
B. (2)All casualties should be stripped of all clothing, residual product should be brushed off, and the casualty should be thoroughly rinsed with copious amounts of cold water
C. (3)All casualties should be stripped of all clothing, residual product should be brushed off, and the casualty should be thoroughly rinsed with copious amounts of warm water
D. (4)All casualties should be stripped of all clothing, residual product should be brushed off, and the casualty should be thoroughly rinsed with copious amounts of hot water
E. (5)All casualties should be stripped of all clothing, residual product should be brushed off, and the casualty should be thoroughly rinsed with copious amounts of a 50:50 mix of cold water and bleach solution

28. Which of the following items is considered personal protective equipment that should be worn by a healthcare practitioner, during a CBRNE incident?

A. (1)Surgical Mask
B. (2)Respirator
C. (3)N-95 Respirator
D. (4)Latex gloves
E. (5)Nitrile Gloves
F. (6)Chemical protective suit

29. Have you been fitted, trained, and had the chance to practice the proper wear of CBRNE Personal Protective Equipment (PPE)?

A. (1)Yes, I've been fitted, trained, and had the chance to practice the proper wear of PPE
B. (2)I've been fitted and trained, but have not had the chance to practice the proper wear of PPE
C. (3)I've been fitted, but have never been trained on the proper wear, and have never had the chance to practice the proper wear of PPE
D. (4)No, I have no experience with PPE
E. (5)I am unsure/I do not know

30. How should healthcare practitioners manage the clothing, jewelry, and personal effects from victims of a CBRNE incident?

A. (1)Discarded in a trash bag
B. (2)Handed to security personnel
C. (3)Discarded in a red biohazard bag, and handed to security personnel
D. (4)Discarded in a red biohazard bad, tagged with date, time, and name of casualty, and handed to security personnel
E. (5)Discarded in a red biohazard bad, tagged with date, time, and name of casualty, and handed to law enforcement personnel

31. Where is the hospital's external disaster management protocol stored?

A. (1)On the hospital's Internet page
B. (2)On the hospital's intranet page
C. (3)In the office of the emergency preparedness coordinator
D. (4)In the office of Risk Management
E. (5)In the Emergency Department

32. During an external disaster, who is the hospital incident commander?

A. (1)The Risk Management Coordinator
B. (2)The Emergency Department Attending Physician
C. (3)The Emergency Department Charge Nurse
D. (4)The Nursing Shift Supervisor
E. (5)The hospital Chief Executive Officer

DEMOGRAPHIC/PRACTICE/EXPERIENCE QUESTIONS

33. Which of the following best describes your gender?

A. (1)Female
B. (2)Male

34. Which of the following best describes your race/ethnicity? (**choose all that apply**)

A. (1)African American
B. (2)Caucasian
C. (3)Hispanic/Latino
D. (4)Asian
E. (5)Indian
F. (6)Arabic
G. (7)Pacific Islander
H. (8)Native American
I. (9)Other

35. Which of the following best describes your age group, in terms of number of years?

A. (1)26-30
B. (2)31-35
C. (3)36-40
D. (4)41-45
E. (5)46-50
F. (6)51-55
G. (7)56-60
H. (8)>60

36. Which of the following best describes your profession/occupation in the hospital?

A. (1)Attending Physician
B. (2)Nurse
C. (3)Nurse Practitioner
D. (4)Physician Assistant
E. (5)Resident Physician

37. Which of the following best describes your number of years in practice/years of experience?

A. (1)<1
B. (2)1-5
C. (3)6-10
D. (4)11-15
E. (5)16-20
F. (6)21-25
G. (7)26-30
H. (8)>30

38. If you are a resident physician, what is your current level of training, in terms of PGY year?

A. (1)PGY1
B. (2)PGY2
C. (3)PGY3
D. (4)PGY4
E. (5)Not a Resident Physician

39. Have you ever managed a patient who was a victim of a CBRNE incident?

A. (1)Yes, one time
B. (2)Yes, less than five times
C. (3)Yes, five or more times
D. (4)No, I've never mentioned a victim from a CBRNE incident
E. (5)I don't know/ I'm not sure

40. Have you ever taken a Hospital Emergency Incident Command System (HEICS) course, or been trained in the HEICS principles?

A. (1)No, I have never taken a HEICS course
B. (2)Yes, within the past 6 months
C. (3)Yes, within the past 12 months
D. (4)Yes, more than 12 months ago
E. (5)I don't know/ I'm not sure

THANK YOU FOR YOUR PARTICIPATION! THIS COMPLETES THE QUESTIONNAIRE.

DM

ORIGINAL ARTICLE

Intraosseous hydroxocobalamin versus intravenous hydroxocobalamin compared to intraosseous whole blood or no treatment for hemorrhagic shock in a swine model

Vikhyat S. Bebarta, MD, FACEP, FACMT; Normalynn Garrett, PhD; Susan Boudreau, RN, BSN; Maria Castaneda, MS

Abstract

Objective: *To determine if intraosseous (IO) hydroxocobalamin can improve systolic blood pressure (SBP) in a swine model after severe hemorrhagic shock.*

Methods: *Thirty six swine (45-55 kg) were anesthetized, intubated, and instrumented with continuous femoral and pulmonary artery pressure monitoring and then hemorrhaged such that 30 percent of their blood volume was extracted over 20 minutes. Five minutes later, animals were randomly assigned to receive 500 mL IO whole blood, 150 mg/kg IO or intravenous (IV) hydroxocobalamin in 180 mL of saline, or no treatment and then monitored for 60 minutes. A sample size of eight animals per group was based on a power of 80 percent, an alpha of 0.05, and a small effect size to detect a difference in SBP between groups. Outcome data were analyzed using repeated measures analysis of variance (RMANOVA).*

Results: *RMANOVA outcome analysis detected a significant difference between groups ($p < 0.05$). IO whole blood, IO hydroxocobalamin, and IV hydroxocobalamin groups were similar to each other, but significantly different compared to controls regarding SBP, mean arterial pressure (MAP), systemic vascular resistance, and heart rate. Differences in SBP and MAP were sustained throughout the experiment. At 60 minutes, the comparison among the groups, IO whole blood, IO hydroxocobalamin, IV hydroxocobalamin, and control, was the following: SBP 78.2 versus 83.7 versus 75.1 versus 55.3 mm Hg; MAP 62.7 versus 65 versus 60 versus 43 mm Hg. There was a significant interaction by time in lactate values ($p < 0.01$) such that control animal lactate values increased over time (3.3 mmol/L) compared to IO whole blood, IO or IV hydroxocobalamin treated animals (1.1, 1.6, 1.3 mmol/L).*

Conclusions: *IO hydroxocobalamin improved SBP, MAP, compared to no treatment and was similar to IO whole blood and IV hydroxocobalamin in this animal model of severe hemorrhage. Moreover, whereas serum lactate was improving in all treated groups, it was deteriorating in the control group.*

Key words: hydroxocobalamin, intraosseous infusion, swine, hemorrhage, resuscitation

Introduction

Hemorrhage is a leading cause of potentially preventable traumatic death.[1] Rapidly establishing venous access is central to treatment of hemorrhagic shock in the prehospital setting. However, establishing intravenous (IV) access under austere conditions can be challenging or impossible. For this reason, the Committee on Tactical Combat Casualty Care recommends intraosseous (IO) resuscitation when IV access is not obtainable.[2] Although published studies evaluating the efficacy of resuscitation treatments using an IO administration route are limited, IO catheters have been placed in hundreds of injured combat troops.[3] Because of the limited number of controlled studies, additional studies using IO administration for resuscitation are needed to validate the safety and efficacy of using IO devices for resuscitation.

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Selecting the amount and type of fluid to be infused for hemorrhagic resuscitation is equally challenging. The most recent recommendations are to limit resuscitation fluids such that risks of coagulopathies, hyperinflammatory response, and exsanguination are minimized.[4,5] Hydroxocobalamin has been shown to improve blood pressure when administered in a small volume[6] and may be an ideal resuscitation treatment under austere conditions. It is safe, approved by the United States Food and Drug Administration (FDA), and effective for cyanide-induced shock.[7] We have previously reported that a small volume of hydroxocobalamin (90-180 mL) can improve blood pressure and survival after severe cyanide toxicity in an animal model.[8] Likewise, hydroxocobalamin has been shown to effectively increase blood pressure in cyanide-induced cardiac arrest and endotoxin-induced hypotension.[9,10] Hence, hydroxocobalamin may be a viable alternative to other fluids currently used in hemorrhagic resuscitation with fewer associated risks.

There are no published reports comparing IV to IO hydroxocobalamin in a hypotensive, hemorrhagic, animal model. Results from our most recently published study suggest hydroxocobalamin is effective in increasing blood pressure as well as systemic vascular resistance (SVR) in a hypovolemic hemorrhagic swine model.[11] Moreover, at the dose of 150 mg/kg of hydroxocobalamin, systolic blood pressure (SBP) does not exceed recommendations by the Committee on Tactical Combat Casualty Care,[12] hence, mitigating effects of over increasing blood pressure which can subsequently increase mortality.[13-15]

Goal of this investigation

Our primary hypothesis is that IO hydroxocobalamin is more effective than no treatment in reversing hypotension associated with potentially survivable hemorrhage. Secondarily, we posited that IO or IV hydroxocobalamin will be significantly better than no treatment and equivalent to IO whole blood. Specifically, we compared SBP over time in animals that had 30 percent of their blood volume removed (class III hemorrhagic shock) and were subsequently treated with IO or IV hydroxocobalamin, IO whole blood (positive control), or not treated (negative control).

Methods

Study design and setting

We conducted a comparative laboratory investigation approved by our Institutional Animal Care and Use Committee at the Wilford Hall Ambulatory Surgical Center Clinical Research Division and funded by the US Air Force Office of the Surgeon General. All procedures involving animals complied with the regulations and guidelines of the Animal Welfare Act, the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and the American Association for Accreditation of Laboratory Animal Care. The housing of animals and the performance of the study took place in the Animal Care Facility at our institution.

Animal subjects

Female Yorkshire swine (*Sus scrofa*) (N = 36, weighing 45-55 kg) were premedicated with intramuscular ketamine 10 mg/kg. General anesthesia was induced with isoflurane via nose cone. Following endotracheal intubation, animals were mechanically ventilated with a volume-limited, time-cycled ventilator (Drager-Siemens, Fabius GS anesthesia machine, New York City, NY), and maintained with inhaled isoflurane (1-3 percent) and oxygen (FiO_2 of 0.4-0.45). Tidal volume was initially 8-10 mL/kg and respiratory rate was 12 breaths/min. Minute ventilation was adjusted to maintain an end tidal CO_2 value between 38 and 42 mm Hg as measured by inline capnography. Lead II of the surface electrocardiogram was monitored continuously. Temperature was maintained at 37.5-39.0°C.

Interventions

Invasive hemodynamic variables were measured with an eight-French Swan-Ganz CCOmbo V pulmonary artery catheter (Model 777F8) and the Edwards Vigilance II monitor (Edwards Lifesciences, Irvine, CA). Measurements included continuous cardiac output, SVR, mixed venous oxygen saturation, central venous pressure, pulmonary artery pressure, and core temperature. Catheter ports were flushed with saline and placed via cut-down in the right external jugular. Aortic pressure was measured continuously through the femoral artery. An 8.5 French introducer (Arrow, Reading, PA) was

placed in the carotid artery for laboratory sampling and another was placed in the internal jugular for medication administration. Animals received a warmed saline IV bolus (10 mL/kg) during procedure setup to assure adequate hydration prior to experimentation. There were no significant differences in central venous pressure values prehemorrhage among the groups ($p = 0.5$). The Fabius GS anesthesia data collection software embedded in the ventilator's computer was used for data acquisition. Animals in the IO groups had an adult (25 mm) IO needle placed in the proximal tibia (EZ-IO, Shavano Park, TX) prior to hemorrhage. IO needle placement was confirmed by marrow aspiration and ease of flush.

Baseline biochemical measurements included arterial blood gases (ABL 800 Flex blood gas analyzer, Radiometer America, Westlake, OH), prothrombin time (PT), partial thromboplastin time (PTT), (STA-R Evolution, Diagnostic Stago Inc., Parsippany, NJ), and platelet count (Advia 120, Siemens, Norwood, MA).

After instrumentation, isoflurane was reduced to 0.5-1.5 percent after which animals were acclimated and blood pressure stabilized for 10 minutes before hemorrhage began. Animals were then hemorrhaged using a modified Frankel et al.[16] and modified White et al.[17] model such that 1.42 mL/kg/min of blood was removed for 7 minutes then 0.76 mL/kg/min of blood was removed for the remaining 13 minutes. Five minutes after hemorrhage, animals were assigned to receive 150 mg/kg IO or IV hydroxocobalamin (Meridian Medical Technologies, Columbia, MD) solubilized in 180 mL of saline, 500 mL IO fresh whole blood, or no treatment. Isoflurane anesthesia was standardized between groups such that there was no significant difference between groups during or after hemorrhage (mean isoflurane control, 1.2 percent; IO, 1.7 percent; IV, 1.5 percent). Administration time of treatments was standardized such that it was infused over 4-6 minutes. Ten milliliters of saline was infused before and after treatment after which animals were monitored for 60 minutes.

Methods of measurement and outcome measures

The primary outcome measure was SBP over time after treatment or no treatment from hemorrhage (time zero) to 60 minutes. A 60-minute observation period was selected to represent the 1 hour time frame in which a trauma victim's best chance for survival is to be transported to an operating room. We also compared cardiac output, mean arterial pressure (MAP), SVR, and heart rate. Hemodynamic measurements were recorded at 1-minute intervals and analyzed at 10-minute intervals. Serum blood sampling was taken at baseline, immediately after hemorrhage and at 5, 10, 20, 30, 40, 50, and 60 minutes after treatment/no treatment.

Primary data analysis

Power was assessed using G*Power Version 3.0.10., a β of 0.05 and a small effect size, *f*, of 0.25 to detect more than 1 standard deviation difference in SBP between groups. Based on this design, a total of 32 subjects (8 subjects × 4 groups) would be required to detect a difference between the treatment groups. Because the data from control and IV hydroxocobalamin groups were from previous experiments, those groups have 10 each, therefore the total number of subjects was 36.

Descriptive statistics were analyzed using multivariate analysis of variance (MANOVA). Outcome variables were modeled using repeated measures multivariate analysis of variance (RMANOVA) with adjustment for treatment, time, and the interaction of treatment by time with an autoregressive covariance structure assumed. Post hoc analysis was performed on all variables that showed a significant treatment by time interaction, for which treatment contrasts were measured at each post-treatment time point with a Bonferroni adjustment for multiple testing applied. Values for serum lactate concentrations, PT, PTT, and platelet counts were compared among groups using RMANOVA for times zero, 60 minutes.

All statistical testing was two sided with a significant level of alpha of 0.05 and completed using SAS version 9.3 (Cary, NC, USA). All graphical presentations were made using R version 2.15.1. Our study was funded by the United States Air Force Office of the Surgeon General.

Results

Characteristics of study subjects

At baseline, the groups had similar vital signs and biochemical variables (MANOVA $p > 0.05$; Table 1). At

Table 1. Baseline characteristics of the animals 30 min before hemorrhage				
Characteristics	**IO HOC (N = 8)**	**IV HOC (N = 10)**	**IO WB (N = 8)**	**Control (N = 10)**
Weight, kg	49.5 (2.9)	48.2 (2.6)	52.2 (4.0)	51.8 (2.4)
Heart rate, beats/min	95 (13.6)	92 (16.3)	88.7 (13.7)	88 (16.2)
Systolic blood pressure, mm Hg	115.6 (10.3)	103.3 (5.9)	98.7 (5.8)	102.7 (11.6)
Mean arterial pressure, mm Hg	92.8 (11.3)	81.2 (7.0)	79.2 (7.3)	78.3 (11.2)
Cardiac output, L/min	4.5 (0.6)	5.1 (0.9)	4.5 (1.1)	5.2 (1.1)
Systemic vascular resistance, dyne s/cm^{-5}	1,545 (222)	1,186 (267)	1,400 (5,170)	1,102 (257)
Lactate, mmol/L	1.0 (0.3)	1.0 (0.2)	0.8 (0.2)	1.0 (0.3)
Hemoglobin, g/dL	8.0 (0.7)	7.3 (0.7)	8.2 (0.5)	8.9 (0.5)
Prothrombin time, s	13.6 (0.6)	13.6 (0.4)	13.7 (0.7)	13.4 (0.5)
Partial thromboplastin time, s	32.6 (6.1)	28.8 (3.7)	30.7 (6.4)	32.3 (7.3)
Platelet count, 10^9/L	268 (43)	343 (83)	241 (63)	328 (82)

HOC, hydroxocobalamin; WB, whole blood; IV, intravenous; IO, intraosseous; kg, kilograms; mm Hg, millimeters of mercury; L/min, liter per minute; dyne s/cm^{-5}, dynes-seconds per centimeter^{-5}; mmol/L, millimoles per liter; gm/dL, grams per deciliter; s, seconds; L, liter. Data presented as means (standard deviation).

time zero, predefined as 5 minutes posthemorrhage, there were no significant differences between groups (Table 2). It is noteworthy that the cardiovascular response to hemorrhage in our swine population was similar to findings of Frankel. Whereas MAP and SBP show an immediate response to hemorrhage induced over 20 minutes in pigs maintained under 1-2 percent isoflurane, heart rate does not respond as quickly.[16] One of the control animals died after 40 minutes.

Main results

SBP (Figure 1a), the primary outcome variable, was similar between the treatment groups over time. This was significantly different from the nontreated group. By 10 minutes after treatment, SBP values in the treated groups were significantly greater than those in the nontreated group; $p < 0.01$. This difference continued for the rest of the observation period such that at 60 minutes, mean SBPs for IO and IV hydroxocobalamin were 83.7 (SD ± 17.3) and 75.1 (SD ± 7.5) mm Hg, whole blood 78.25 (SD ± 15.8), compared to 55.3 (SD ± 12.9) mm Hg for control; $p < 0.01$. Similar to SBP, MAP significantly improved over time in treated groups but not in the control group (Figure 1b).

Heart rate (Figure 1c) was not different among the three treated groups at any time point; however, 20 minutes after treatment, there was a significant difference between the IO whole blood (97.8 [SD ± 16.7] BPM) and IV hydroxocobalamin (99.2 [SD ± 25.6] BPM) animals compared to control (139.6 [SD ± 40.9] BPM) such that heart rate was significantly slower in these treated groups compared to control ($p < 0.03$). This difference was sustained over the 60-minute observation period. Although IO hydroxocobalamin (114.8 [SD ± 31.7] BPM; 20-minute value reported)-treated animals displayed a slower heart rate compared to control throughout the 60-minute observation period, this difference was not statistically significant. Heart rate values are presented in Table 3.

In the IO hydroxocobalamin group, SVR was higher compared to the IV hydroxocobalamin or IO

Table 2. Immediate posthemorrhage characteristics of the animals				
Characteristics	**IO HOC (N = 8)**	**IV HOC (N = 10)**	**IO WB (N = 8)**	**Control (N = 10)**
Blood loss, mL	974 (74.8)	955 (47.2)	1,023 (73.8)	1, 018 (37.0)
% of total blood volume	30 (0.00)	30 (0.01)	30 (0.01)	30 (0.01)
Heart rate, beats/min	102 (27.9)	95 (23.8)	96 (26.4)	108 (30.5)
Systolic blood pressure, mm Hg	41.3 (9.6)	47.1 (9.2)	41.3 (9.2)	36.6 (9.0)
Mean arterial pressure, mm Hg	33.6 (2.9)	38.5 (8.6)	35 (7.5)	29.5 (6.1)
Cardiac output, L/min	2.4 (0.5)	3.5 (0.9)	2.8 (0.5)	3.0 (0.8)
Systemic vascular resistance, dyne s/cm^{-5}	1,030 (266)	790.1 (235)	893 (158)	815 (272)
Lactate, mmol/L	1.7 (0.6)	1.21 (0.3)	1.2 (0.6)	1.39 (0.6)
Hemoglobin, g/dL	7.4 (0.8)	7.5 (0.6)	7.6 (0.6)	8.3 (0.5)
Prothrombin time, s	13.7 (0.7)	13.4 (0.4)	13.7 (0.7)	13.6 (0.3)
Partial thromboplastin time, s	37.7 (12)	27.5 (4.2)	30.76 (6.4)	31.9 (7.8)
Platelet count, 10^9/L	273 (60)	361 (71)	240.5 (63)	350 (71)

HOC, hydroxocobalamin; WB, whole blood; IV, intravenous; IO, intraosseous; mL, milliliters; mm Hg, millimeters of mercury; L/min, liter per minute; dyne s/cm^{-5}, dynes-seconds per centimeter^{-5}; mmol/L, millimoles per liter; g/dL, grams per deciliter; s, seconds; L, liter. Data presented as means (standard deviation). Estimated total blood volume = 66 mL/kg weight.

whole blood group at T + 10 minutes (ie, 10 minutes after treatment), but by 20 minutes, SVR between the three treated groups was not significantly different (Figure 1d). Although the IO whole blood group demonstrated a significantly higher SVR compared to control from 10 minutes through 30 minutes after treatment, both hydroxocobalamin treatment groups continued to have significantly higher SVR values compared to control over the entire 60-minute observation period (mean SVR IO whole blood 1,119 [SD ± 117]; IV hydroxocobalamin 1,316 [SD ± 216]; IO hydroxocobalamin 1,547 [SD ± 330]; control 882 [SD ± 270] dyne s/cm^{-5}; $p < 0.01$; 60-minute values reported).

This statistically significant difference in SVR did not affect cardiac output (Figure 1e). There was no difference among the groups over time (4.2 vs 3.2 vs 3.4 vs 3.3 L/min; $p = 0.5$; 60-minute values reported).

Lactate measures (Figure 2) demonstrated a significant interaction by time such that control animal lactate values increased over time (3.4 [SD ± 4.8] mmol/L) compared to IO hydroxocobalamin (1.6 [SD ± 0.6] mmol/L), IV hydroxocobalamin {1.4 (SD ± 0.3) mmol/L, or IO whole blood lactate values over time (1.05 [SD ± 0.4] mmol/L); 60-minute values reported}. We collected near infrared spectroscopy (NIRS) data (Covidien INVOS 5 100C, Minneapolis, MN) and compared pretreatment values. There were no significant differences ($p = 0.8$) however, because hydroxocobalamin is a dark-red analog of vitamin B-12, it interferes with NIRS measurements.[18] Post-treatment evaluation of NIRS is impossible. Arterial blood gas values are presented in Table 4.

Prothrombin, PTT, and platelet counts were normal among the three groups. Mean PT, PTT, and platelet counts for IO versus IV hydroxocobalamin versus IO whole blood versus no treatment at 60 minutes were the following: PT 14.8 versus 14.6 versus 13.5 versus 13.6 seconds; PTT 34.0 versus 33.8 versus

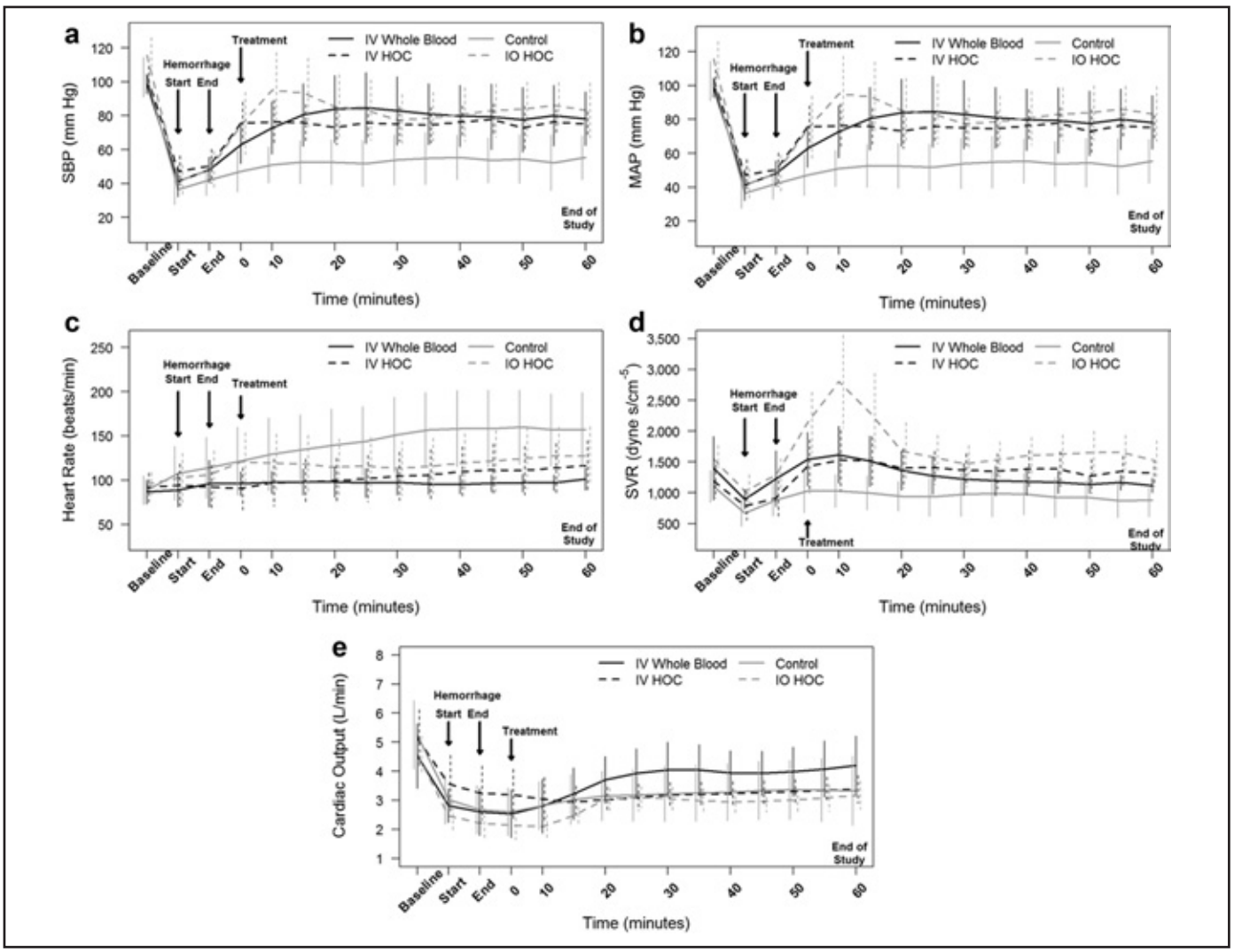

Figure 1. Hemodynamic variables (systolic blood pressure [SBP], mean arterial pressure [MAP], systemic vascular resistance [SVR], heart rate, and cardiac output) measured in animals over time until the end of the experiment. Animals were hemorrhaged such that 30 percent of the total blood volume was removed over 20 minutes. Five minutes after hemorrhage animals were treated with intravenous hydroxocobalamin (IV HOC; dashed black line), n = 10, intraosseous whole blood (IV whole blood; solid black line). n = 8, intraosseous hydroxocobalamin (IO HOC; solid gray line), n = 8, or not treated (control; dashed gray line) n = 10, and observed for 60 minutes. mm Hg, millimeters of mercury; dyne s/cm^{-5}, dynes-seconds per centimeter^{-5}; beats/min, beats per minute; L/min, liters per minute.

30.98 versus 33.2 seconds; platelet count 249 versus 329 versus 241.6 versus 359 × 10^9/L.

Discussion

We found that in a class III hemorrhagic shock model, the administration of IO hydroxocobalamin improved SBP and MAP as compared to control and was similar to IV hydroxocobalamin and IO fresh whole blood. Because lactate levels are a good reflection of the severity of hemorrhagic shock,[19] decreasing lactate levels for the hydroxocobalamin and whole blood groups compared to increasing lactate levels for the control group support the efficacy of hydroxocobalamin for hemorrhagic shock compared to no treatment. In fact studies suggest that a lactate of greater than 2 mmol/L, as was found only in the control group in our study, is a predictor of increased risk of mortality.[20-22] Contrary to the control group, serum lactate remained

Table 3. Heart rate post-treatment by time in minutes					
Time post-treatment, min	**IO HOC (N = 8)**	**IV HOC (N = 10)**	**IO WB (N = 8)**	**Control (N = 10)**	**p value (vs control)**
At treatment	106.3 (27)	92.4 (24)	96.1 (26)	114.2 (34)	
Treatment + 10	119.1 (33)	97.3 (26)	97.5 (12)	129.5 (41)	
Treatment + 20	114.8 (31)	99.2 (25)*	97.8 (16)*	139.6 (40)	$p < 0.02$
Treatment + 30	113.5 (30)	104.5 (27)*	97.5 (14)*	151.5 (42)	$p < 0.02$
Treatment + 40	119.5 (33)	109.4 (28)*	95.3 (10)*	158.3 (42)	$p < 0.02$
Treatment + 50	124.6 (34)	110.8 (27)*	96.8 (9)*	160.0 (41)	$p < 0.02$
Treatment + 60	127.3 (33)	116.5 (28)*	101.1 (12)*	157.3 (41)	$p < 0.02$
HOC, hydroxocobalamin; WB, whole blood; IV, intravenous; IO, intraosseous. Data presented as means (standard deviation). *All p values were <0.02.					

below 2 mmol/L in the treated groups throughout the observation period.

Heart rate was not different among the three treated groups at any time point, but by 20 minutes after treatment and for the remainder of the observation period, the IO whole blood and IV hydroxocobalamin groups displayed a significantly slower heart rate compared to control. Although heart rate in animals treated with IO hydroxocobalamin was slower than control, the values were not statistically lower. Nevertheless, a slower heart rate post drug administration suggests that animals receiving treatment were recovering from hemorrhagic shock compared to the control group.

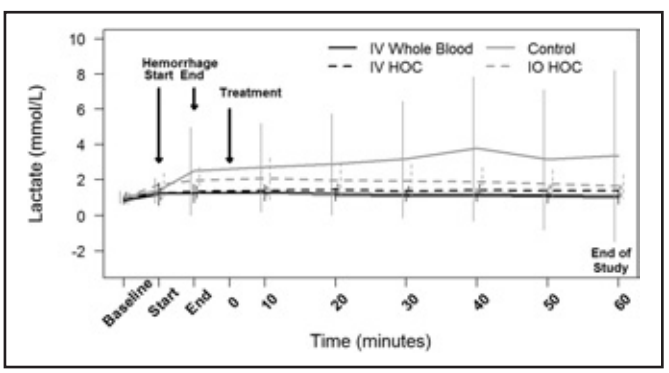

Figure 2. Lactate measurements measured in the animals over time until the end of the experiment. Animals were hemorrhaged such that 30 percent of the total blood volume was removed over 20 minutes. Five minutes after hemorrhage, animals were treated with intravenous hydroxocobalamin (IV HOC; dashed black line), n = 10, intraosseous whole blood (IV whole blood; solid black line), n = 8, intraosseous hydroxocobalamin (IO HOC; solid gray line), n = 8, or not treated (control; dashed gray line) n = 10, and observed for 60 minutes. mmol/L, millimoles per liter.

The difference between the heart rate found in IO hydroxocobalamin treatment group compared to IV hydroxocobalamin treatment group animals may also be partially explained by the route of administration. IO drug administration, specifically in animal resuscitation models, has been shown to yield longer times to maximum concentration (Tmax) and lower maximum concentrations (Cmax) of drug compared to IV routes[23] which may explain the lag in heart rate decline in animals administered hydroxocobalamin by IO compared to IV infusion. Increases in Tmax and decreases in Cmax using IO drug administration appear to be limited to delivering drug in resuscitation models. Others have reported no difference in Tmax or Cmax when comparing route administration in nonresuscitation models.[24] Further research is needed to clarify this controversy.

At T + 10 minutes (ie, 10 minutes after treatment), IO hydroxocobalamin produced a significant increase in SVR compared to IV hydroxocobalamin, IO whole blood, and control, however, by 20 minutes, there was no difference in SVR between the treated groups, whereas SVR was significantly lower in

Table 4. Arterial blood gas values by time in minutes				
Time post-treatment, min	**IO HOC (N = 8)**	**IV HOC (N = 10)**	**IO WB (N = 8)**	**Control (N = 10)**
Lactate (mmol/L)*				
Treatment + 10	2.0 (1.1)	1.3 (0.2)	1.27 (0.4)	2.7 (2.4)
Treatment + 30	1.9 (0.9)	1.3 (0.2)	1.1 (0.3)	3.1 (3.2)
Treatment + 60	1.6 (0.6)	1.3 (0.2)	1.0 (0.3)	3.3 (4.8)
pH				
Treatment + 10	7.40 (0.03)	7.40 (0.03)	7.41 (0.03)	7.44 (0.03)
Treatment + 30	7.43 (0.03)	7.41 (0.03)	7.44 (0.02)	7.44 (0.04)
Treatment + 60	7.45 (0.03)	7.42 (0.03)	7.45 (0.03)	7.45 (0.06)
PCO^2, mm Hg				
Treatment + 10	42.0 (4.0)	42.7 (3.6)	44.7 (3.3)	41.0 (3.9)
Treatment + 30	40.7 (3.5)	41.3 (3.1)	41.9 (3.8)	37.5 (3.5)
Treatment + 60	39.8 (3.4)	41.3 (4.5)	41.8 (2.3)	37.2 (6.0)
HCO^3, mmol/L				
Treatment + 10	25.7 (1.6)	26.1 (1.2)	27.1 (1.9)	27.8 (2.9)
Treatment + 30	26.5 (1.2)	25.9 (1.3)	28.2 (1.5)	26.5 (3.8)
Treatment + 60	27.7 (1.0)	26.4 (0.7)	28.8 (2.0)	26.9 (5.1)

HOC, hydroxocobalamin; WB, whole blood; IV, intravenous; IO, intraosseous; mm Hg, millimeters of mercury; mmol/L, millimoles per liter; min, minutes. Data presented as means (standard deviation). There was a statistically significant interaction by time and group for lactate values.
*The significant interaction for lactate was $p < 0.01$.

controls. Whereas hydroxocobalamin-treated animals continued to exhibit significantly higher SVR values compared to control through the 60-minute observation period, SVR values in animals treated with whole blood decreased such that by 40 minutes, there was no significant difference in SVR between control and whole blood groups. Because hydroxocobalamin regulates nitric oxide synthase in an organ-dependent manner,[25] the increase in SVR compared to treatment with whole blood was expected.

The difference in SVR between the two hydroxocobalamin treatment groups at 10 minutes postadministration is more difficult to explain. We speculate that, as expected, all groups demonstrated the usual physiologic response to shock, that is, vasoconstriction. However, because of the slower Tmax under resuscitative conditions when using the IO route of administration, animals in the IO groups displayed physiologic vasoconstriction superimposed on the increase in SVR produced by hydroxocobalamin at 10 minutes after treatment. Because we found no difference in cardiac output between the hydroxocobalamin groups, we are uncertain of the clinical significance of the differences in SVR in our model.

Often, when casualties present in severe shock, it is difficult to obtain IV access and a more technically demanding, and time consuming surgical venous cutdown or central venous catheter is required. This technique is not available in the prehospital setting and delays in gaining vascular access may cause further

deterioration in the patients' condition. One viable alternative is an IO catheter. The use of IO catheters is gaining considerable support in the first responder community. Findings from investigations of IO catheter use for traumatic injuries or medical emergencies in prehospital settings suggest that placement of IO catheters is quick and learning correct placement is easy for novices. Moreover, once IO access is established and used for resuscitation, it becomes easier to establish more traditional means of IV access.

There is considerable ongoing research regarding the type and amount of fluid to use for hemorrhage resuscitation. For example, in 2003, Balogh et al.[26] showed that trauma patients administered lower volumes of crystalloid compared to those were administered higher volumes had an increased incidence of multiple organ failure, and death. Further confirmation of the deleterious effects of large crystalloid infusion for trauma resuscitation has been shown in recent military operations in Iraq and Afghanistan.[27,28] Findings from those conflicts have shown that large volume crystalloid resuscitation can dilute coagulation factors and increase the risk of bleeding and death from hemorrhage. Colloids, such as hydroxyethyl starch or hypertonic saline, may provide the modest increase in blood pressure necessary to maintain tissue oxygenation with smaller infused volumes until definitive surgical intervention is obtained, but colloids have disadvantages similar to crystalloids. For example, hydroxyethyl starch may interfere with coagulation by reducing the speed of clot formation and increasing clot lysis,[29] and hypertonic saline provided no clear benefit when compared to normal saline in a large National Institutes of Health sponsored clinical trial. In fact, the study was stopped early for potential safety concerns.[30] Moreover, results regarding damage to tissue when hypertonic saline is infused via an IO catheter have been mixed.[31,32] Hemoglobin-based oxygen carriers may become good alternatives to blood product transfusions, but results from animal studies have been limited by clinical side effects, lack of efficacy, and increased deaths.[33] Last, blood products are not available under austere conditions, expensive, and carry infection risks. A safe, small volume, durable drug is needed for early resuscitation in the field and the emergency department for hemorrhagic shock.

Hydroxocobalamin is FDA approved for cyanide toxicity and has been successfully used to treat cyanide-induced shock since 2006.[7] Hydroxocobalamin concomitantly binds cyanide and ameliorates shock. The mechanism by which hydroxocobalamin ameliorates shock is not fully known but purported to be via modulation of nitric oxide synthase.[25,34] In an endotoxemic model of shock, hydroxocobalamin produced an organ-dependent regulation of nitric oxide synthase that was beneficial, unlike other compounds that have been investigated that scavenge or reduce nitric oxide in shock models.[35] Additionally, our data suggest that hydroxocobalamin is less likely to worsen hemorrhagic coagulopathy as compared to crystalloid or hydroxyethyl starch infusions.[36] This may be attributed to the small volume (90-180 mL) of hydroxocobalamin required to effectively increase blood pressure compared to crystalloids or colloids. We have previously reported that hydroxocobalamin increases SVR, and correspondingly increases blood pressure, within 1-2 minutes of IV administration.[8,9] These data are congruent with pharmacokinetic data previously reported.[37] Moreover, the relatively long T ½ alpha of hydroxocobalamin may negate the need for multiple injections such as is necessary with routinely used vasopressors. Because it is effective in small volumes, hydroxocobalamin is easily transportable under austere conditions. Taken together, hydroxocobalamin shows promise as a prehospital treatment for hemorrhage that may support blood pressure and improve acidosis associated with shock. Further investigation is warranted.

Limitations

Our study had several limitations. Although animals have been crucial to the discovery of new drugs, animal models do not always translate into effective therapeutic interventions in clinical trials. Failure to generalize animal model findings to human trials may be due to the use of inappropriate models or underpowered sample size. We have attempted to mitigate these problems through appropriate sample size calculations. We have also used a swine model that has been shown to be an acceptable model for IO catheter placement and has been used in numerous published

investigations of hemorrhagic shock.[31,38] Swine cardiovascular physiologic and compensatory responses to hemorrhage are comparable to human responses, hence our swine model is an appropriate one.[39] Second, we used a controlled hemorrhage model rather than an uncontrolled hemorrhage model. Our results may not be reproducible in an uncontrolled model of hemorrhage. Moreover, we modified previously established controlled hemorrhage models such that we removed 1.42 mL/kg/min of blood over 7 minutes then 0.76 mL/kg/min of blood over the remaining 13 minutes. This modification provided a consistent 30 percent blood loss in all groups, that is, IO hydroxocobalamin versus IV hydroxocobalamin versus IO whole blood versus no treatment (mean blood loss 974, 955, 1,023, 1,018 mL). However, because our hemorrhage model has not been tested by other investigators, it remains a limitation. To provide support for results from this study, we have planned future studies in which we will use a model of uncontrolled hemorrhage, specifically a groin injury model. Likewise, larger volume percentages of blood loss may have demonstrated different outcomes. Finally, a longer observation period may have shown other differences or similarities between groups over time. We used the 1 hour time frame to simulate optimal prehospital treatment time.

Conclusions

In summary, we found that IO hydroxocobalamin modestly improved blood pressure and MAP as compared to control and was similar to IV hydroxocobalamin and IO whole blood in our prehospital class III hemorrhage model. There was a significant interaction in lactate values among the groups such that control lactate values were increasing as treated group lactate values were decreasing. Lactate in the treated groups remained below 2 mmol/L, whereas lactate in the control group was greater than 2 mmol/L and rising. Coagulation parameters remained normal throughout the study.

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Vikhyat S. Bebarta, MD, FACEP, FACMT, Professor, Medical Toxicology, Department of Emergency Medicine, Department of Pharmacology, University of Colorado, School of Medicine, Aurora, Colorado.

Normalynn Garrett, PhD, CREST Research Program, Department of Emergency Medicine, San Antonio Military Medical Center, Fort Sam Houston, Texas.

Susan Boudreau, RN, BSN, CREST Research Program, Department of Emergency Medicine, San Antonio Military Medical Center, Fort Sam Houston, Texas.

Maria Castaneda, MS, San Antonio Military Medical Center, Fort Sam Houston, Texas.

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ORIGINAL ARTICLE

The pharmacokinetics of intraosseous atropine in hypovolemic swine

Jonathan Yost, CRNA, MSN; Phillip Baldwin, CRNA, MSN; Sarah Bellenger, CRNA, MSN; Freida Bradshaw, CRNA, MSN; Edna Causapin, CRNA, MSN; Richelle Demotica, CRNA, MSN; Michael Livingston, CRNA, MSN; Cynthia Lee, CRNA, MSN; Brian Gegel, CRNA, DNAP; James Burgert, CRNA, DNAP; Adam Claessens, DO; Don Johnson, PhD; Michael Loughren, CRNA, PhD

Abstract

Objective: *Compare the pharmacokinetics of atropine administered via the intravenous (IV), intramuscular (IM), and intraosseous (IO) routes in a normovolemic and hypovolemic swine model.*

Design: *Prospective, between subjects, experimental study.*

Setting: *Vivarium.*

Subjects: *Yorkshire-cross swine (N = 36).*

Intervention: *Atropine was administered via IV, IM, or IO routes to normovolemic and hypovolemic swine. Blood samples were drawn at regular intervals after atropine administration and analyzed for plasma atropine concentration. Pharmacokinetic parameters were obtained from modeling the plasma concentrations.*

Main outcome measurements: *Pharmacokinetic parameters, maximum concentration (C_{max}) and time to maximum concentration (T_{max}).*

Results: *The IV and IO groups in both the normovolemic and hypovolemic models reached peak plasma concentration immediately and had a very rapid distribution phase with no apparent absorption phase for the IO groups. Peak plasma concentration and time to reach peak concentration were both significantly lower for the IM groups. There was a significant increase in absorption time with IM administration in the hypovolemic model compared to the normovolemic model.*

Conclusion: *The IO route is an effective method of administering atropine and is comparable to the IV route even under conditions of significant hemorrhage. Therapeutic levels of atropine may be delayed and possibly difficult to obtain via IM injection in the presence of hypovolemic shock.*

Key words: intraosseous, intramuscular, atropine, nerve agent, shock, pharmacokinetics

Introduction

The use of chemical warfare, specifically nerve agents, continues to be a major threat for soldiers and civilians. The lethality of nerve agents and the ongoing threat of their use underscore the need for prompt, effective administration of antidotes. Standard treatment of nerve agent exposure includes atropine and the acetylcholinesterase reactivator, pralidoxime chloride (2-PAM chloride).[1] Ideally for rapid and dependable results, these agents should be administered intravenously to the casualty. However, intravenous (IV) access is not practical for multiple reasons including limitations of the provider's performance in full protective gear, time constraints of mass casualty scenarios, and patient factors such as extremity injuries and hypovolemia. Consequently, the standard practice is to administer these medications via intramuscular (IM) injection.[1,2] Drugs in aqueous solution are absorbed rapidly after IM injection and have the advantage of being appropriate for self-administration.[3] Absorption from the muscle is improved by the use of autoinjectors, which delivers the medication over a larger surface area.[4] Even with improved absorption, IM peaks later than IV administration. Absorption of most drugs after IM injection is perfusion rate limited; increases in blood flow hasten

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Table 1. Summary of the treatment groups					
Normovolemic			Hypovolemic		
Treatment	Number	Data collection	Treatment	Number	Data collection
Atropine IV	6	Blood sampling 0-2 h	Atropine IV	5	Blood sampling 0-2 h
Atropine IM	6	Blood sampling 0-2 h	Atropine IM	6	Blood sampling 0-2 h
Atropine IO	6	Blood sampling 0-2 h	Atropine IO	6	Blood sampling 0-2 h

absorption and decreases in blood flow slow absorption.[5] Hence, in hypovolemic shock, where there is a diversion of blood from skeletal muscle, absorption may be slowed to such an extent that therapeutic levels are not obtained. Casualties exposed to chemical weapons may also suffer from conventional injuries leading to hemorrhage and subsequent shock.

The development of new devices for inserting intraosseous (IO) needles now gives healthcare personnel another option in the treatment of nerve agents. IO administration of atropine provides rapid onset and a pharmacokinetic profile similar to IV injection with the speed and ease of insertion that was previously only afforded by IM injection.[6] The potential for improved outcomes with IO delivery of atropine was demonstrated in a study of simulation-based treatment of chemical warfare casualties in which the use of an IO infusion device increased the survival rate from 3.3 to 73.4 percent.[7] There is a need to compare the pharmacokinetics of IV, IO, and IM atropine in cardiovascular collapse to determine the extent to which hypovolemic shock retards IM atropine absorption and if IO administration is an effective alternative.[6]

The aims of this study were to determine the pharmacokinetics of atropine when administered via the IO, IV, and IM routes in a hypovolemic pig model and to determine if there is a difference in the rate and extent of absorption of atropine when administered via the IO, IV, and IM routes compared to a normovolemic pig model.

Methods

This study was a prospective, between subjects, experimental design. The study protocol was approved by the local Institutional Animal Care and Use Committee. Animals involved in this study were maintained in accordance with the "Guide for the Care and Use of Laboratory Animals" published by the National Research Council/Institute of Laboratory Animal Research (ILAR).

Thirty-six Yorkshire-cross swine weighing between 58 and 71 kg were observed for 3 days to ensure a good state of health, fed a standard diet, and restricted to nothing by mouth after midnight the day of the experiment. On the day of the experiment, they were randomly assigned to one of six treatment groups (Table 1). General anesthesia was induced with an IM injection of tiletamine HCl and zolazepam HCl (4-8 mg/kg) (Telazol, Zoetis Incorporated, Kalamazoo, MI). The animals were then orally intubated and maintained with isoflurane (1 percent). Physiologic variables were monitored throughout the experiment, and the temperature of the pig was maintained at greater than 36.0°C with the use of a forced air warmer as needed. For all groups, the investigators cannulated a catheter into the carotid artery for blood pressure monitoring and sample collection. In the hypovolemic group, an additional catheter was placed in the internal jugular vein for exsanguination. Hemorrhage was accomplished similar to the hemorrhage model published by the US Army Institute for Surgical Research.[8] The internal jugular catheter was used to exsanguinate 35 percent of the estimated blood volume (24.5 mL/kg) over 30 minutes. If the mean arterial pressure dropped below 40 mm Hg, the investigators slowed the rate of hemorrhage. Once hemorrhage was complete, the pigs were allowed to stabilize for 15 minutes.

After obtaining a baseline blood sample, the investigators administered 2 mg of atropine (APP Pharmaceuticals, Schaumburg, IL) in a single bolus

either via an 18-gauge IV catheter placed in an ear vein or a 15-gauge IO needle (Vidacare Corporation, San Antonio, TX) inserted in the proximal area of the tibia, or by IM autoinjection (ATROPEN, Meridian Medical Technologies, Columbia, MD) into the gluteal muscle. Both IV and IO injections were followed by a 10-mL normal saline flush. IO placement was confirmed prior to drug administration with aspiration of bone marrow and easy irrigation of 10 mL of normal saline. A standard dose of 2 mg was used instead of a weight-based dose because the autoinjector dose was fixed.

In the IV and IO groups, blood samples (10 mL) were obtained at 0.5, 1, 2.5, 5, 7.5, 10, 20, 30, 45, 60, 75, 90, and 120 minutes after injection. In the IM group, samples were obtained at 1, 2.5, 5, 7.5, 10, 15, 20, 30, 45, 60, 75, 90, and 120 minutes after injection. The times were altered in the IM group to better characterize absorption. Blood samples were placed in lithium heparin tubes and immediately placed on ice. Samples were centrifuged for 10 minutes at 4,000 rpm. Plasma was transferred to 2 mL microcentrifuge tubes and frozen at –40°C. Samples were then shipped to the University of Washington's Pharmacokinetic Laboratory for analysis.

The analysis of atropine in pig plasma used protein precipitation and high-performance liquid chromatography (HPLC) with mass selective detection. Briefly, 100 µL plasma was combined with 200 µL acetronitrile and 10 ng scopolamine as an internal standard. The sample was vortexed and centrifuged for 10 minutes at 14,000 rpm. The supernatant was then transferred to a 96-well microtiter plate. A standard calibration curve was prepared similarly. The dynamic range of the calibration curve was 0-500 ng/mL. The sample (1 µL) was injected onto the HPLC column. The HPLC-mass spectrometry (MS) system consisted of an Agilent Technologies 1100 series HPLC including pump, thermostatted autosampler, and column compartment. The mass spectrometer was an Agilent Technologies series 1100 SL. The column was an Agilent Zorbax C-8, 100 mm × 2.1 mm × 3.5 µm and was maintained at 30°C. The mobile phase (82:18) was ammonium formate, 2 mM, pH 3.3 and acetronitrile combined isocratically. The sample tray was maintained at 4°C. The mass spectrometer was operated in the positive electrospray SIM mode monitoring ions 290 m/z for atropine, 304 m/z for scopolamine. All ions had a dwell time 289 ms. The fragmentor was set to 160 volts for atropine and scopolamine. The capillary was set to 1,500 V.

Pharmacokinetic parameters were determined by a standard two stage approach. Data were modeled using compartmental models in WinNonlin (Pharsight, St Louis, MO). Means and standard deviations were calculated for each group. A multivariate analysis of variance was used to determine differences in the groups relative to the pharmacokinetic parameters with a post hoc least significant difference test. An alpha of 0.05 was used for significance. All analyses were performed with SPSS version 18 (SPSS Inc, Chicago, IL).

Results

A total of 36 pigs were used in the study; one of which was excluded from data analysis. Specifically, one pig in the hypovolemic IV administration group died in the final minutes of the experiment. The data from that pig were analyzed and modelled but the results were vastly different (greater than 3 standard deviations) from the rest of the group and therefore, excluded from statistical analysis.

Raw plasma concentration versus time curves for all groups is presented in Figure 1. Both IV and IO peaked immediately and had a very rapid distribution phase. There was no apparent absorption phase for the IO administration. As expected, the peak

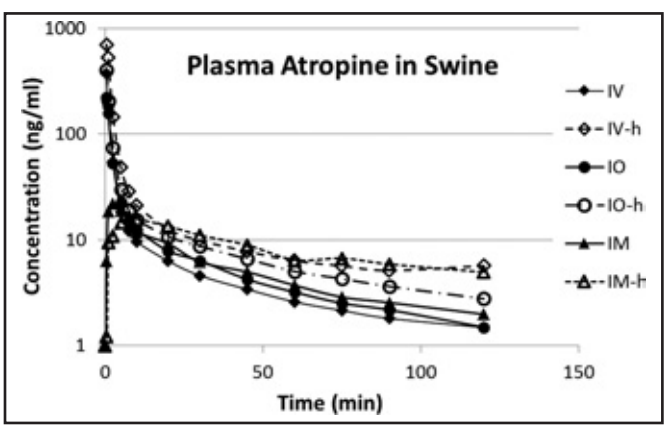

Figure 1. Pharmacokinetic profiles of atropine by route of administration.

Table 2. Derived pharmacokinetic parameters (mean ± SD) of atropine in normovolemic and hypovolemic swine							
Parameters	**Units**	**Normovolemic**			**Hypovolemic**		
		IV	**IO**	**IM**	**IV**	**IO**	**IM**
V1	L	6.5 ± 3.3	11.1 ± 7.2	65.2 ± 44.3	4.4 ± 1.6	7.7 ± 3.1	
AUC	min ng/mL	912 ± 334	1,023 ± 384	937 ± 183	1,599 ± 392	1,470 ± 523	1,247 ± 168
Cl	mL/min	2,523 ± 1,105	2,184 ± 756	2,200 ± 408	1,314 ± 329	1,462 ± 345	1,627 ± 217
t½-alpha	min	0.9 ± 0.2	1.3 ± 0.4	7.3 ± 6.1	1.1 ± 0.1	1.2 ± 0.2	
t½-beta	min	38.3 ± 4.6	38.0 ± 6.9	106.0 ± 86.2	46.2 ± 5.3	48.9 ± 14.8	
C_{max}	ng/mL	374 ± 166	300 ± 250	20 ± 8	513 ± 221	309 ± 168	14 ± 5
T_{max}	min	0	0	6.6 ± 3.1	0	0	19.5 ± 9.8*
*p = 0.011.							

concentration and time to peak concentration were significantly lower for IM administration. The hypovolemic IO and IV groups had very similar results to the normovolemic groups, peaking immediately and having a rapid distribution. Compared to the normovolemic groups, peak concentrations were higher in the IO and IV hypovolemic groups and concentrations remained higher for the duration of the experiment (Figure 1). Hypovolemia did not delay the circulation time or create an absorption phase with IO administration. However, hypovolemia significantly delayed absorption after IM administration (6.6 vs 19.5 minutes, p = 0.011, Table 2).

Both normovolemic and hypovolemic IV data were modeled using a two compartment model with IV bolus and first-order elimination. No appreciable absorption phase was noted in the IO data; therefore, it was modeled using the same model as the IV data. The normovolemic IM data were modeled using a two compartment model, first-order absorption and elimination. The hypovolemic IM data had such slow absorption that no distribution was observed in the concentration time curve and could not be modeled using the same model as the IM normovolemic data. Therefore, a one compartment model was used for modeling. The pharmacokinetic parameters derived from compartmental modeling are reported in Table 2. The peak concentration or concentration maximum (C_{max}) and time to peak concentration (T_{max}) for the IM hypovolemic group were significantly lower than the hypovolemic IV and IO administration groups, as well as, significantly lower than all of the normovolemic groups.

Discussion

The aims of this study were to determine the pharmacokinetics of atropine when administered via the IO, IV, and IM routes in a hypovolemic swine model and determine the impact of hypovolemia on the rate and extent of absorption when administered via these routes. This study demonstrated that hypovolemia has a dramatic effect on the absorption of atropine delivered by IM autoinjection. We expected absorption from IM injection to decrease with the peripheral vasoconstriction associated with hypovolemia, but the threefold increase in T_{max} was more than we anticipated. Conversely, the pharmacokinetics of IV and IO deliveries were less affected by hypovolemia. We hypothesized that peripheral vasoconstriction caused by hypovolemia might delay uptake of atropine with IO administration and create an absorption phase in its pharmacokinetic profile. In theory, the drug could distribute to the bone marrow of the tibia, which is primarily fat, and slowly absorb over time. We did not see any evidence of this in our study. The pharmacokinetic

changes we saw with hypovolemia after IO and IV administration were not unexpected. We expected that a 35 percent reduction in blood volume would cause a decrease in the initial volume of distribution and that the diminished liver blood flow associated with shock would decrease drug clearance. Similar changes were observed in an investigation of fentanyl pharmacokinetics during hemorrhagic shock.[9]

Our findings are consistent with those of Murray et al.,[6] whose study on the bioavailability of nerve agent antidotes in minipigs demonstrated rapid and complete bioavailability of atropine after IO administration. However, in the same study, the manual IM injection of atropine resulted in a more rapid absorption (3.5 vs 6.6 minutes) and higher peak concentrations (33.6 vs 20 ng/mL) than we observed with the use of an autoinjector.[6] Autoinjection has previously been found to have more rapid absorption and higher peak plasma concentrations than traditional IM injection.[4] Perhaps these differences are related to the muscle used for injection and/or the type of swine used for the experiment. The quadriceps muscle of a 20-kg Gottingen minipig may have greater blood flow than the gluteal muscle of a 70-kg Yorkshire cross. In humans, the IM administration of a 2-mg dose of atropine into the anterolateral aspect of the upper leg with the MARK 1 autoinjector resulted in a mean peak plasma concentration of 12.9 ng/mL and a median time to peak concentration of 6.5 minutes.[10]

Our results indicate that therapeutic levels of atropine may be delayed and possibly difficult to obtain via IM injection in the presence of hypovolemic shock. In the only firsthand accounts of battlefield nerve agent casualty management, Iranian Doctor Syed Abbas Foroutan described the use of very large doses of IV atropine in the treatment of nerve agent poisoning.[11] Dr. Foroutan stated "A critical point in treating chemical warfare victims in emergency situations is to administer the highest required dosage of atropine in the shortest period of time."[11] NATO doctrine advocates the use of three 2 mg IM autoinjections in the field. Once the casualty reaches a medical treatment facility, 2 mg IM doses should continue every 5-10 minutes until IV access can be obtained.[1,2] Iranian soldiers also received a 6-mg IM dose in the field. However, once they reached the medical treatment facility, Dr. Foroutan used from 20 to 200 mg of IV atropine for cases of severe exposure. His standard treatment included an initial 4 mg IV dose, followed in 1-2 minutes by an additional IV dose of 5 mg over 5 minutes if there were no signs of atropinization (an increase in pulse by 20-30 beats/min). However, at times, he would administer doses of 50 mg every 5 minutes.[11] Because IV and IO administration distribute very rapidly, frequent boluses are needed to maintain a therapeutic level as demonstrated in Dr. Foroutan's experience. Treatment protocols of an IO bolus followed by an infusion or some combination of IO and IM administration may be needed to maintain therapeutic levels. It should be noted that the Iranians did not use any oxime therapy in the field and limited quantities were used at the medical treatment facility.[11] This omission in management may have contributed to the seemingly large doses of atropine needed to achieve atropinization.

This study emphasizes the potential difficulty of treating nerve agent poisoning solely with IM atropine and the feasibility of treating nerve agent casualties with IO administration of atropine. This route of administration may be particularly advantageous when the casualty has had a severe exposure or is in hypovolemic shock.

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Jonathan Yost, CRNA, MSN, Department of Anesthesia and Operative Services, Madigan Army Medical Center, Joint Base Lewis-McChord, Washington.

Phillip Baldwin, CRNA, MSN, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Sarah Bellenger, CRNA, MSN, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Freida Bradshaw, CRNA, MSN, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Edna Causapin, CRNA, MSN, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Richelle Demotica, CRNA, MSN, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Michael Livingston, CRNA, MSN, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Cynthia Lee, CRNA, MSN, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Brian Gegel, CRNA, DNAP, Veteran Anesthesia Services, San Antonio, Texas.

James Burgert, CRNA, DNAP, Research Scientist, Geneva Foundation, Tacoma, Washington.

Adam Claessens, DO, Pharmacokinetics Lab, University of Washington, Seattle, Washington.

Don Johnson, PhD, Director of Research and Professor, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Michael Loughren, CRNA, PhD, Department of Anesthesia and Operative Services, Madigan Army Medical Center, Joint Base Lewis-McChord, Washington.

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ORIGINAL ARTICLE

Examining the importance of incorporating emergency preparedness and disaster training core competencies into allied health curricula

Tammy Curtis, PhD, RT(R)(CT)(CHES)

Abstract

Preparation for responding to emergency events that does not warrant outside help beyond the local community resources or responding to disaster events that is beyond the capabilities of the local community both require first responders and healthcare professionals to have interdisciplinary skills needed to function as a team for saving lives. To date, there is no core emergency preparedness and disaster planning competencies that have been standardized at all levels across the various allied health curricula disciplines.

Objective: *To identify if emergency preparedness and disaster training content are currently being taught in allied health program courses, to identify possible gaps within allied health curricula, and to explore the perceptions of allied health college educators for implementing emergency preparedness and disaster training core competencies into their existing curricula, if not already included.*

Design: *A quantitative Internet-based survey was conducted in 2013.*

Setting: *Convenient sample.*

Participants: *Fifty-one allied health college educators completed the survey.*

Findings: *Descriptive statistics indicated that the majority of allied health college instructors do not currently teach emergency preparedness and disaster training core competency content within their current allied health discipline; however, their perceived level of importance for inclusion of the competencies was high. The results of this study supported the need for developing and establishing a basic national set of standardized core emergency preparedness and disaster planning competencies at all levels across various allied health curricula disciplines to ensure victims receive the best patient care and have the best possible chance of survival.*

Key words: emergency preparedness, disaster training, core competencies, allied health curricula

Background

The terrorist attacks of the September 11, 2001, the aftermath of Hurricane Katrina and Rita in 2005, the devastation of Hurricane Sandy in 2012, the massacre at Sandy Hook Elementary school in 2012, the Boston Marathon bombing in 2013, the first Ebola outbreak in the United States in 2014, and the current terrorist threats on US soil have prompted healthcare organizations to expand their strategies for addressing emergency preparedness, bioterrorism, and disaster training for responding and aiding the community in the event of a crisis.[1-4] In 2010, approximately 303,750 deaths resulted from natural and human-caused disasters which were the highest number of deaths worldwide since 1976.[5] In 2011, a total of 325 catastrophic events occurred, with 150 human-caused disasters and 175 natural disasters claiming another 35,000 lives.[6] The impact of these events demonstrates the need for improved emergency preparedness and response management practices among health professionals. Hospitals in the United States have emergency and disaster plans in place as required by state licensure or The Joint Commission (TJC); however, successful implementation of these plans depends on the skills and training of allied health professionals. Equally important, collegiate programs in emergency management, emergency preparedness, emergency response, disaster training, and homeland security

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have expanded as a result of the tragic terrorists attacks on September 11, 2001, and the devastation aftermath of Hurricane Katrina and Rita in 2005.[7] Overall, in the United States, a total of 465 academic programs with titles such as emergency management, homeland security, international disaster management, humanitarian assistance, and related higher education programs have been identified.[7] In addition to the expansion of emergency academic programs, a number healthcare programs have incorporated emergency preparedness and response competencies into their courses. Furthermore, core competency models have been recommended and developed for health professionals. In 2000, the Center for Public Health Preparedness at the Columbia University partnered with the New York City Department of Health and Mental Hygiene and developed basic competencies in emergency and bioterrorism readiness for all public healthcare workers.[8,9]

Furthermore, TJC parallels the competencies that were developed by Columbia University Mailman School of Public Health and School of Nursing in their emergency management standards for healthcare organizations. TJC's emergency management standards mandate that all healthcare organizations which are accredited by TJC and offer emergency services must have an emergency management program.[10] According to TJC, this plan is based on the concept that hospital workers and leaders possess core skills and abilities for responding to emergencies.[11] Following Hurricane Katrina in 2005, surge hospitals were staffed by medical volunteers that included physicians, university faculty, psychiatrists, nurses, pharmacists, respiratory therapists, allied healthcare workers, healthcare students, information technology experts, social service workers, and food service personnel.[12] As a result of the various surge hospitals that responded to Hurricane Katrina, TJC is considering implementing minimum standards for ensuring safe quality patient care at the surge hospitals. TJC has not published the surge hospital standards as of to date.[12] Academic programs prepare healthcare workers to act as emergency management leaders and first responders when catastrophic events occur, therefore, having a foundation in emergency preparedness and disaster training will help equip these workers in fulfilling their roles.

Statement of problem

An initial review of literature revealed the development of proposed emergency preparedness and disaster training competencies among public health workers, nurses, emergency medical services personnel, and emergency physicians, but no core emergency preparedness and disaster planning competencies have been standardized at all levels across the various allied health curricula disciplines.[13-16] Key problems associated with the absence of core competencies among healthcare professionals include the following: limited preparedness; personnel shortages; unorganized relations with hospitals and community responders; lack of accountability; lack of interdisciplinary teamwork skills, inadequate training, equipment, and funding; lack of national standards for training and credentialing; and limited understanding of effectiveness.[17-19] This pilot study was designed to explore the existence or "nonexistence" of emergency preparedness core competencies among allied health curricula and the current perceptions of educators for incorporating and implementing emergency preparedness core competencies into their existing curricula.

Purpose of the study

The purposes of this pilot study was to collect background data on existing emergency preparedness and disaster training competencies within allied health curricula, to identify possible gaps in allied health curricula, and to explore the current perceptions of college educators for implementing emergency preparedness core competencies into their existing curricula, if not already included. Data obtained from this study demonstrated the importance of incorporating emergency preparedness core competencies that are consistent across all allied health discipline curricula; furthermore, data supported recommendations for developing and establishing a national standard for training and credentialing allied health professionals who act as first responders during a disaster. These skills could help to better prepare new allied health graduates for operating on interdisciplinary

levels when responding to emergencies. Allied health professionals are required to become certified in basic cardiopulmonary resuscitation (CPR) in an effort to save lives; likewise, increasing knowledge in emergency preparedness and disaster response could also play a critical role in preserving lives.

Research questions

1. What emergency preparedness and disaster training competencies exist among current allied health curricula?

2. What is the perceived importance among college instructors for incorporating emergency preparedness and disaster training core competencies into allied health curricula?

3. What are perceived barriers among college instructors for incorporating emergency preparedness and disaster training competencies into current allied health curricula?

4. What are perceived benefits among college instructors for incorporating emergency preparedness and disaster training competencies into current allied health curricula?

Review of literature

A review of literature revealed only a few studies that examined the existence of bioterrorism, emergency response, or disaster training competencies among physicians, nursing, or public health workers' academic programs; however, no specific study was found that investigated the existence or absence of emergency preparedness and disaster training core competencies among multiple allied health programs as a whole. For example, an article by Markenson et al.,[15] discussed a review of 25 medical schools' core curricula which found only one program that included bioterrorism training. A second example by Buyum et al.[20] reported that 38 nursing educators, who attended one of two school of nursing summits, indicated that 50 percent or more nursing school curriculum in Georgia were lacking in emergency preparedness and disaster training to include response to bioterrorism, mass casualty events, and infectious disease outbreaks. A third example presents a study conducted by the American Association of Community Colleges (AACC) in which 760 community college presidents and chancellors were asked to identify existing programs that supported homeland security efforts. Community colleges reported that 79 percent had programs that train first responders, 36 percent focused on cybersecurity, 32.4 percent trained for security and protective services, and 9.3 percent involved education for counterterrorism and national security.[21] A fourth descriptive study conducted in 2003 by the International Nursing Coalition for Mass Casualty Education (INCMCE) in collaboration with the National League for Nursing investigated the existing level of disaster preparedness content being taught in nursing programs at all levels from LPN to PhD. The sample consisted of a total of 2,013 deans and directors of nursing schools across the United States, of which 348 responded to an online survey. Results indicated that nursing schools taught approximately 4 hours of disaster preparedness content throughout their existing program curricula. In addition, findings demonstrated that 75 percent of respondents indicated that they felt inadequately prepared to teach content related to disaster preparedness. A major barrier noted was little room to add disaster preparedness content into an already packed curriculum. This study demonstrated a need for establishing baseline content covering disaster preparedness and response to all hazards among nursing curricula.[22]

An additional objective of this study was to explore perceptions of college instructors regarding the implementation of emergency preparedness and disaster training core competencies into their existing curricula. To date, few studies explored the relationship among physician perception, faculty perception, or student perception, and mass casualty events, bioterrorism, or Chemical, Biological, Radiological, Nuclear, and Explosives (CBRNE) topics. Furthermore, no specific study was identified that investigated allied health educator's perception of the importance for inclusion and implementation of emergency preparedness and disaster training core competencies into existing allied health

programs. For example, Chen et al.[23] found that of 614 family physicians, 82 percent had no bioterrorism training, yet 93 percent felt that bioterrorism training was needed. Another example is a survey of 166 nursing educators, conducted by Whitty and Burnett,[24] which found that nursing faculty had little mass casualty incident training, but perceived mass casualty incident content as important for teaching nursing students. A third example by Jasper et al.[25] found that 47 percent of 130 intern students, who attended Thomas Jefferson University Hospital, received CBRNE training prior to their residency portion of their program; however, 45-60 percent of interns indicated that they perceived themselves as not being proficient in disaster management.

Methodology

The objectives of this study were twofold: first, to identify the existence or absence of emergency preparedness and disaster training core competencies within allied health program curricula, and second, to assess the current perceptions of college instructors implementing these core competencies into their existing curricula. To accomplish these objectives, the following method of exploration was conducted. This study surveyed participants who currently teach as allied health educators at the three chosen community colleges. The principal investigator e-mailed the link of the survey to department heads of the allied health programs. Next, the department heads forwarded the electronic survey to their program directors and allied health educators at their institution using faculty e-mail addresses. The responses of the surveys were electronically and anonymously collected via SurveyMonkey.

Sample population

Three community colleges with a total of 115 full-time and part-time faculty members representing 46 programs and 479 courses collectively were conveniently selected. These community colleges were selected due to the number and variety of allied health programs that prepare graduates to work in healthcare settings who could take on the role of first responder in an emergency and disaster operation response plan. Of the 115 participants targeted, 51 participated in this study yielding a response rate of 44 percent.

Study instrument

A survey instrument was adopted with permission. The formatting of the instrument was modeled after the original survey used in two previous publications by the same author.[16,24] The survey was originally designed to assess nursing faculty training for responding to mass casualty events, and to assess nursing faculty perceptions of the importance of teaching mass casualty event content.[16] The same survey was used in a second publication designed to assess whether a relationship existed between knowledge of responding to mass casualty events among nursing faculty and their perceived importance for teaching mass casualty content in their nursing programs.[24] The reliability coefficient of Cronbach's alpha-test for a five-point anchored scale was 0.989 in the second study.[24] The electronic version of the survey was designed within SurveyMonkey, an electronic survey software platform. Furthermore, to help explore the research questions for this study, 12 emergency preparedness and disaster training core competencies for public healthcare workers were adopted as a framework and incorporated into the online survey of participants[8,26,27] (see Table 1). The estimated time commitment for participants to complete the survey was 10 minutes. The survey was geared toward identifying both existing and nonexistent content throughout the allied health curricula that are components of emergency preparedness and disaster training education. Furthermore, the survey assessed the faculty's perception of importance, benefits, barriers, and implementation of the core competencies into allied health curricula across all disciplines.

The content validity and usability of the instrument were assessed by administering the questionnaire to eight faculty members who currently teach in allied health programs. The survey was revised based on minor feedback.

Data collection procedures

Approval from the Internal Review Board (IRB) at Texas Woman's University was sought and granted to

Table 1. Emergency preparedness and disaster training core competencies for public healthcare workers	
Core competency	**Description**
1	Define and describe mass casualty events, biological, nuclear, chemical, radiological, explosive, terrorism, or natural disasters
2	Identify federal and state resources that contribute to emergency and disaster response, as well as, basic legal and regulatory issues to include healthcare (eg, Strategic National Stockpile, Disaster Medical Assistance Team, Metropolitan Medical Response System, FEMA)
3	Describe the public health role in emergency response in a range of emergencies that may arise (eg, disease surveillance, investigation, public information in disease outbreaks, collaboration with other community agencies, or weather emergencies)
4	Locate and use the section of the hospital emergency response plan that applies to your position
5	Describe your emergency response role and be able to demonstrate patient care skills during drills or actual emergencies
6	Describe your responsibilities for communicating with or referring requests for information from other employees, patients and families, media, general public or your own family, and demonstrate these responsibilities during drills or actual emergencies
7	Maintain risk communication skills during emergency or disaster response such as communicating with patients, families, other employees, the general public, and the media
8	Demonstrate the ability to seek assistance through the chain of command during emergency situations or drills
9	Define an incident command system and how it functions at the federal, state, local, agency, and institutional level
10	Examine importance of critical thinking, creative problem-solving skills, modifying routine procedures, and trauma protocols when responding to emergencies or disasters within the hospital setting
11	Identify personal limits to knowledge/skill/authority and be able to identify key system resources for referring matters when necessary
12	Recognize usual events that may indicate an emergency and describe appropriate actions
FEMA, Federal Emergency Management Agency.	

ensure protection of human subjects. The responses of the surveys were electronically and anonymously collected via SurveyMonkey. The survey remained open for the period of 4 weeks and a reminder e-mail was sent to encourage participation.

Data analysis

Data were analyzed using two popular software tools: Statistical Package for the Social Sciences (SPSS) and SurveyMonkey. Means, frequency, and standard deviations were computed.

Results

Demographics

Table 2 displays a total of 51, of 115, faculty members who participated in completing the survey. Overall, participants represent 20 different allied health programs. Faculty members (n = 51) were asked to report their current teaching position, their number of years teaching, and their highest level of education. The majority of participants hold the rank of an instructor (49 percent), have taught for 11–20

Table 2. Allied health programs as reported by participants		
Allied health discipline (n = 51)	**Responses**	**Percent**
Dietetic Technician	2	4
ECG/Telemetry Tech	1	2
Funeral Service Education	2	4
Health Information Technology	3	6
Medical Assistant	2	4
Medical Coding	2	4
Medical Laboratory Technician	2	4
Medical Office Specialist	2	4
Nuclear Medicine	1	2
Occupational Therapy Assistant	3	6
Ophthalmic Medical Assistant	1	2
Paramedic/EMS	5	10
Pharmacy Technician	4	8
Phlebotomy Program	2	4
Physical Therapist Assistance	4	8
Radiation Therapy	2	4
Radiologic Technology	4	8
Respiratory Therapy	4	8
Sonography	2	8
Surgical Technology	3	6
ECG, electrocardiogram; EMS, emergency medical services.		

years (37 percent), and obtained a master's degree (45 percent).

Existing core competency content

Participants were asked to identify whether they currently incorporate any of the 12 public health worker's emergency preparedness core competencies into their existing courses (see Table 1). Results indicated that there were a higher percentage of participants who did not currently teach emergency preparedness and disaster training core competency content for each allied health discipline than the number of participants who did (see Table 3). The competencies that were least incorporated into existing courses were "defining an incident command system and how it functions at the federal, state, local, agency and institutional level" (82 percent) and "identifying federal and state resources that contribute to emergency and disaster response, as well as, basic legal and regulatory issues to include health care" (78 percent). Even though there was a higher percentage of participants who did not teach each competency, the competency incorporated the most was "defining and describing mass casualty events, biological, nuclear, chemical, radiological, explosive, terrorism, or natural disasters" (45.1 percent).

Perceived level of importance for core competencies

Using a Likert scale, participants were asked to rate their perception of the level of importance for incorporating each of the 12 competencies into their allied health program's curriculum. Responses were categorized using the following five-point response scale: 5 = very important, 4 = quite important, 3 = fairly important, 2 = slightly important, and 1 = not important at all. The competency perceived as most important was "defining discipline's scope of practice, functional roles, and knowing when it is necessary to refer matters that exceed scope of practice when responding to an emergency or disaster" (50 percent). The competency perceived as least important was "describing the hospital chain of command structure and community chain of command structure, their roles, and responsibilities during emergency and disaster response" (20 percent) and "discussing direct patient care when responding to an emergency such as mass casualty events, terrorism, or natural disasters within a hospital setting" (18 percent) (see Table 4).

Perceived barriers

The percentages and frequencies of perceived barriers to incorporating the basic emergency preparedness

Table 3. Inventory of existing emergency core competency content			
Emergency preparedness core competency (n = 51)	**Responses**	**Yes (percent)**	**No (percent)**
Do you currently incorporate emergency or disaster preparedness content, such as defining and describing mass casualty events, biological, nuclear, chemical, radiological, explosive, terrorism, or natural disasters, in any of your course lessons, activities, or discussions?	51	45.1	54.9
Identify federal and state resources that contribute to emergency and disaster response, as well as, basic legal and regulatory issues to include healthcare (eg, Strategic National Stockpile, Disaster Medical Assistance Team, Metropolitan Medical Response System, FEMA).	50	22.0	78.0
Discuss the public health's role in an emergency or disaster response (eg, disease surveillance, investigation, public information in disease outbreaks, collaboration with other community agencies, or weather emergencies).	50	42.0	58.0
Describe hospital emergency response plans as mandated by The Joint Commission's emergency management standards (eg, the hospital emergency response plans at your students' local clinical sites such as emergency staffing, surge capacity for triage, patient isolation, acquisition of additional supplies, emergency evacuation, shelters-in-place, safety and security, staff responsibilities, or fatality management).	50	42.0	58.0
Discuss direct patient care when responding to an emergency such as mass casualty events, terrorism, or natural disasters within a hospital setting (eg, medical history related to event, psychological trauma, physical exam, personal protective equipment, decontamination, isolation, waste disposal, surge capacity).	50	38.0	62.0
Discuss how to maintain communication channels in the hospital setting during emergencies such as phones, cell phones, intercom systems, digital pagers, fax machines, two-way radios, and runners.	50	26.0	74.0
Explain the fundamentals for establishing risk communication skills during emergency or disaster response such as communicating with patients, families, other employees, the general public, and the media.	49	30.6	69.4
Describe the hospital chain of command structure and community chain of command structure, their roles, and responsibilities during emergency and disaster response.	48	27.1	72.9
Define an incident command system and how it functions at the federal, state, local, agency, and institutional level.	50	18.0	82.0
Examine importance of critical thinking, creative problem solving, and modifying routine protocols when responding to emergencies or disasters within the hospital setting.	50	38	62
Define your discipline's scope of practice, functional roles, and knowing when it is necessary to refer matters that exceed your scope of practice when responding to an emergency or disaster.	50	42.0	58.0
Explain how to recognize unusual events that may indicate an emergency and appropriate follow-up action (eg, recognize patterns, signs, and symptoms of biological, chemical, or radiological exposure).	50	42.0	58.0

Table 4. Perceived level of importance for inclusion of core competencies (*n* = 51)						
Emergency preparedness core competency	**Percentages (response count)**					
	n	**5**	**4**	**3**	**2**	**1**
Do you currently incorporate emergency or disaster preparedness content, such as defining and describing mass casualty events, biological, nuclear, chemical, radiological, explosive, terrorism, or natural disasters, in any of your course lessons, activities, or discussions?	39	38.5 (15)	20.5 (8)	17.9 (7)	17.9 (7)	5.1 (2)
Identify federal and state resources that contribute to emergency and disaster response, as well as, basic legal and regulatory issues to include healthcare (eg, Strategic National Stockpile, Disaster Medical Assistance Team, Metropolitan Medical Response System, FEMA).	36	22.2 (8)	8.3 (3)	36.1 (13)	19.4 (7)	13.9 (5)
Discuss the public health's role in an emergency or disaster response (eg, disease surveillance, investigation, public information in disease outbreaks, collaboration with other community agencies, or weather emergencies).	36	36.1 (13)	19.4 (7)	16.7 (6)	19.4 (7)	8.3 (3)
Describe hospital emergency response plans as mandated by The Joint Commission's emergency management standards. For example, the hospital emergency response plans at your students' local clinical sites such as emergency staffing, surge capacity for triage, patient isolation, acquisition of additional supplies, emergency evacuation, shelters-in-place, safety and security staff responsibilities, or fatality management.	39	38.5 (15)	12.8 (5)	15.4 (6)	17.9 (7)	15.4 (6)
Discuss direct patient care when responding to an emergency such as mass casualty events, terrorism, or natural disasters within a hospital setting (eg, medical history related to event, psychological trauma, physical exam, personal protective equipment, decontamination, isolation, waste disposal, surge capacity).	38	39.5 (15)	23.7 (9)	2.6 (1)	15.8 (6)	18.4 (7)
Discuss how to maintain communication channels in the hospital setting during emergencies such as phones, cell phones, intercom systems, digital pagers, fax machines, two-way radios, and runners.	36	38.9 (14)	19.4 (7)	2.8 (1)	22.2 (8)	16.7 (6)
Explain the fundamentals for establishing risk communication skills during emergency or disaster response such as communicating with patients, families, other employees, the general public, and the media.	37	32.4 (12)	18.9 (7)	18.9 (7)	16.2 (6)	13.5 (5)
Describe the hospital chain of command structure and community chain of command structure, their roles, and responsibilities during emergency and disaster response.	35	34.3 (12)	14.3 (5)	8.6 (3)	22.9 (8)	20.0 (7)
Define an incident command system and how it functions at the federal, state, local, agency, and institutional level.	35	22.9 (8)	22.9 (8)	17.1 (6)	20.0 (7)	17.1 (6)
Examine importance of critical thinking, creative problem solving skills, modifying routine procedures, and trauma protocols when responding to emergencies or disasters within the hospital setting.	39	43.6 (17)	17.9 (7)	15.4 (6)	7.7 (3)	15.4 (6)

Table 4. Perceived level of importance for inclusion of core competencies (*n* = 51) (continued)						
Emergency preparedness core competency	**Percentages (response count)**					
	n	**5**	**4**	**3**	**2**	**1**
Define your discipline's scope of practice, functional roles, and knowing when it is necessary to refer matters that exceed your scope of practice when responding to an emergency or disaster.	38	50.0 (19)	15.8 (6)	15.8 (6)	7.9 (3)	10.5 (4)
Explain how to recognize unusual events that may indicate an emergency and appropriate follow-up action (eg, recognize patterns, signs, and symptoms of CRBNE exposure).	37	37.8 (14)	18.9 (7)	21.6 (8)	5.4 (2)	16.2 (6)
Note: Response scale: 5 = very important, 4 = quite important, 3 = fairly important, 2 = slightly important, and 1 = not important at all.						

core competencies into existing allied health curriculum are displayed in Table 5. The top barriers identified by participants were adequate resources (48.6 percent), finding time to train faculty (40.5 percent), implementation of competencies (40.5 percent), evaluating competency skills (40.5), and time constraints during class (40.5). The barrier identified as the least challenging was faculty buy in (10.8 percent).

Perceived benefits

The percentages and frequencies of perceived benefits to incorporating the basic emergency preparedness core competencies into existing allied health curriculum are displayed in Table 6. The top benefits identified by participants were to better prepare graduates with emergency and disaster response skills (83.7 percent) and to reduce stress during emergency response (71.4 percent). The benefit perceived as the least attractive was grant opportunities (6.1 percent).

Table 5. Perceived barriers to incorporating emergency core competencies (*n* = 37)		
Perceived barriers	**Percent**	*n*
Adequate resources	48.6	18
Curriculum change process	32.4	12
Finding time to train faculty	40.5	15
Faculty buy in	10.8	4
Evaluating competency skills	40.5	15
Development of assignments	35.1	13
Implementation of competencies	40.5	15
Time constraints during class	40.5	4
Note: A total of 37 participants responded to this question, and 14 participants skipped this question.		

Level of concern

The percentages and frequencies of participant's level of concern that a catastrophic event such as a flood, terrorist threat, or mass casualty event could affect their local community are displayed in Table 7. Most participants were only moderately concerned (39.2 percent), followed by very concerned (25.5 percent). Only one participant was not concerned at all.

Perceived readiness of graduates

The percentages and frequencies of the faculty's opinion of how well they feel their new graduates will function in the healthcare setting when responding to a mass casualty event in their local community are displayed in Table 7. The majority of participants felt that their new graduates will function moderately well (60.8 percent) in the healthcare setting when responding to a mass casualty event. Participants indicated that none of their new graduates would function extremely well. On the opposite end, participants indicated that none of their new graduates would function poorly under the same circumstances. When comparing

Table 6. Perceived benefits to incorporating emergency core competencies (*n* = 49)

Perceived benefits	Percent	*n*
Interdisciplinary teamwork	65.3	32
Help establish national standard	46.9	23
Reduce stress during emergency response	71.4	35
Better prepare graduates with emergency and disaster response skills	83.7	41
Increase consistency for training and credentialing	26.5	13
Promote community partnerships	30.6	15
Engage stakeholders	10.2	5
Increase sensitivity to other disciplines	42.9	21
Share accountability with other disciplines	36.7	18
Collaboration with others	55.1	27
Networking	38.8	19
Grant opportunities	6.1	3

Note: A total of 49 participants responded to this question, and two skipped this question.

Table 7. Perceived level of concern for local catastrophic event occurring and perceived readiness level of new graduates to respond to a mass casualty event (*n* = 51)

Level of concern	Percent (*n*)	Readiness level	Percent (*n*)
Extremely concerned	19.6 (10)	Extremely well	0 (0)
Very concerned	25.5 (13)	Very well	27.5 (14)
Moderately concerned	39.2 (20)	Moderately well	60.8 (31)
Slightly concerned	13.7 (7)	Slightly well	11.8 (6)
Not at all concerned	2.0 (1)	Not at all well	0 (0)

the perceived readiness levels of new graduates to respond to a mass casualty event and the perceived level of concern for a local catastrophic event to occur, findings demonstrate an even distribution of correlations. For example the highest perceptions are found in the moderate level of concern that an event will occur and the moderate level of readiness for students to respond. The lowest perceptions are found in the category of "slightly concerned" an event will occur and the perception that students are "slightly well" prepared to respond (see Table 7).

Perceived level of comfort

The percentages and frequencies of how comfortable participants feel teaching basic emergency preparedness core competency content are displayed in Table 8. The majority of participants indicated that they are quite comfortable (31.4 percent) or fairly comfortable (25.5 percent) teaching the basic emergency core competency content. A small number of participants felt very comfortable (9.8 percent), while another small number of participants were not comfortable at all (11.8 percent).

Related participant inquiries

Related to teaching, participants (n = 51) were asked if they have earned continuing education credits regarding emergency preparedness or disaster training. Most participants indicated they have not engaged in continuing education credits for emergency or disaster training (68.6 percent). A smaller portion indicated they have completed the specified

Table 8. Perceived level of comfort teaching emergency preparedness core competencies (*n* = 51)

Comfort level	Percent	*n*
Very comfortable	9.8	5
Quite comfortable	31.4	16
Fairly comfortable	25.5	13
Slightly comfortable	21.6	11
Not at all comfortable	11.8	6

training (31.4 percent). Furthermore, participants (n = 51) were asked if they believe that all allied health programs should include emergency and disaster response core competencies into program curricula across all disciplines. The majority of participants indicated yes (75.5 percent). The minority of participants indicated no (24.5 percent). Finally, the participants were given the opportunity to provide additional comments concerning the incorporation of emergency and disaster preparedness core competencies into their existing curriculum as well as perceived need for faculty development or any other thoughts related to this topic. Only a few participants (n = 9) responded upon which a pattern emerged indicating that the majority of participants feel allied health students should be introduced to emergency preparedness and disaster training before they graduate. Concerns were the need for faculty development in this area and limited class time.

Discussion

Research questions

The first research question inventoried the existence or absence of emergency preparedness and disaster training competencies within current allied health curricula. Participants were asked to identify if they currently teach any of the 12 public health workers competencies in their existing courses. Data reported by the participants revealed an overall lower percentage of participants who currently teach emergency and disaster-related content in their courses than the majority who indicated they did not (see Table 3).

The second research question asked the participants to rate their perceived level of importance for incorporating each of the 12 public health workers emergency preparedness core competencies into their specific allied health program's curriculum. Using a five-point scale, findings demonstrated the competency perceived as the most important for incorporation was "defining discipline's scope of practice, functional roles, and knowing when it is necessary to refer matters that exceed scope of practice when responding to an emergency or disaster." A possible explanation could be that most health professionals are concerned with legal and regulatory issues within their scope of practice and keeping compliance with holding a professional license to practice. This same rationale could help explain why the second highest perceived competency of importance was "critical thinking, creative problem-solving skills, modifying routine procedures, and trauma protocols when responding to emergencies or disasters within the hospital setting." For each competency, a range of two to seven participants selected "Not important at all" while the range for "Very important" was 8-19. For the majority, there were a higher number of educators who indicated the competencies were perceived as "very important" and "quite important" for inclusion in their courses, than participants who indicated "not important" or "slightly important." The competency perceived as least important was "describing the hospital chain of command structure and community chain of command structure, their roles and responsibilities during emergency and disaster response." This competency would be most important for emergency management team leaders but would also apply to hospital drills among all employees. A related inquiry on the survey was geared toward answering the second research question regarding perceived level of importance for inclusion of emergency preparedness core competencies, which simply asked straight forwardly, "Do you believe that all allied health programs should include emergency and disaster response core competencies into program curricula across all disciplines?" Most participants (75.5 percent) indicated yes. This particular question targeted the researcher's proposal for supporting a national standardized set of emergency preparedness and disaster training core competencies across all allied health disciplines for more consistent education and preparation among healthcare professionals working as a team in emergency response and prevention efforts.

The third research question asked participants (college instructors) to identify perceived barriers for incorporating emergency preparedness and disaster training competencies into current allied health curricula. Findings communicated the top level of concerned areas were having adequate resources, finding

time to train faculty, strategies for implementing competencies, evaluating competency skills, and time constraints during class sessions. Additional concerns were development of assignments and the process of changing the curriculum. The participants were least concerned about faculty buy in to include the competencies. Another concern that emerged as a repeated pattern from an open ended question was that most participants agreed allied health students should be introduced to emergency preparedness and disaster training before they graduate. Drawing from a different question on the survey to help assess the amount of training faculty believed they might need to help teach the competencies, participants were requested to rate their current level of comfort to teaching the basic emergency preparedness core competencies. Most participants indicated that they are quite comfortable or fairly comfortable teaching the basic emergency core competency content. The least amount of participants felt very comfortable while the minority was not comfortable at all. Furthermore, educators were asked to if they have previously earned continuing education credits regarding emergency preparedness or disaster training. Most participants indicated they had not engaged in continuing education credits for emergency or disaster training. While some educators felt more comfortable teaching the emergency and disaster-related content than others, faculty development in this area could strengthen a more consistent presentation across all allied health disciplines and support interdisciplinary skills for their graduates.

The fourth research question requested participants to identify perceived benefits for incorporating emergency preparedness and disaster training competencies into current allied health curricula. Findings indicated the most beneficial reasons for including the competencies were to better prepare graduates with skills for responding to emergency and disaster-related events and to reduce stress levels during emergency response. The benefits ranked just under these top two in order of importance were interdisciplinary teamwork, collaboration with others, and establishing a national standard. The benefit perceived as the least attractive was grant opportunities.

Conclusion

The literature review and findings of this pilot study supported a need to link academic allied health program curricula content and public health practice concerning emergency preparedness and disaster core competency content. This pilot study also contributed to a gap in literature concerning the identification of the absence of core emergency preparedness and disaster training competencies among allied health discipline curricula. The importance of adopting and implementing emergency preparedness and disasters training core competencies that are consistent across all allied health discipline curricula was emphasized. Interdisciplinary connections between academia and healthcare organizations ensure proper safety measures toward prevention and preparation for responding to catastrophic events affecting communities. The benefits of establishing and developing a national standardized set of core emergency preparedness and disaster planning competencies across all allied health curricula include interdisciplinary teamwork, communication, collaboration, networking, technical skills, shared accountability, and stress reduction. Most importantly, this unified and collaborative approach will help save and protect lives. Last, this pilot study demonstrated that what healthcare workers needed to know before September 11, 2001, and before Hurricane Katrina in 2005 is different than what healthcare workers need to know today concerning emergency preparedness and disaster training competency skills. It is not a matter of if a mass casualty event, major natural disaster, infectious disease outbreak, or terrorist attack will occur, but when. In the duration of conducting this study between 2012 and 2014, more natural disasters, threats, and shootings took place that were not included for the purpose of ending this study.

Limitations and recommendations for future studies

This study had several limitations. A small convenience, homogeneity sample was used; therefore, the subjects are not considered to be representative of the entire population which results in a low external validity of the study. Random selection of allied health programs is recommended for representation

of the entire population. The investigator recommends the study be repeated using a larger sample size to include more allied health programs. The sample could also be expanded to include other geographic areas outside the state of Louisiana. For example, different geographic regions experience different natural hazards such as tornadoes in the Great Plains, hurricanes along the Gulf Coast or the Atlantic Coast, flooding and mudslides in the Southwest, tsunamis around the Pacific Basin, droughts in the mid-western states, and wildfires in western United States.[28] The sample could also be extended to include bachelor level programs that offer more advanced courses.

The data collection method limited the number of potential respondents to the online survey. Not all of the participant's e-mail addresses were posted on the community college Web sites; therefore, the investigator was dependent on the department heads of the colleges to forward the link to the online survey to their allied health faculty. There was no guarantee that all participants were included on the e-mail. Furthermore, spam filters could have prevented the survey from reaching the potential participants' e-mail accounts. The timing of the release of the survey was dependent on the participation of the college department heads and out of the control of the principal investigator. The investigator recommends that future researchers seek IRB approval for obtaining the participant's e-mail addresses in future studies so that there is more control over the release and collection of data. Collectively, these limitations are significant and could affect the generalizability of the conclusions in this study.

An additional recommendation for future studies include investigating the correlation between the participant's perceived level of concern that a catastrophic event could affect their local community and the amount of time the participants have lived in their local community. Findings from this study indicated that the majority (39 percent) of participants were only moderately concerned that a catastrophic event could occur, and 14 percent were slightly concerned. These results were interesting because of the participants live in the state of Louisiana where Hurricane Katrina occurred in 2005.

Tammy Curtis, PhD, RT(R)(CT)(CHES), Associate Professor, School of Allied Health, Northwestern State University, Shreveport, Louisiana.

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DM

ORIGINAL ARTICLE

A decision support framework for characterizing and managing dermal exposures to chemicals during Emergency Management and Operations

G. Scott Dotson, PhD, CIH; Naomi L. Hudson, DrPH; Andrew Maier, PhD, DABT, CIH

Abstract

Emergency Management and Operations (EMO) personnel are in need of resources and tools to assist in understanding the health risks associated with dermal exposures during chemical incidents. This article reviews available resources and presents a conceptual framework for a decision support system (DSS) that assists in characterizing and managing risk during chemical emergencies involving dermal exposures. The framework merges principles of three decision-making techniques: 1) scenario planning, 2) risk analysis, and 3) multicriteria decision analysis (MCDA). This DSS facilitates dynamic decision making during each of the distinct life cycle phases of an emergency incident (ie, preparedness, response, or recovery) and identifies EMO needs. A checklist tool provides key questions intended to guide users through the complexities of conducting a dermal risk assessment. The questions define the scope of the framework for resource identification and application to support decision-making needs. The framework consists of three primary modules: 1) resource compilation, 2) prioritization, and 3) decision. The modules systematically identify, organize, and rank relevant information resources relating to the hazards of dermal exposures to chemicals and risk management strategies. Each module is subdivided into critical elements designed to further delineate the resources based on relevant incident phase and type of information. The DSS framework provides a much needed structure based on contemporary decision analysis principles for 1) documenting key questions for EMO problem formulation and 2) a method for systematically organizing, screening, and prioritizing information resources on dermal hazards, exposures, risk characterization, and management.

Key words: chemicals, decision analysis, dermal, Emergency Management and Operations, risk analysis, hazards

Introduction

Recent world events demonstrate the need for high-quality resources specifically designed to assist Emergency Management and Operations (EMO) personnel in making informed decisions during both natural (eg, hurricanes and tsunamis) and human-caused disasters (eg, terrorist events and transportation accidents). Numerous efforts are underway to develop resources that address both the broader topic of EMO, in addition to specific scenarios or hazards. For instance, the Federal Emergency Management Agency (FEMA) created the National Incident Management System (NIMS) to provide a comprehensive national approach to incident management.[1] Additionally, a collaborative effort between the National Library of Medicine (NLM), the Office of the Assistant Secretary for Preparedness and Response (ASPR) of the US Department of Health and Human Services (US HHS) and US Department of Homeland Security (US DHS) is actively developing multiple web-based decision-making resources, such as Wireless Information System for Emergency Responders (WISER) and Chemical Hazards Emergency Medical Management (CHEMM).[2,3] These integrative web-based resources provide critical data, facts, and guidance during mass casualty events involving hazardous materials during each of the life cycle phases of an emergency incident.[2,3]

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Despite the availability of numerous high-quality resources designed to guide EMO, data gaps continue to exist for specific hazards or scenarios. Dermal contact is an important exposure pathway and may present significant health risks during chemical incidents.[4,5] Chemicals, such as nerve agents, cyanides, vesicants, acids, and bases, cause numerous adverse health effects ranging from mild skin irritation to paralysis and death following acute dermal contact,[5] but there are few information resources that provide guidance related to dermal exposures. For example, the US DHS had identified several data gaps in patient decontamination planning guidance and research associated with dermal exposures.[5]

Limited data are available on the characterization or management of dermal hazards. Table 1 identifies chemicals commonly involved in both fixed facility and transportation incidents,[6] along with their associated skin hazard classifications based on the Globally Harmonized System of Classification and Labeling of Chemicals (GHS).[7] While the data captured by the National Toxic Substance Incident Program (NTSIP) describe fixed facility and transportation events and collect information on the incident, health effects, and contributing factors to the incident, the surveillance system does not collect route-specific data.[6] As such, it is difficult to determine how many of the injured or ill persons experienced health effects due to dermal exposure, as health effects may also include neurological, gastrointestinal, and other systemic effects.[4,5] A review of published studies revealed several investigations describing adverse health outcomes associated with dermal exposures to various chemicals. These studies provide supplemental evidence of the consequences of dermal exposures during chemical emergencies that included skin damage (ie, irritation and corrosion) and dermal absorption of a recognized carcinogenic agent (ie, polycyclic aromatic hydrocarbons) released as pyrolysis products.[6,8,9] Additionally, the US Occupational Safety and Health Administration (US OSHA) identifies dermal exposures as a significant workplace health hazard and reports that both the number of cases and the rate of skin disease in the United States exceeded recordable respiratory illnesses.[10]

Table 1. Chemicals commonly involved in fixed facility and transportation incidents coupled with their Globally Harmonized System of Classification and Labeling of Chemicals (GHS) dermal hazard designations*

Chemicals	GHS designation†	GHS hazard statement
Ammonia	Acute Dermal Toxicity Category 3 Skin Corrosion Category 1B	Toxic in contact with skin Causes severe skin burns
Sulfuric acid	Skin Corrosion Category 1A	Causes severe skin burns
Hydrochloric acid	Skin Corrosion Category 1B	Causes severe skin burns
Chlorine	Skin Irritation Category 2	Causes skin irritation
Sodium hydroxide	Skin Corrosion Category 1A	Causes severe skin burns
Potassium hydroxide	Skin Corrosion Category 1A	Causes severe skin burns
Benzene	Skin Irritation Category 2	Causes skin irritation
Sulfur dioxide	Acute Dermal Toxicity Category 3 Skin Corrosion Category 1B	Toxic in contact with skin Causes severe skin burns

*List based on data retrieved from the National Toxic Substance Incident Program (NTSIP) Annual Report. 2010.[6] These chemicals are located in both the top 20 most common chemicals in fixed facility events and in the top 10 of the most common chemicals in transportation events.
†European Union.[7]

Despite the absence of EMO resources pertaining to dermal exposures to chemicals, informed decisions need to be made to successfully manage and respond to chemical emergencies. A thorough examination of all aspects of dermal risk is very complex and rarely conducted during the response phase of an incident. This typically results in the use of general guidelines instead of substance-specific guidance (eg, chemical protective clothing [CPC] requirements for initial response and decontamination procedures)[11] or quick guides for a selected range of release scenarios.[12-14] These general procedures can be protective, but failure to provide dermal-specific technical guidance can place responders at increased risk. For example, wearing an inappropriate CPC ensemble may provide a false sense of security by providing an inadequate barrier to chemical penetration or may increase heat loads that enhance dermal absorption and result in elevated physiological burden (eg, heat stress).[15,16] Furthermore, inadequate decontamination procedures may lead to increased exposure to a chemical. The use of an aqueous solution consisting of soap and water may be ideal for decontamination of water-soluble chemicals; however, for more lipophilic (non-water) soluble chemicals (eg, organic solvents and some pesticides), potential for dermal exposure may increase by spreading the chemical over a larger surface area to potentially "wash in" the chemical.[15,16] Efforts underway in the federal government provides supplemental evidence of the complexities associated with dermal exposures to chemicals with an emphasis on the decontamination following mass casualty events.[6]

Purpose

A conceptual framework is presented for a decision support system (DSS) to assist EMO personnel during chemical incidents involving dermal exposures. The framework incorporates scenario planning, risk analysis, and decision analysis as the basis of the DSS. Several key issues are addressed, including 1) the complexities of dermal risk assessment, 2) the critical criteria and primary assumptions that govern the decision process, and 3) the identification, integration, and prioritization of relevant information resources.

Framing The Problem: Decision Making In Emergency Management And Operations

Effective decision making and problem solving are critically important for the management of chemical emergencies. The decision process should consider potential risks and magnitude of uncertainty in an interactive process of developing an incident management strategy. The successful development of these strategies relies on the availability of appropriate information resources. Tools and resources exist to guide decision making that governs the overall incident; however, information is often limited for aspects of the incident requiring special expertise. Thus, a specific issue, such as dermal exposures, may be overlooked because of the absence of readily available information that addresses all dimensions of dermal risk. To illustrate this, approximately 300 resources (see Appendix table) were identified that contained information that could be useful for addressing dermal exposure during chemical incidents. However, the current suite of available resources on dermal risk issues lacks a system, such as the CHEMM and WISER resources, to link disparate resources in a way that facilitates decision making.[2,3]

An effective dermal risk management strategy requires a decision process that addresses key risk assessment and management questions. As the process for answering these questions relies on complex data from numerous sources, a DSS can be a valuable aid to the incident command structure. Numerous examples of decision approaches used in EMO context to identify, organize, and integrate complex data in all emergency phases exist and support the development of a similar process for dermal risks.[17-20]

Risk analysis and decision making

Problems associated with dermal exposures during a chemical emergency can be framed using risk analysis, which is a systematic approach used to assess and manage the risk associated with a specific hazard, event, or situation and guide decision making related to potential risk management outcomes.[21] It consists of two distinct components: 1) risk assessment and 2) risk management. Risk assessment is concerned with the characterization of risks associated with a

specified hazard.[21] Risk management focuses on the application of these findings to make decisions and policies to control the risk.[21] Both of these steps are also refined through iterative risk communication processes that include stakeholder involvement. For dermal exposures, risk analysis would aid in identifying the hazards and risks, and assist EMO personnel in formulating control strategies ranging from selection of CPC, medical management, and decontamination.

An initial step in risk analysis is problem formulation. In EMO, this is often accomplished via scenario planning, which is a strategic approach used to characterize potential threats or events to determine the level of readiness, vulnerabilities, and needs.[22-24] In the context of this article, dynamic scenario planning allows for the identification and integration of the key questions related to dermal exposures. This form of scenario planning allows for the construction of scenarios designed for preparedness planning that incorporate factors and variables that are readily adjustable to actual response conditions. The inclusion of such factors and variables results in flexible models that ensure that preparedness efforts parallel response activities more precisely. For issues like CPC selection during an actual response, this helps to mitigate the natural tendency to recommend defaults in the absence of information that are "over-protective" and may create a more hazardous situation for engaged EMO personnel. The key questions identified as a component of the dynamic scenario planning serve as the first stage of a dermal DSS. Table 2 provides a list of recommended key questions that can serve as a dermal checklist tool to guide resource review and data evaluation. The checklist is the first component of a dermal DSS by systematically organizing information using the primary principles of risk analysis with specific data divided between risk assessment (ie, hazard characterization, exposure assessment, and risk characterization) and risk management (ie, exposure control approaches, decontamination, and medical surveillance).

Framing the problem using risk analysis and dynamic scenario planning enhances the decision-making process and serves as the basis of a DSS. A variety of decision-making tools are available that can be applied to EMO problems.[20,24,36,37] One such tool is multicriteria decision analysis (MCDA). This is a group of methods applied to understand complicated decisions and assist in choosing among alternatives via systematic analyses of risk levels, uncertainty, and valuation based on multiple criteria.[37-40] The MCDA approach has a successful history of application in the field with ongoing refinement based on incident review processes.[41]

Case Study: Application of the Dermal Checklist Tool

Each chemical incident presents numerous challenges based on scenario-specific factors, such as type of emergency, location, and chemical of concern. These distinctions affect the actions needed to both manage the incident and protect EMO personnel. To illustrate this point, case studies were developed that demonstrate the challenges and difficulties associated with conducting a dermal risk assessment during two distinct chemical emergencies. The first scenario involves a fixed facility release of sulfuric acid (CAS# 7664-93-9). The second scenario describes a transportation-related incident involving the release of benzene (CAS# 71-43-2). Table 2 applies the previously described checklist of recommended key questions to assist in characterizing and managing the scenario-specific hazards, exposures, and risk to the case studies.

The information in Table 2 demonstrates that the complexity of conducting rigorous dermal risk assessments for chemical emergencies varies based on the scenario and hazard. The use of standard operating procedures and generic risk management practices, which are "one size fits all" or designed to accommodate a wide range of issues, represents one approach applied to assist in the management of chemical incidents. These approaches are useful, but in many cases are not the most appropriate: that is they may result in risk management actions that generate unintended risks. For example, the hazard characterization presented in Table 2 demonstrates that the hazards of dermal contact with sulfuric acid and benzene are very different. Sulfuric acid is capable of causing immediate and severe corrosion with dermal absorption and targeted systematic effects of less concern.[30] In

Table 2. Case studies illustrating the complexities associated with assessing dermal risks during emergency response activities involving chemicals

Risk analysis activity		Case study 1	Case study 2
		Scenario description: Spill of sulfuric acid (CAS# 7664-93-9) from a drum puncture in a manufacturing facility warehouse	Scenario description: Uncontrolled release of benzene (CAS# 71-43-2) from a tanker truck arising from a traffic accident
Risk assessment	**Key questions**		
1. Hazard characterization	1a. Are chemicals present that represent a skin hazard (direct or systemic effects)?	1a. Yes: Direct effects*,†,‡,§,¶,**,††	1a. Yes: Direct and systemic effects*,†,‡,§,¶,**,‡‡,§§,¶¶
	1b. Are the effects acute (ie, immediate), acute delayed, or chronic?	1b. Immediate: Skin irritation and corrosion*,†,‡,§,¶,**,††	1b. Immediate: Skin irritation; Delayed: Target organ toxicity (neurotoxicity, cancer, and noncancer effects on the blood)*,†,‡,§,¶,**,§§,¶¶
	1c. Are other stressors present that may affect the hazard?	1c. Chemical reacts violently with water generating fumes and the potential for dermal absorption†,¶,***	1c. Hot environment may increase vapor exposure and the potential for dermal absorption†,¶,***
	1d. Can chemical be dermally absorbed following direct contact?	1d. No: Not expected to be readily absorbed*,†	1d. Yes: Dermal absorption may occur in sufficient amounts to cause adverse health outcome*,†,‡,§,¶,***,§§
	1e. Can dermal absorption occur following indirect contact (ie, vapors or aerosols)?	1e. Not expected; vapors may be irritating or corrosive*,†,‡,§,¶,**,††	1e. Yes.*,†,‡,§,¶,***,‡‡,§§ *Note*: Vapor uptake via the skin is less than direct contact with liquid form§§
	1f. Is the chemical a systemic toxicant?	1f. No*,†,‡,§,¶,***	1f. Yes*,†,‡,§,¶,‡‡,§§
	1g. Are dermal absorption rates known?	1g. No	1g. Yes: Data indicate that dermal uptake may be significant: Quantified estimates available‡‡,§§
2. Exposure assessment	2a. Is dermal contact possible in immediate release zone?	2a. Yes: Dermal exposure may occur via contact with liquid following splashes or other pathways†,***	2a. Yes: Dermal exposure may occur via contact with liquid following spills/splashes or other pathways†,***
	2b. Is dermal contact likely outside the immediate release zone?	2b. Yes: Reaction with water will generate heat and increase the concentration of fumes in the air,†,†† therefore, it is likely that dermal contact may occur outside the immediate release zone	2b. Yes: Dermal exposure to benzene vapors may occur outside the immediate release zone as benzene may be encountered in liquid or vapor phases†,¶,***,§§

Table 2. Case studies illustrating the complexities associated with assessing dermal risks during emergency response activities involving chemicals (continued)

Risk analysis activity		Case study 1	Case study 2
		Scenario description: Spill of sulfuric acid (CAS# 7664-93-9) from a drum puncture in a manufacturing facility warehouse	Scenario description: Uncontrolled release of benzene (CAS# 71-43-2) from a tanker truck arising from a traffic accident
Risk assessment	**Key questions**		
	2c. Can dermal exposures occur during the transport of potentially contaminated materials or patients?	2c. Yes: Be careful to avoid contact with contaminated objects and clothing†	2c. Yes: Be careful to avoid contact with contaminated objects and clothing†
	2d. Are sampling methods/tools available to assess dermal exposures?	2d. No: No dermal methods identified; Multiple air sampling methods identified*	2d. No: No dermal methods identified; Analytical sampling methods for air, water, soil, and sediment identified*,***
	2e. Are dermal exposure estimation models available?	2e. No	2e. Yes: Numerous dermal exposure models available to estimate dermal absorption§§
	2f. Do surface sampling techniques exist for the chemical of concern? If so, are they validated?	2f. Skin SWYPEs may be used to determine if there is any skin exposure†††	2f. No: None identified
	2g. Is biological monitoring an option?	2g. No	2g. Yes: Biological monitoring methods exist that rely on the measure metabolites in breath and biological samples (ie, blood, urine, and other tissues)§§
3. Risk characterization	3a. Are quantitative exposure limits for dermal exposures available?	3a. No: None identified	3a. Yes: A LOAEL was identified for acute exposure—mucous membrane and skin irritation§§
	3b.Is there a means to interpret or compare surface sampling results such as surface exposure limits?	3b. No: None identified	3b. No: None identified
	3c. Are other dermal-related exposure recommendations available?	3c. No: None identified	3c. No: None identified
	3d. Can exposures be compared to existing limits to support a risk characterization?	3d. No: None identified	3d. Yes: Concentrations of benzene in blood correspond to higher levels of exposure§§

Table 2. Case studies illustrating the complexities associated with assessing dermal risks during emergency response activities involving chemicals (continued)

Risk analysis activity		Case study 1	Case study 2
		Scenario description: Spill of sulfuric acid (CAS# 7664-93-9) from a drum puncture in a manufacturing facility warehouse	Scenario description: Uncontrolled release of benzene (CAS# 71-43-2) from a tanker truck arising from a traffic accident
Risk management	**Key questions**		
4. Exposure mitigation	4a. What control techniques are needed to reduce the potential for direct dermal contact in the release zone?	4a. Water spray may be used to reduce fumes (*do not* allow the water to come in contact with the liquid sulfuric acid) or a *small* spill needs to be covered with dry sand or other noncombustible material[†,¶,***] Neutralization procedures are also recommended[†,¶,***]	4a. A vapor suppressing foam or water spray may be used to reduce vapors and liquids may be absorbed or covered with dry earth, sand, or other noncombustible material and transfer to containers[†,¶,***]
	4b. Are controls needed to reduce indirect dermal contact in the release zone?	4b. Yes: Controls measures for fumes are needed to reduce dermal contact in the release zone[†,¶,***]	4b. Yes: Controls measures for vapors are needed to reduce dermal contact in the release zone[†,¶,***]
5. Protective equipment	5a. What chemical protection ensemble is needed?	5a. Follow ERG guidelines (137)[‡‡‡] or similar CPC guidance based on response zone, concentration and presence of fuming[§§§]	5a. Follow CPC guidance based on response zone[§§§,¶¶]
	5b. Are specific CPC selection guidelines available?	5b. Yes: Guidelines are available[§§§]	5b. Yes: Guidelines are available[§§§]
	5c. What barrier material is needed to prevent dermal contact during activities in each response zone?	5c. Protective clothing barriers are recommended to prevent dermal contact for sulfuric acid >70 percent, including Butyl rubber, Polyethylene (PE), Viton®, Viton®/Butyl Rubber®, Barrier (PE/PA/PE), Silver Shield/4H® (PE/EVAL/PE), Trellchem® HPS, Trellchem® VPS, Tychem® SL (Saranex®), Tychem® CPF3, Tychem® F, Tychem® BR/LV, Tychem® Responder®, Tychem® TK for 8 h and PE for >4 h[§§§]	5c. Protective clothing barriers are recommended to prevent dermal contact, including Polyvinylalcohol, Viton®, Barrier (PE/PA/PE), Silver Shield/4H® (PE/EVAL/PE), Tychem® CPF3, Tychem® F, Tychem® BR/LV, Tychem® Responder®, Tychem® TK for 8 h and Viton®/Butyl Rubber for >4 h[§§§]
	5d. What metrics (eg, breakthrough time, compatibility data) are available to aid in selecting CPC?	5d. Breakthrough times are available to aid in CPC[‡‡‡,§§§]	5e. Breakthrough times are available to aid in CPC[§§§]

Table 2. Case studies illustrating the complexities associated with assessing dermal risks during emergency response activities involving chemicals (continued)

Risk analysis activity		Case study 1	Case study 2
		Scenario description: Spill of sulfuric acid (CAS# 7664-93-9) from a drum puncture in a manufacturing facility warehouse	Scenario description: Uncontrolled release of benzene (CAS# 71-43-2) from a tanker truck arising from a traffic accident
Risk management	**Key questions**		
6. Decontamination	6a. What specific decontamination procedures are needed?	6a. Decontamination processes include removal from the area, removal of contaminated clothing, and washing any exposed skin thoroughly with soap and water[†] or flush with running water for at least 20 min[‡‡‡]	6a. Decontamination processes include removal from the area, removal of contaminated clothing unless it is adhering to the skin, and washing any exposed skin thoroughly with soap and water[†,¶¶] or flush with running water for at least 20 min[‡‡‡]
	6b. Are specific assays available to demonstrate the efficacy of decontamination?	6b. Skin SWYPEs may be used to determine if there is any of the chemical on the skin[†††]	6b. No: None identified
7. Medical surveillance	7. Are there specific medical surveillance requirements for exposed persons?	7. Medial surveillance for potentially exposed personnel is not recommended due to the immediate nature of the effects of dermal exposure to sulfuric acid	7. Persons with significant exposure to benzene should be followed for up to 72 h to monitor for the delayed effects, such as fluid in the lungs[¶¶]

[*]Ref. 25.
[†]Ref. 26.
[‡]Ref. 27.
[§]Ref. 7.
[¶]Ref. 28.
[**]Ref. 29.
[††]Ref. 30.
[‡‡]Ref. 31.
[§§]Ref. 32.
[¶¶]Ref. 13.
[***]Ref. 33.
[†††]Ref. 34.
[‡‡‡]Ref. 14.
[§§§]Ref. 35.

comparison, benzene has limited potential as a skin irritant, but is capable of being dermally absorbed and contributing to the onset of acute and delayed systematic effects including blood cancers.[32] These chemicals represent unique health risks following dermal exposure scenarios resulting in the need for specialized risk management practices. Thus, generic guidance would indicate the need for CPC but would not guide the user to the specific recommendations for each of these two different exposure scenarios. Subsequent considerations address the characterization and validation of dermal contact through surface sampling, decontamination needs, and medical surveillance. EMO personnel are in need of a decision support tool to assist in making informed decisions regarding both broad and specific issues during chemical emergencies involving dermal exposures. The dermal checklist tool serves to identify in a systematic manner the questions that need to be addressed for the scenario under review.

Conceptual Framework for the Dermal Dss

The conceptual framework intended to facilitate the development of a dermal DSS to provide resources to answer the resulting set of key dermal risk questions is outlined in this section. The framework consists of three primary modules: 1) Resource Compilation, 2) Prioritization, and 3) Decision. Figure 1 presents the overall flow of the framework.

Resource compilation

The foundation of any decision process is a robust database comprised of high-quality data collected from multiple sources. The primary objective of this module is to identify, collect, and organize relevant resources to facilitate the compilation of a searchable dataset. This task is challenging due to the large volume of resources that are available and relevant to EMO activities involving chemical incidents coupled with the lack of a coherent link among the resources. For this reason, a classification system to organize resources is critical. Three elements of the classification system should include 1) incident phase, 2) information categories, and 3) resource categories. Figure 2 illustrates the relationship of the core elements of the resource compilation module.

The incident phase element serves as a descriptor that captures objectives and critical questions relevant to specific scenarios. This takes into account that the resource needs will vary during each of the distinct life cycle phases of an emergency incident (ie, preparedness, response, or recovery) for a given scenario. The resources compiled need to exhibit duality that allows for their application in both broad terms for use in multiple situations, but be sufficiently narrow to provide guidance under specified conditions. For example, a train derailment and terrorist event involving an office building would require different information resources to guide EMO. The second element of the resource compilation module pertains to information categories. The categories illustrated in Figure 2 reflect that the data needs are not consistent among scenarios. The case studies in Table 2 vary in the nature of the presented hazard highlighting the need to identify specialized resources. Another benefit of categorizing data in the manner presented in Figure 2 is that it allows specialists to rapidly identify resources specific to their roles, such as exposure modeling or medical management. The final element of the resource compilation module is resource categories. This is particularly important based on the incident phase, which are often subject to time constraints. For example, less accessible resources that have a high depth of information are more appropriate for the preparedness phase than for the response phase. In essence, the resource compilation module provides a specialized resource library pertaining to dermal exposures to chemicals that allows for effective sorting consistent with EMO needs.

Prioritization

A further enhancement to the dermal DSS enables prioritization of resources on top of, or in addition to, a single compilation of resources. This enhancement is conceptually consistent with the MCDA approach. In the prioritization module, an approach is applied that captures for each information resource the value for addressing user-defined scenarios. The process incorporates a weighting of the impacts of an information resource for the assessment being conducted. One such approach is value of information (VOI) scoring,

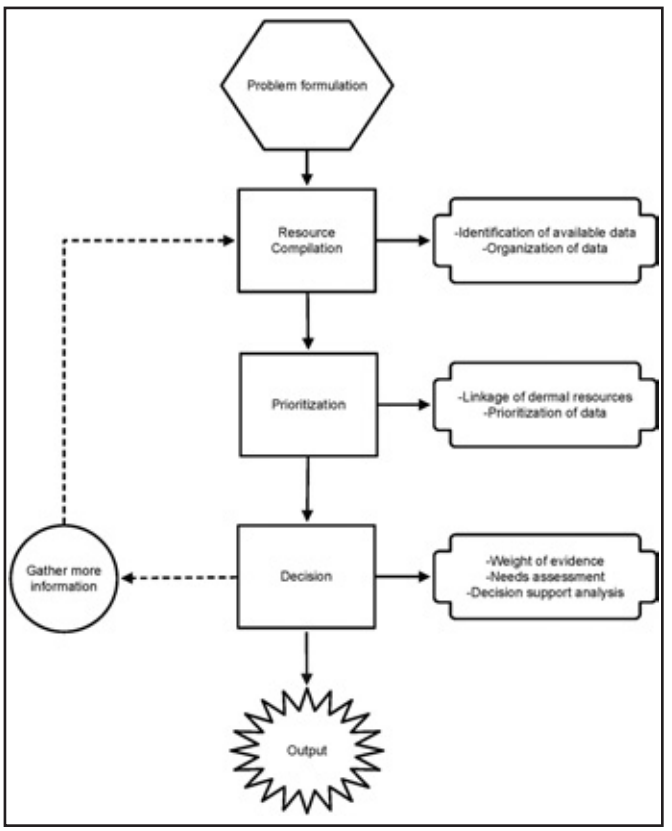

Figure 1. Conceptual framework and relationship of the primary modules of the decision support system. The image illustrates the conceptual framework for a dermal decision support system. This framework consists of three primary modules: 1) resource compilation, 2) prioritization, and 3) decision. Each module represents a key function in the decision support system to ensure that critical information is available to users to aid in protecting emergency management and response personnel during chemical incidents involving dermal exposures.

which facilitates the systematic prioritization of large volumes of resources to limit uncertainty in decision making.[42] Figure 3 demonstrates the relationship of the core elements of the prioritization module.

In the context of the dermal DSS, application of VOI scores ensures that information resources are prioritized based on the critical needs of EMO personnel. Two important criteria for EMO resources are accessibility and reliability. Accessibility is a critical criterion because of the time dependence of decision making that varies by incident phase. For example, during the early response, rapidly accessible information is crucial and therefore should be readily identifiable from a resource library. Multiple factors governing the accessibility criterion are 1) cost (paid vs free resources), 2) format (hard copy textbook vs online databases), and 3) usability and ease of finding the relevant information within the resource (searchable databases vs hard copy textbooks). One potential drawback to giving high weight to accessibility is that common or highly accessible resources may not include information to meet a specific need. This is illustrated in the recommendations for CPC selection for benzene summarized in Table 2. The *Emergency Response Guidebook*, which is a common high access resource, does not provide specific CPC recommendations for benzene.[14] In contrast, other resources that might have lower accessibility scores provide specific CPC recommendations for benzene.[43]

The second criterion for a VOI score is reliability, which reflects the level of confidence in the information resource and its relevance to EMO. Elements of reliability include 1) the source of the information (government document vs unpublished resources), 2) the publication date, 3) the level of scrutiny (ie, peer review), and 4) relevance to dermal risk in EMO settings. This criterion is important for selecting the most appropriate resource for the scenario and is of particular importance when existing resources provide conflicting recommendations. For example, in evaluating the decontamination procedures for benzene and sulfuric acid, different organizations provide varying guidance on decontamination (as seen in Table 2).

The overall prioritization process can be further refined to address specific user needs by customizing the weights of the different criteria and factors. Strategic combinations of the accessibility and reliability criteria and factors allow for further stratification of resources. In addition, modifying factors or new criteria can be used to customize the VOI to allow consideration of additional variables and provide dynamic range in the process to further refine resource prioritization. For example, additional weight could be placed on free and Internet-accessible resources in a chemical emergency response or history of use or familiarity among the user community. Techniques such as MCDA, as described earlier, provide a tool for applying different weights to

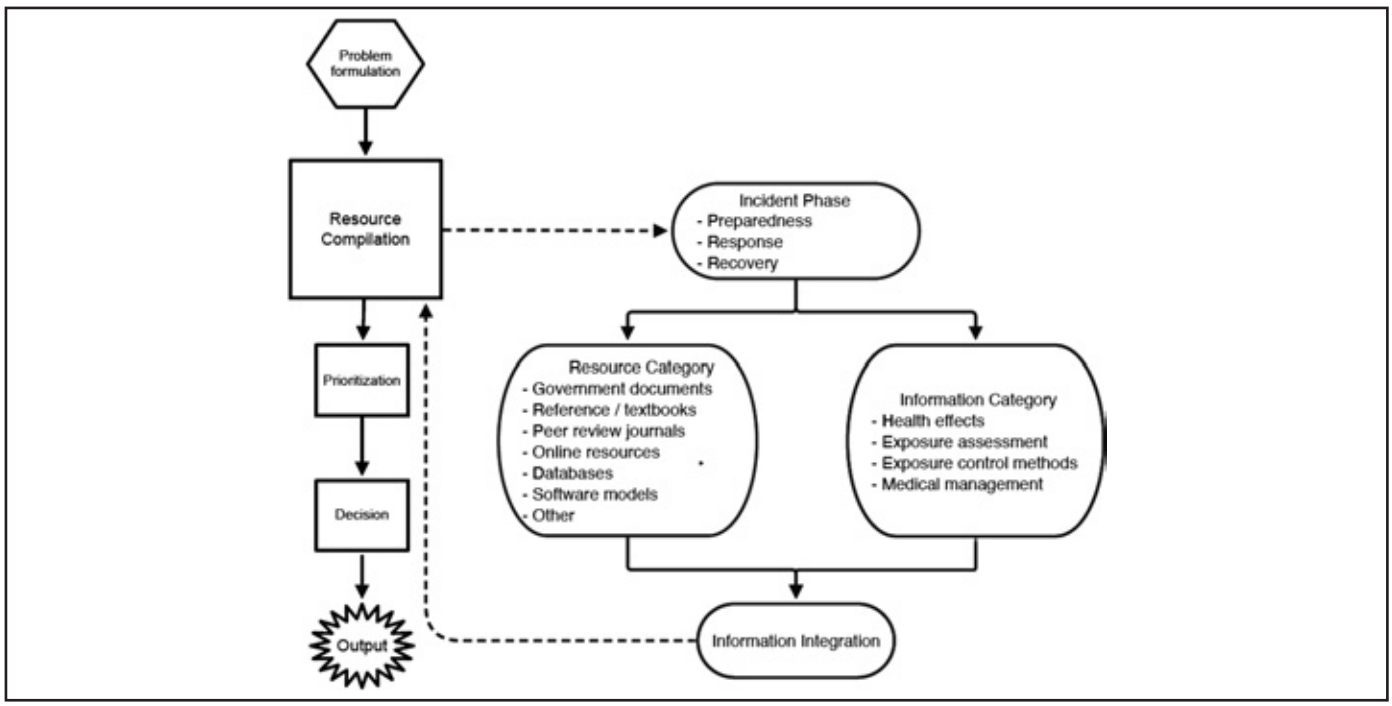

Figure 2. Core elements of the resource compilation module of the decision support system. The image identifies the key elements included in the resource compilation module of the decision support system. These elements guide the classification and integration of relevant information resources according to 1) incident phase, 2) resource categories, and 3) information category. By classifying and integrating information resources, the resource compilation module provides a specialized resource library pertaining to dermal exposures to chemicals that effectively sorts data based on emergency management and response needs.

individual decision criteria such that the final prioritization emphasizes the component factors that are most important. The flexibility afforded by this technique for different scenarios is helpful in the EMO arena. For example, factors related to accessibility might be weighted more highly for the response than the planning phase. This preference can be built into the scoring approach using the MCDA concept.[39-41] Although there are many potential structures for such VOI-score-based resource rankings, an example approach that captures several key elements is shown in Table 3.

In practice, once the definition of the assignment criteria (ie, scores or weights) are completed, implementing the VOI score concept for dermal risk resources pertinent to emergency response scenarios requires ongoing refinement to ensure that new developments in resource utility are captured. The initial assignment process can employ any one of many expert elicitations or focus group methods.[44] The primary goal is to involve subject matter experts (SMEs) that represent the breadth of expertise of the key content as well as the needs of the end users of the resource. EMO is a dynamic field with a significant history of applying lessons learned to improve performance on future responses. The dermal DSS (or any such resource for EMO) should reflect this feature of continuous improvement. Thus, the resource prioritization derived based on inputs of small numbers of SMEs should be refined based on actual user experience and preference. Mechanisms to capture user feedback or real-time data updates are a critical design component of the dermal DSS. Relevant techniques for capturing such data include user feedback surveys or usage tracking techniques for electronic resource libraries (eg, number of downloads of a mobile application). More advanced methods that build in automatic features for prioritization based on user selection (eg, number of "hits") would provide a mechanism to ensure the tool reflects user preferences. These feedback tools are critical because the EMO community is composed of hundreds

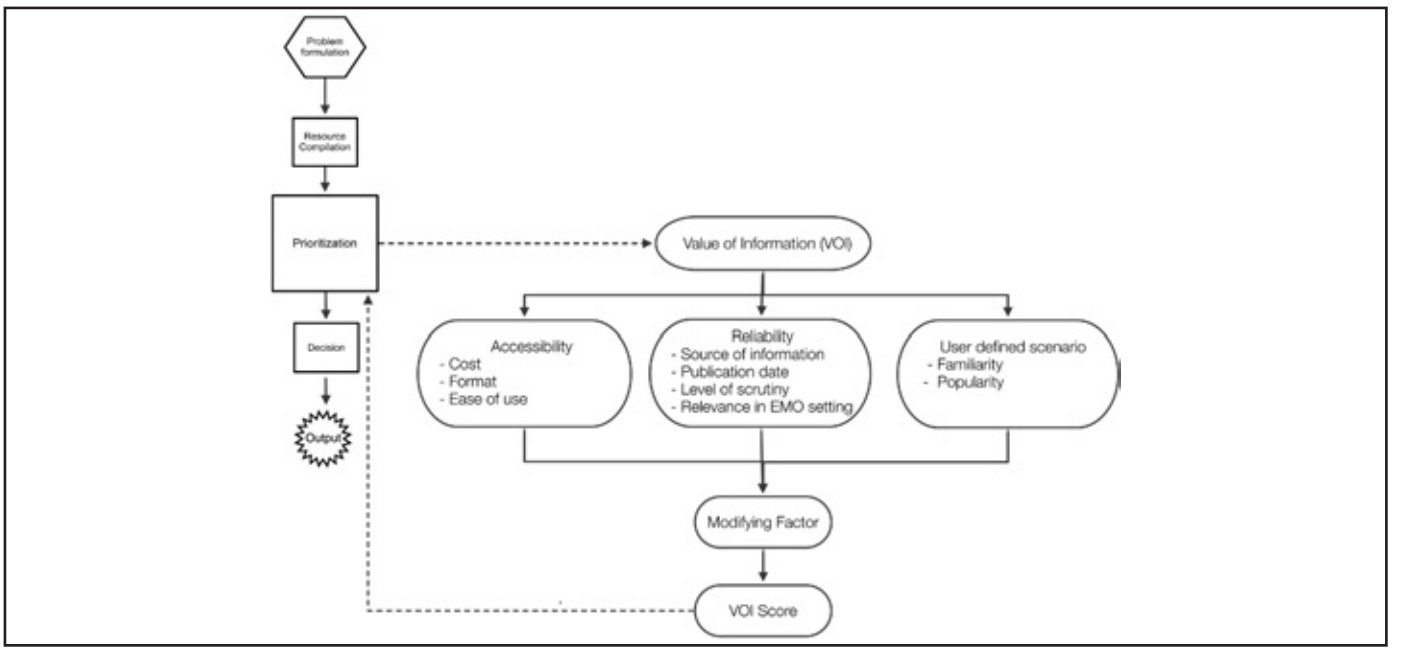

Figure 3. Core elements of the prioritization module of the decision support system. The image illustrates the primary elements of the prioritization module of the decision support system. This module enhances the specialized resource library constructed during the resource compilation module by developing a relative ranking for each information resource. The relative rankings, also known as value of information (VOI) score, allow for key criteria, such as accessibility and reliability, to be incorporated into the prioritization of information resources based on the emergency phase and the associated need of involved personnel.

of thousands of active members and the ability of a small expert group to capture the sentiments of such a large and dynamic community is limited.

Decision

EMO reflects a demanding decision-making environment. The current state of the field is that the decision process occurs at the incident command level where judgments are made based on the weight of evidence. In many cases, the response requires the command structure to support numerous high impact decisions, often made in a rapid manner. The nature of the information needed is driven by the scenario. Because of the challenging demands in EMO decision making, the information inputs need to be optimized. The dermal DSS incorporates prioritized information as the input to the overall decision process as a basic step toward the goal of effective decision making. The decision process can be enhanced and facilitated with additional tools that integrate information, rather than just providing access to information. There are many examples of such decision tools that apply to dermal EMO needs. Most of the currently available tools take the form of hardcopy or online documents or databases that incorporate data with a decision logic component. Examples include the decision frameworks that weigh complex information datasets such as the NIOSH Skin Notation Methodology or databases that direct the user to a recommendation based on specific and limited inputs, such as the CPC selection guidance.[4,43] Decision tools are advancing to include probabilistic recommendations or other indications of likelihood based on user inputs. One example is CHEMM Intelligent Syndromes Tool (CHEMM-IST), which provides an indication of the likelihood for a particular toxidrome being present.[3] Overall, such decision tools are of significant value, and the demand for such products and the availability of technology to make them more available will increase their impact. Clearly, the nature of the decision tools is evolving from traditional methods (eg, from paper resources and decision logic documents) to electronic tools and computer-based applications that respond to user feedback and have learning features.

Table 3. Illustration of key steps in determining value of information (VOI)-score-based resource rankings		
Key step	**Overview**	**Example**
1	Define primary criteria	(Q) = quality; (A) = accessibility; (F) = familiarity
2	Rate resources for each criterion	Assign a score from 1 to 5 (5 is most desirable)
3	Calculate the crude VOI score (C)	C determined by calculating the average of ratings for criteria Q, A, and F that can reflect multiple subject matter experts (SMEs) inputs
4	Application of a modifying factor (M) for anticipated overall utility of the resource; M is a multiplier included to raise or lower the crude VOI score in the ranking results	Assign a level of low, medium, or high (high is most desirable). For this results, low = −0.25, medium = 0, and high = 0.25.
5	Calculate the final VOI score (V)	$[V = C + (C \times (M)]$
6	Repeat for all candidate resources	Develop ranked list based on highest VOI score.

Although the amount and variety of resources are significant, EMO personnel often lack the data needed to answer important questions that may impact the health and lives of responders and the public. The case studies noted above highlight many opportunities for new data collection. Thus, the dermal DSS includes a practice to research loop as illustrated by the need to gather more information in Figure 1. This loop allows for the identification of important data for future use that were not available for decision support at a prior incident. As highlighted in Table 2, there is a need for dermal exposure guidance for both chemicals. This practice to research loop identifies this topic as a research need to ensure that the information is available for future emergencies involving benzene or sulfuric acid. Under ideal circumstances, the use of this component of the dermal DSS is during the planning phase of EMO, which allows new data collection to support an anticipated need (eg, a new dermal surface exposure limit). In the incident phase, documentation of data gaps can provide insights to prioritize new data development for future dermal DSS users and to support research agenda development.[45] As new data are collected or identified via this process linkage to the information resource, the compilation step will support access to the new data for future EMO needs.

Discussion

Decision making in the context of the incident command structure for EMO is complex and integrates multiple health and safety hazards. The resulting complexity necessitates the use of simplifying assumptions and precautionary methods where information resources and decision tools are not immediately at hand. Dermal risks are one component of the EMO scenario in need of better decisions tools.

As an initial step to meet this need, the conceptual framework for a DSS is presented to provide an organization structure for EMO-related dermal risk information. To assist EMO, a dermal checklist tool was developed to guide users through critical considerations to ensure that dermal exposure and risk are fully considered during chemical incidents. This checklist provides a systematic process to identify dermal risk information resources needed for the scenario being evaluated. This checklist serves as the initial step in a dermal DSS strategy that is designed to identify key information needs for EMO by providing a structure for 1) documentation of key questions for EMO problem formulation and 2) the organization of information resources on dermal hazards, exposures, risk characterization, and management. The checklist and DSS provide practical guides to allow EMO personnel to develop and implement a customized preparedness and response plan to address an often overlooked risk during chemical incidents. The dermal DSS complements the suite of information resources often used in EMO but aims to provide a specific focus on dermal risk resources that might be overlooked by a superficial review of existing data. The dermal DSS was also organized for compatibility with existing EMO

practices focusing on inputs that are made by health specialists at the level of the incident command structure.

An additional consideration that should be included in the management of any incident is the identification of potential hazards. In many cases, EMO personnel responding to an incident may not know what chemicals are present or which ones represent the greatest health hazard. The absence of this information may result in execution of critical decisions that are incorrect, such as the selection of an inappropriate CPC that is not protective and places EMO personnel at unacceptable health risks. To assist in overcoming this issue, EMO personnel and decision makers responsible for providing guidance on a chemical incident should use available tools to aid in chemical identification. For example, WISER and CHEMM-IST are capable of quickly assisting users in identifying a chemical based on numerous variables including physical proprieties, signs, and symptoms of exposure or National Fire Protection Association or DOT placards. Once identified, application of the DSS would allow EMO personnel make better informed decisions and risk to their lives and health.

Because EMO practice is continually improving, the dermal DSS is envisioned as an approach to be refined over time. Thus, it embeds feedback processes both to refine the prioritization of existing resources and to emphasize the ability to drive research from practical needs in the field. A case study approach was used to highlight many areas where chemical-specific guidance for EMO is not available from general guidance resources. For example, many common resources for EMO personnel denote the need for CPC but do not recommend specific products or materials that are found in specialized resources. Other areas that appear to be ready for new research include validated dermal exposure monitoring methods and dermal exposure limits.

Conclusion

The goal of the dermal DSS is to provide a systematic framework to identify and organize EMO resources to assist users in making informed decisions regarding the management of the risks of dermal exposures with chemicals. As outlined in this article, the DSS provides a platform for individual users to organize their own stock of resources. Future enhancements can include incorporation of the concept in venues for training and outreach regarding dermal risks for EMO. The increased access to Internet-based information or mobile device applications that function without Internet access opens the door to the development of shared information resource databases constructed on the principles provided in the dermal DSS. Resources from the US NLM, such as WISER and CHEMM, are potential sites for linkage to online or downloadable applications of the dermal DSS. Such a development would reflect the natural extension of current databases to create virtual libraries or electronic tools that harness smart search technologies and provide decision-making tools to protect EMO personnel from dermal risks.

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G. Scott Dotson, PhD, CIH, Education and Information Division, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, Ohio.

Naomi L. Hudson, DrPH, Education and Information Division, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cincinnati, Ohio.

Andrew Maier, PhD, DABT, CIH, Department of Environmental Health, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

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Appendix

Dermal-related resources for use during chemical incidents with potential for dermal exposure			
Resource name	**Resource type**	**Source**	**URL**
12th report on carcinogens	Government document	National Toxicology Program (NTP)	*http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf*
2012 Emergency Response Guidebook	Online	US Department of Transportation	*http://phmsa.dot.gov/staticfiles/PHMSA/DownloadableFiles/Files/Hazmat/ERG2012.pdf*
A Guide to the Globally Harmonized System of Classification and Labeling of Chemicals (GHS)	Online	Occupational Safety and Health Administration (OSHA)	*https://www.osha.gov/dsg/hazcom/ghs.html*
AEGL Chemicals	Online	Environmental Protection Agency (EPA)	*http://www.epa.gov/oppt/aegl/pubs/chemlist.htm*
AIHA 2011 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook	Reference/text book	American Industrial Hygiene Association (AIHA)	*http://www.aiha.org/get-involved/AIHAGuidelineFoundation/EmergencyResponsePlanningGuidelines/Pages/default.aspx*
Air International Regulations for shippers of dangerous goods	Reference/text book	AIR Shipper (Labelmaster)	*http://www.labelmaster.com/shop/books/air-transport/a-i-r-shipper*
American Industrial Hygiene Association Industrial Hygienists' Role and Responsibilities in Emergency Preparedness and Response White Paper	Online	AIHA	*https://www.aiha.org/get-involved/VolunteerGroups/Documents/IPRWG-EPRWhitePaper_Final.pdf*
AOAC: Official Methods of Analysis (19th ed.) and Supplements	Reference/text book	Association of Official Analytical Chemists (AOAC)	*http://www.aoac.org/imis15_prod/AOAC/Publications/Official_Methods_of_Analysis/About/AOAC_Member/Publications/OMA/AOAC_Official_Methods_of_Analysis.aspx?hkey=ccc1fa5c-3e0f-4f76-87ab-1604b266f9df*
Areal Location of Hazardous Atmospheres (ALOHA)	Online	EPA/NOAA	*http://www.epa.gov/osweroe1/content/cameo/aloha.htm*
Ashford's Dictionary of Industrial Chemicals	Reference/text book	R.D. Ashford	*http://www.industrialchemistry.org/100pagesAddict3.pdf*
Ashgate Handbook of Pesticides and Agricultural Chemicals	Reference/text book	G.W.A. Milne, ed.	*http://www.waterstones.com/waterstonesweb/products/g+w+a+milne/ashgate+handbook+of+pesticides+and+agricultural+chemicals/5928867/*
Best Practices for Protecting EMS Responders During Treatment and Transport of Victims of Hazardous Substance Releases	Online	OSHA	*https://www.osha.gov/Publications/OSHA3370-protecting-EMS-respondersSM.pdf*
Biological Monitoring Methods for Industrial Chemicals (2nd ed.)	Reference/text book	R.C. Baselt	*http://www.clinchem.org/content/27/3/516.full.pdf*
Biological Monitoring: An Introduction	Reference/text book	S. Que Hee, ed.	*http://www.amazon.com/Biological-Monitoring-Introduction-Shane-Que/dp/0471290831/ref=sr_1_1?s=books&ie=UTF8&qid=1382993441&sr=1-1*
CAMEO chemicals	Online	National Oceanic and Atmospheric Administration (NOAA)	*http://www.epa.gov/osweroe1/content/cameo/cameo.htm*
CAMEO chemicals: mobile site	Online	NOAA	*http://m.cameochemicals.noaa.gov/search/simple*
CAMEO Chemicals: online version	Online	NOAA	*http://www.cameochemicals.noaa.gov/*
Cargo Decoder Mobile App	Online	Strategies in Software	*http://www.strategiesinsoftware.com/current-projects/cargo-decoder*
Casarett and Doull's Toxicology: The Basic Science of Poisons (8th ed.)	Reference/text book	C.D. Klaassen, ed.	*http://www.amazon.com/Casarett-amp-Doulls-Toxicology-Science/dp/0071769234*
Catalog of Teratogenic Agents (13th ed.)	Reference/text book	T.H. Shepard	*http://www.amazon.com/Catalog-Teratogenic-Agents-Thomas-Shepard/dp/080189784X*
CG ICS Site Safety Plan (SSP) checklists	Online	OSHA	*https://www.osha.gov/SLTC/etools/ics/pdf/ics_uscg_ssp_checklists.pdf*
Chemcyclopedia	Reference/text book	J.H. Kuney, ed. (American Chemical Society)	*http://books.google.com/books/about/Chemcyclopedia_1992.html?id=Cv4UQwAACAAJ*
Chemical Properties Handbook: Physical, Thermodynamic, Environmental, Transport, Safety and Health Related Properties for Organic and Inorganic Chemicals	Reference/text book	C.L. Yaws	*https://www.aiha.org/marketplace/Pages/Product-Detail.aspx?productid=%7B453AFAC6-092E-E411-B502-005056B20848%7D*

Dermal-related resources for use during chemical incidents with potential for dermal exposure			
Resource name	**Resource type**	**Source**	**URL**
Chemical Protective Clothing (2nd ed.)	Reference/text book	D.H. Anna (AIHA)	*https://webportal.aiha.org/Purchase/ProductDetail.aspx?Product_code=ab99f67d-4778-de11-96b0-0050568361fd*
Chemical Reactivity Worksheet	Online	NOAA	*http://response.restoration.noaa.gov/reactivityworksheet*
Chemical Warfare Agents: Toxicity at Low Levels	Reference/text book	S.M. Somani, J.S. Romano Jr, eds.	*http://www.amazon.com/Chemical-Warfare-Agents-Toxicity-Levels-ebook/dp/B001AOO9RA*
Chemical Warfare Agents: Toxicology and Treatment (2nd ed.)	Reference/text book	T.C. Marrs, R.L. Maynard, F.R. Sidell	*http://books.google.com/books?hl=en&lr=&id=nzVF04525ukC&oi=fnd&pg=PR5&dq=%22Chemical+warfare+agents:+toxicology+and+treatment%22&ots=FVbQCGvXrf&sig=vA_Gj5_Ks6vmjreUO6Vjg1YaxmE#v=onepage&q=%22Chemical%20warfare%20agents%3A%20toxicology%20and%20treatment%22&f=false*
Chemical Hazards Emergency Medical Management (CHEMM)	Online	US Department of Health and Human Services (HHS)	*http://www.chemm.nlm.nih.gov/*
Chemical Protective Clothing Performance Index	Reference/text book	Krister Forsberg and Lawrence H. Keith	*http://www.amazon.com/Chemical-Protective-Clothing-Performance-Index/dp/0471328448/ref=sr_1_1?s=books&ie=UTF8&qid=1429196112&sr=1-1&keywords=chemical+protective+clothing+performance*
CHEMM: Decontamination Procedures	Online	US HHS	*http://chemm.nlm.nih.gov/decontamination.htm*
CHEMM: Information for Incident Preparedness	Online	US HHS	*http://chemm.nlm.nih.gov/incidentpreparedness.htm*
CHEMM: Information for the First Responders	Online	US HHS	*http://chemm.nlm.nih.gov/firstresponders.htm*
CHEMM: Intelligent Syndromes Tools (CHEMM-IST)	Online	US HHS	*http://chemm.nlm.nih.gov/chemmist.htm*
CHEMM: On-site Activities	Online	US HHS	*http://chemm.nlm.nih.gov/onsite.htm*
CHEMM: PPE	Online	US HHS	*http://chemm.nlm.nih.gov/ppe.htm*
CHEMM: Strategy for Developing a Community Chemical Response Plan	Online	US HHS	*http://chemm.nlm.nih.gov/responseplanstrategy.htm*
CHEMM: Triage Guidelines	Online	US HHS	*http://chemm.nlm.nih.gov/triage.htm*
CHEMM: Types and Categories of Hazardous Chemicals	Online	US HHS	*http://chemm.nlm.nih.gov/agentcategories.htm*
CHEMM: What Kind of Emergency?	Online	US HHS	*http://chemm.nlm.nih.gov/typesofevents.htm*
CHEMTREC Operations Center	Online	CHEMTREC	*http://www.chemtrec.com/responder/services/Pages/OpCen.aspx*
Contact and Occupational Dermatology (3rd ed.)	Reference/text book	J.G. Marks Jr, V.A. DeLeo	*http://www.sciencedirect.com/science/book/9780323014731*
Coping with an attack: A quick guide to dealing with biological, chemical and "dirty bomb" attacks	Online	National Defense University	*http://dhhs.ne.gov/Documents/WMD_Poster.pdf*
CRC Handbook of Chemistry and Physics (94th ed.)	Reference/text book	W.M. Haynes, ed.	*http://www.crcpress.com/product/isbn/9781466571143*
Critical Care Toxicology: Diagnosis and Management of the Critically Poisoned Patient	Reference/text book	J. Brent, et al., eds.	*http://books.google.com/books?hl=en&lr=&id=WuA4LsWXXWEC&oi=fnd&pg=PA70&dq=Critical+care+toxicology:+diagnosis+and+management+of+the+critically+poisoned+patient&ots=ijKt8D3EJj&sig=1Uf5FDxdmUkrDAL7pIhyxKCzHfw#v=onepage&q=Critical%20care%20toxicology%3A%20diagnosis%20and%20management%20of%20the%20critically%20poisoned%20patient&f=false*
Dangerous Goods Regulations (55th ed.)	Reference/text book	International Air Transport Association, Dangerous Goods Board (IATA)	*http://www.iata.org/publications/dgr/Pages/index.aspx*
Decontamination at health facilities	Online	World Health Organization (WHO)	*http://www.who.int/environmental_health_emergencies/deliberate_events/decontamination_en.pdf*
Dermal (Skin)	Online	Agency for Toxic Substances and Disease Registry (ATSDR)	*http://www.atsdr.cdc.gov/substances/toxorganlisting.asp?sysid=2*
Dermal Exposure	Online	OSHA	*https://www.osha.gov/SLTC/dermalexposure/index.html*
Dermal Exposure Assessment: Principles and Applications	Online	EPA	*http://rais.ornl.gov/documents/DERM_EXP.PDF*
Dermal Exposure Monitoring	Online	OSHA	*https://www.osha.gov/SLTC/dermalexposure/exposuremonitoring.html*

Dermal-related resources for use during chemical incidents with potential for dermal exposure			
Resource name	**Resource type**	**Source**	**URL**
Dermatotoxicology (8th ed.)	Reference/text book	H.I. Maibach, K.P. Wilhelm, H. Zhai	*http://www.amazon.com/Dermatotoxicology-Eighth-Edition-Klaus-Peter-Wilhelm/dp/1841848557/ref=dp_ob_title_bk*
Disaster Response and Recovery, (Wiley Pathways) (2nd ed.)	Reference/text book	D. McEntire	*http://www.wiley.com/WileyCDA/WileyTitle/productCd-1118673026.html*
Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning (2nd ed.)	Reference/text book	M.J. Ellenhorn, S. Schonwald, G. Ordog, J. Wasserberger	*http://www.clinchem.org/content/44/2/366.full*
Emergency Action for Chemical and Biological Warfare Agents	Reference/text book	D.H. Ellison	*http://www.amazon.com/Emergency-Action-Chemical-Biological-Warfare/dp/0849302412*
Emergency Care for Hazardous Materials Exposure (3rd ed.)	Reference/text book	A.C. Bronstein, P.L. Currance, eds.	*http://www.cne.go.cr/CEDO-CRID/CEDO-CRID%20V4/pdf/eng/doc2972/doc2972-1a.pdf*
Emergency Decontamination Corridor System	Online	US Army	*http://www.au.af.mil/au/awc/awcgate/army/firefighter_quick_ref.pdf*
Emergency Handling of Hazardous Materials in Surface Transportation	Reference/text book	Association of American Railroads (Bureau of Explosives)	*http://www.boepublications.com/hazmat.html*
Emergency Preparedness and Response	Online	OSHA	*https://www.osha.gov/SLTC/emergencypreparedness/index.html*
Emergency Response Guidebook	Government document	US Department of Transportation (PHMSA)	*http://phmsa.dot.gov/staticfiles/PHMSA/DownloadableFiles/Files/Hazmat/ERG2012.pdf*
Emergency Response Guidebook Mobile App	Online	US Department of Transportation	*http://www.phmsa.dot.gov/portal/site/PHMSA/menuitem.ebdc7a8a7e39f2e55cf2031050248a0c/?vgnextoid=f6db5aaa0581d310VgnVCM1000001ecb7898RCRD&vgnextchannel=c8e71dec94973110VgnVCM1000009ed07898RCRD&vgnextfmt=print*
Emergency Response Resources	Online	CDC	*http://www.cdc.gov/niosh/topics/emres/responders.html*
Emergency Response Resources: Personal Protective Equipment	Online	CDC	*http://www.cdc.gov/niosh/topics/emres/ppe.html*
Encyclopaedia of occupational health and safety	Government document	International Labour Office	*http://www.ilo.org/safework/info/publications/WCMS_113329/lang-en/index.htm*
Environmental and Occupational Medicine (5th ed.)	Reference/text book	W.N. Rom, ed.	*http://www.amazon.com/Environmental-Occupational-Medicine-William-Rom/dp/0781762995*
Evaluation Guidelines for Surface Sampling Methods	Online	OSHA	*https://www.osha.gov/dts/sltc/methods/surfacesampling/surfacesampling.html*
Field Management of Chemical Casualties Handbook	Online	USAMRICD	*https://www.rke.vaems.org/wvems/Libraryfiles/Dis/E_04.pdf*
Fire Protection Guide to Hazardous Materials (2010 ed.)	Reference/text book	National Fire Protection Association (NFPA)	*http://catalog.nfpa.org/Fire-Protection-Guide-to-Hazardous-Materials-2010-Edition-P14118.aspx*
Goldfrank's Toxicologic Emergencies (9th ed.)	Reference/text book	L.R. Goldfrank	*http://goldfrankstoxicology.com/*
Goodman and Gilman's the Pharmacological Basis of Therapeutics (12th ed.)	Reference/text book	L. Brunton, B. Chabner, B. Knollman	*http://accessmedicine.com/resourceTOC.aspx?resourceID=651*
Guidance Document on Dermal Absorption	Online	European Commission	*http://ec.europa.eu/food/plant/protection/evaluation/guidance/wrkdoc20_rev_en.pdf*
Guidance on Emergency Responder Personal Protective Equipment (PPE) for Response to CBRN Terrorism Incidents	Online	CDC	*http://www.cdc.gov/niosh/docs/2008-132/pdfs/2008-132.pdf*
Guide for the Selection of Personal Protective Equipment for Emergency First Responders	Online	National Institute of Justice	*https://www.ncjrs.gov/pdffiles1/nij/191518.pdf*
Guide to Occupational Exposure Values	Reference/text book	American Conference of Governmental Industrial Hygienists (ACGIH)	*https://www.acgih.org/store/ProductDetail.cfm?id=2332*
Guidelines for Mass Casualty Decontamination During a Terrorist Chemical Agent Incident	Online	US Army Soldier and Biological Chemical Command (SBCCOM)	*http://www.au.af.mil/au/awc/awcgate/army/sbccom_decon.pdf*
Guidelines for Responding to a Chemical Weapons Incident	Online	US Army	*http://www.au.af.mil/au/awc/awcgate/army/sbccom_chem_response.pdf*

Dermal-related resources for use during chemical incidents with potential for dermal exposure			
Resource name	**Resource type**	**Source**	**URL**
Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose (4th ed.)	Reference/text book	S.W. Borron, M. Burns, M.W. Shannon	*http://www.amazon.com/Winchesters-Clinical-Management-Poisoning-Overdose/dp/0721606938*
Hamilton & Hardy's Industrial Toxicology (5th ed.)	Reference/text book	R.D. Harbison	*http://www.amazon.com/Hamilton-Hardys-Industrial-Toxicology-5e/dp/0815141815*
Handbook of Chemistry and Physics (94th ed.)	Reference/text book	R.C. Weast, ed. (The Chemical Rubber Company)	*http://www.hbcpnetbase.com/*
Handbook of Environmental Data on Organic Chemicals (5th ed.)	Reference/text book	K. Verschueren	*http://www.amazon.com/Handbook-Environmental-Data-Organic-Chemicals/dp/0470171723*
Handbook of Poisoning (13th ed.)	Reference/text book	R.H. Dreisbach	*http://www.amazon.com/Dreisbachs-Handbook-Poisoning-Prevention-Thirteenth/dp/1850700389/ref=sr_1_1?s=books&ie=UTF8&qid=1381776580&sr=1-1*
Handbook of Reactive Chemical Hazards (7th ed.)	Reference/text book	L. Bretherick, P. Urben	*http://www.sciencedirect.com/science/book/9780123725639*
Hawley's Condensed Chemical Dictionary (15th ed.)	Reference/text book	R.J. Lewis Sr, ed.	*http://www.scribd.com/doc/94910911/Hawley%E2%80%99s-Condensed-Chemical-Dictionary-Fifteenth-Edition*
Hayes' Handbook of Pesticide Toxicology	Reference/text book	R. Krieger, ed.	*http://www.sciencedirect.com/science/book/9780123743671*
Haz-MAP	Online	National Library of Medicine (NLM)	*http://hazmap.nlm.nih.gov/index.php*
Hazardous Chemicals Data Book: 1986	Reference/text book	G. Weiss (Noyes Data Corporation)	*http://www.osti.gov/scitech/biblio/6051711*
Hazardous Material Emergency Response: Incident Command	Online	National Institute of Environmental Health Sciences	*http://www.niehs.nih.gov/health/assets/docs_f_o/incident_command_hazardous_material_response.pdf*
Hazardous Substances Data Bank (HSDB)	Online	NLM	*http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB*
HazMatIQ Federal Resources: Videos	Online	HAZMAT IQ	*http://www.hazmatiq.com/video/index.html*
ICS Resource Center	Online	Federal Emergency Management Agency (FEMA)	*http://www.training.fema.gov/EMIWeb/IS/ICSResource/index.htm*
INCHEM: Chemical Safety Information from Intergovernmental Organizations	Online	WHO	*http://www.inchem.org/*
Incident Command System	Online	FEMA	*https://www.fema.gov/incident-command-system-resources*
Incident Command System eTool	Online	OSHA	*https://www.osha.gov/SLTC/etools/ics/index.html*
Incident Commanders Checklist: Emergency Response	Online	Wagner-Meinert, Inc.	*http://www.wagner-meinert.com/Portals/0/Incident_Commanders_Checklist.pdf*
International Cosmetic Ingredient Dictionary & Handbook (15th ed.)	Reference/text book	Personal Care Products Council (Formally CTFA)	*https://access.personalcarecouncil.org/eweb/DynamicPage.aspx?Action=Add&ObjectKeyFrom=1A83491A-9853-4C87-86A4-F7D95601C2E2&WebCode=ProdDetailAdd&DoNotSave=yes&ParentObject=CentralizedOrderEntry&ParentDataObject=Invoice%20Detail&ivd_formkey=69202792-63d7-4ba2-bf4e-a0da41270555&ivd_cst_key=00000000-0000-0000-0000-000000000000&ivd_prc_prd_key=AD961222-3580-4D73-961F-68013ECCFE40*
Jane's CBRN Response Handbook (4th ed.)	Reference/text book	A. Garcia, D. Rand, J.H. Rinard	*http://www.ihs.com/products/janes/security/cbrn-response-handbook.aspx*
Joint Information Center Model. Collaborative Communications During Emergency Response	Online	National Response Team	*http://www.au.af.mil/au/awc/awcgate/nrt/jic-model.pdf*
Kirk-Othmer Encyclopedia of Chemical Technology, Vol 1 (4th ed.)	Reference/text book	Kirk-Othmer	*http://onlinelibrary.wiley.com/book/10.1002/0471238961*
Management of Terrorist Events Involving Radioactive Material (NCRP Report No. 138)	Reference/text book	National Council on Radiation Protection and Measurements	*http://www.ncrppublications.org/Reports/138*
Managing Hazardous Materials Incidents (MHMIs)	Online	ATSDR	*http://www.atsdr.cdc.gov/MHMI/index.asp*
Managing Hazardous Materials Incidents (MHMIs) (PDF Version)	Online	ATSDR	*http://www.atsdr.cdc.gov/MHMI/mhmi_v1_2_3.pdf*
Mapping Applications for Response, Planning, and Local Operational Tasks (MARPLOT)	Online	EPA/NOAA	*http://www.epa.gov/osweroe1/content/cameo/marplot.htm*

Dermal-related resources for use during chemical incidents with potential for dermal exposure			
Resource name	**Resource type**	**Source**	**URL**
Martindale: The Complete Drug Reference (37th ed.)	Reference/text book	S.C. Sweetman, ed.	*http://www.amazon.com/Martindale-Complete-Reference-Edition-Package/dp/085369933X/ref=pd_sim_sbs_b_1*
Medical Aspects of Chemical and Biological Warfare. Chapter 15: Decontamination	Online	US Army	*http://www.au.af.mil/au/awc/awcgate/medaspec/Ch-15electrv699.pdf*
Medical Aspects of Chemical Warfare	Online	US Army	*http://www.cs.amedd.army.mil/borden/Portlet.aspx?id=d3d11f5a-f2ef-4b4e-b75b-6ba4b64e4fb2*
Medical Aspects of Chemical Warfare: Chapter 14. Field Management of Chemical Casualties	Online	US Army	*http://www.hsdl.org/?view&did=18081*
Medical Aspects of Chemical Warfare: Chapter 15. Triage of Chemical Casualties	Online	US Army	*http://www.hsdl.org/?view&did=18076*
Medical Aspects of Chemical Warfare: Chapter 16. Decontamination of Chemical Casualties	Online	US Army	*http://www.hsdl.org/?view&did=18072*
Medical Management Guidelines (MMGs)	Online	ATSDR	*http://www.atsdr.cdc.gov/mmg/index.asp*
Medical Management Guidelines for Chemical Agents	Online	CDC	*http://www.bt.cdc.gov/chemical/mmg.asp*
Medical Toxicology (3rd ed.)	Reference/text book	R.C. Dart, ed.	*http://books.google.com/books?id=BfdighlyGiwC&pg=PA732&source=gbs_selected_pages&cad=2#v=onepage&q&f=false*
Methodology for Developing Chemical Exposure Guidelines for Deployed Military Personnel (Reference Document 230)	Government document	US Army Public Health Command (USAPHC)	*http://phc.amedd.army.mil/PHC%20Resource%20Library/RD230%20June%202010%20Revision.pdf*
National Incident Management System	Online	FEMA	*http://www.fema.gov/pdf/emergency/nims/NIMS_core.pdf*
National Incident Management System: Appendix B. Incident Command System	Online	FEMA	*http://www.fema.gov/pdf/emergency/nims/NIMS_AppendixB.pdf*
National Response Framework	Online	Homeland Security	*http://www.fema.gov/media-library-data/20130726-1914-25045-1246/final_national_response_framework_20130501.pdf*
NCEA Exposure Factors Handbook. Chapter 6: Dermal.	Online	EPA	*http://www.epa.gov/ncea/pdfs/efh/front.pdf*
NIOSH Emergency Response Safety and Health Database	Online	CDC	*http://www.cdc.gov/niosh/ershdb/default.html*
NIOSH Manual of Analytical Methods (4th ed.)	Government document	National Institute for Occupational Safety and Health (NIOSH)	*http://www.cdc.gov/niosh/docs/2003-154/*
NIOSH Pocket Guide (Full pdf)	Online	NIOSH	*http://www.cdc.gov/niosh/docs/2005-149/pdfs/2005-149.pdf*
NIOSH Pocket Guide Search page	Online	NIOSH	*http://www.cdc.gov/niosh/npg/*
OECD Guiding Principles for Chemical Accident Prevention, Preparedness and Response	Online	Organization for Economic Cooperation and Development (OECD)	*http://www.oecd.org/env/ehs/chemical-accidents/Guiding-principles-chemical-accident.pdf*
OSHA Occupational Chemical Database	Online	OSHA	*https://www.osha.gov/chemicaldata/*
OSHA Safety and Health Standards: 1910	Online	OSHA	*https://www.osha.gov/pls/oshaweb/owastand.display_standard_group?p_toc_level=1&p_part_number=1910*
OSHA Technical Manual Section II: Chapter 2. Occupational Skin Exposure	Online	OSHA	*https://www.osha.gov/dts/osta/otm/otm_ii/otm_ii_2.html*
OSHA/NIOSH Interim Guidance. Chemical-Biological-Radiological-Nuclear (CBRN) Personal Protective Equipment Selection Matrix for Emergency Responders: Blister Agents	Online	OSHA	*https://www.osha.gov/SLTC/emergencypreparedness/cbrnmatrix/blister.html*
OSHA/NIOSH Interim Guidance. Chemical-Biological-Radiological-Nuclear (CBRN) Personal Protective Equipment Selection Matrix for Emergency Responders: Nerve Agents	Online	OSHA	*https://www.osha.gov/SLTC/emergencypreparedness/cbrnmatrix/nerve.html*

Dermal-related resources for use during chemical incidents with potential for dermal exposure			
Resource name	**Resource type**	**Source**	**URL**
OSHA/NIOSH Interim Guidance. Chemical-Biological-Radiological-Nuclear (CBRN) Personal Protective Equipment Selection Matrix for Emergency Responders	Online	OSHA	*https://www.osha.gov/SLTC/emergencypreparedness/cbrnmatrix/index.html*
PAH Guidance Manual. Appendix G: Calculating Exposure Doses	Online	ATSDR	*http://www.atsdr.cdc.gov/hac/PHAManual/appg.html*
Patty's Toxicology Vols 1-9 (6th ed.)	Reference/text book	E. Bingham, B. Cohrssen, C.H. Powell	*http://www.wiley.com/WileyCDA/Section/id-811499.html*
PDR Guide to Terrorism Response	Reference/text book	J.G. Bartlett, M.I. Greenberg, eds.	*http://www.emergencystuff.com/product-p/156363550x.htm*
Personal Protective Equipment	Online	EPA	*http://www.epa.gov/osweroe1/content/hazsubs/equip.htm*
Pesticide Manual (16th ed.)	Reference/text book	J. Turner (British Crop Protection Council)	*http://bcpcdata.com/pesticide-manual.html*
PHA Guidance Manual. Appendix F: Derivation of Comparison Values	Online	ATSDR	*http://www.atsdr.cdc.gov/hac/PHAManual/appf.html*
Physician's Drug Handbook (12th ed.)	Reference/text book	Springhouse: Lippincott Williams & Wilkins	*http://www.amazon.com/Physicians-Drug-Handbook-Springhouse/dp/1582556806*
Physicians' Desk Reference	Reference/text book	PDR Network LLC	*http://www.pdr.net/*
Poisindex	Online	Micromedex (Truven Health Analytics)	*http://micromedex.com/Portals/1/Assets/Brochures/International/INTL_12339_0614_Poisindex_A4_WEB1.pdf*
Poisoning and Drug Overdose (6th ed.)	Reference/text book	K.R. Olson, ed.	*http://www.amazon.com/Poisoning-Drug-Overdose-Sixth-Edition/dp/0071668330*
Prehospital management and medical intervention after a chemical attack	Online	L. Kenar, T. Karayklanoglu (Emergency Medicine Journal)	*http://emj.bmj.com/content/21/1/84.full.pdf*
Principles of Clinical Toxicology (4th ed.)	Reference/text book	J.D. Bricker	*http://www.abebooks.com/9780849353505/Principles-Clinical-Toxicology-Bricker-Douglas-0849353505/plp*
Protective Clothing and Ensembles	Online	CDC	*http://www.cdc.gov/niosh/topics/protclothing/*
Reactive Skin Decontamination Lotion (RSDL)	Online	Bracco Diagnostics	*http://www.rsdecon.com/PDFs/RSDL-MSDS_US.pdf*
Recognition and Management of Pesticide Poisonings (6th ed.) (EPA 735K13001)	Government document	EPA	*http://www2.epa.gov/sites/production/files/documents/rmpp_6thed_final_lowresopt.pdf*
Registry of Toxic Effects of Chemical Substances, Vols 1 and 2	Government document	NIOSH	*http://www.cdc.gov/niosh/docs/97-119/pdfs/97-119.pdf*
Resource Guide for Disaster Medicine and Public Health	Online	NLM	*http://disasterlit.nlm.nih.gov/*
Sax's Dangerous Properties of Industrial Materials (12th ed.)	Reference/text book	R.J. Lewis Sr, ed.	*https://archive.org/details/dangerous proper00saxn*
Sittig's Handbook of Toxic and Hazardous Chemicals and Carcinogens (6th ed.)	Reference/text book	R.P. Pohanish, ed.	*http://www.amazon.com/Sittigs-Handbook-Hazardous-Chemicals-Carcinogens/dp/1437778690*
Skin Exposure and Effects	Online	CDC	*http://www.cdc.gov/niosh/topics/skin/*
Skin Notation Profiles	Online	NIOSH	*http://www.cdc.gov/niosh/topics/skin/skin-notation_profiles.html*
Surface Contamination	Online	OSHA	*https://www.osha.gov/SLTC/surfacecontamination/index.html*
Symptoms of exposure to highly toxic chemicals	Online	WHO	*http://www.who.int/environmental_health_emergencies/deliberate_events/symptoms_en.pdf*
Technical Support Document for Exposure Assessment and Stochastic Analysis: Dermal Exposure Assessment	Online	California Office of Environmental Health Hazard Assessment	*http://oehha.ca.gov/air/hot_spots/pdf/chap6.pdf*
The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals (15th ed.)	Reference/text book	Royal Society of Chemistry	*http://www.rsc.org/Publishing/Merckindex/*
The Pesticide Manual: World Compendium (16th ed.)	Reference/text book	C. MacBean, ed. (British Crop Protection Council)	*http://www.amazon.com/The-Pesticide-Manual-World-Compendium/dp/190139686X*

Dermal-related resources for use during chemical incidents with potential for dermal exposure			
Resource name	**Resource type**	**Source**	**URL**
The United States Pharmacopeia 37/The National Formulary 32	Reference/text book	United States Pharmacopeial Convention	*http://www.uspnf.com/uspnf/login*
The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2009	Online	WHO	*http://www.who.int/ipcs/publications/pesticides_hazard_2009.pdf*
Threshold Limit Values (TLVs) for Chemical Substances and Physical Agents and Biological Exposure Indices (BEIs)	Reference/text book	ACGIH	*http://www.acgih.org/store/ProductDetail.cfm?id=2331*
Toxicology of the Eye (4th ed.)	Reference/text book	W.M. Grant	*http://www.amazon.com/Toxicology-Eye-Chemicals-Minerals-Systemic/dp/0398058601*
TOXNET	Online	NLM	*http://toxnet.nlm.nih.gov/*
Ullmann's Encyclopedia of Industrial Chemistry (7th ed.)	Reference/text book	F. Ullmann	*http://onlinelibrary.wiley.com/book/10.1002/14356007*
Unified Incident Command and Decision Support (UICDS)	Online	UICDS	*http://www.uicds.us/index.php*
WebWISER (Wireless Information System for Emergency Responders): Online version	Online	NLM	*http://webwiser.nlm.nih.gov/getHomeData.do*
WHO Manual: The Public Health Management of Chemical Incidents	Online	WHO	*http://whqlibdoc.who.int/publications/2009/9789241598149_eng.pdf*
WISER (Wireless Information System for Emergency Responders)	Online	NLM	*http://wiser.nlm.nih.gov/*
Workplace Safety and Health Topics: Chemicals	Online	NIOSH	*http://www.cdc.gov/niosh/topics/chemical.html*

DM

ORIGINAL ARTICLE

Rodent-borne infectious disease outbreaks after flooding disasters: Epidemiology, management, and prevention

James H. Diaz, MD, DrPH

Abstract

Objective: *To alert clinicians to the climatic conditions that can precipitate outbreaks of the rodent-borne infectious diseases most often associated with flooding disasters, leptospirosis (LS), and the Hantavirus-caused diseases, hemorrhagic fever with renal syndrome (HFRS) and Hantavirus pulmonary syndrome (HPS); to describe the epidemiology and presenting clinical manifestations and outcomes of these rodent-borne infectious diseases; and to recommend both prophylactic therapies and effective control and prevention strategies for rodent-borne infectious diseases.*

Design: *Internet search engines, including Google®, Google Scholar®, Pub Med, Medline, and Ovid, were queried with the key words as search terms to examine the latest scientific articles on rodent-borne infectious disease outbreaks in the United States and worldwide to describe the epidemiology and presenting clinical manifestations and outcomes of LS and Hantavirus outbreaks.*

Setting: *Not applicable.*

Participants: *Not applicable.*

Interventions: *Not applicable.*

Main outcome measure: *Rodent-borne infectious disease outbreaks following heavy rainfall and flooding disasters.*

Results: *Heavy rainfall encourages excessive wild grass seed production that supports increased outdoor rodent population densities; and flooding forces rodents from their burrows near water sources into the built environment and closer to humans.*

Conclusions: *Healthcare providers should maintain high levels of suspicion for LS in patients developing febrile illnesses after contaminated freshwater exposures following heavy rainfall, flooding, and even freshwater recreational events; and for Hantavirus-caused infectious diseases in patients with hemorrhagic fevers that progress rapidly to respiratory or renal failure following rodent exposures.*

Key words: Hantavirus, New World Hantaviruses, American Hantaviruses, Sin nombre virus, Bayou virus, Black Creek Canal virus, Hantavirus pulmonary syndrome, Old World Hantaviruses, Leptospira interrogans, leptospirosis, Weil's disease, infectious disease outbreaks, climatic factors, rodent-borne

Introduction

Climatic events, especially heavy rains and flooding following periods of drought, have precipitated both arthropod-borne and rodent-borne infectious disease outbreaks.[1] Heavy rainfall encourages excessive wild grass seed production that supports increased outdoor rodent populations; and flooding forces rodents from their burrows near freshwater sources into the built environment and closer to humans.[1-4] Like arthropods, rodents serve as reservoir hosts and vectors for several pathogens and are typically immune to any pathogenic effects.[3-7] The rodent-borne infectious diseases of greatest medical importance include leptospirosis (LS), Hantavirus, monkeypox, and lymphocytic choriomeningitis virus. Although plague is often considered a rodent-borne disease, rodents are the reservoirs and not the vectors of the plague bacterium, *Yersinia pestis*, which is transmitted by the bites of plague-infected rat fleas.

While most other rodent-borne infectious diseases occur rarely and sporadically, regional outbreaks of LS and the Hantavirus-caused diseases, hemorrhagic

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fever with renal syndrome (HFRS) and Hantavirus pulmonary syndrome (HPS), have occurred following periods of heavy rainfall and flooding worldwide.[3,6-10] As a result, the objectives of this review were to alert clinicians to the climatic conditions, common to monsoon and typhoon seasons in the tropics and hurricane seasons in temperate regions, that can precipitate outbreaks of LS and Hantavirus; to describe the epidemiology and presenting clinical manifestations and outcomes of these rodent-borne infectious diseases; and to recommend prophylactic therapies and effective control and prevention strategies for rodent-borne infectious disease outbreaks.

Methods

Internet search engines, including Google®, Google Scholar®, Pub Med, Medline, and Ovid, were queried with the key words as search terms to examine the latest scientific articles on rodent-borne infectious disease outbreaks worldwide to describe the epidemiology and presenting clinical manifestations and outcomes of LS and the Hantavirus-caused diseases, HFRS and HPS; and to recommend both prophylactic therapies and control and prevention strategies for these infectious disease outbreaks. The key words included Hantavirus, New World Hantaviruses, American Hantaviruses, *Sin nombre* virus, Bayou virus, Black Creek Canal virus, hemorrhagic fever with renal syndrome, Hantatavirus pulmonary syndrome; Old World Hantaviruses; *Leptospira interrogans*, leptospirosis, Weil's disease; and infectious disease outbreaks, climatic factors, rodent-borne.

Results

Epidemiology of leptospirosis outbreaks

LS is now the most commonly reported zoonotic disease worldwide.[3,5] LS has historically occurred in people who have had prolonged contact with freshwater following heavy rains and flooding and is more common in males than females, especially in people who have waded in floodwaters.[3] Unanticipated regional outbreaks of LS following heavy rainfall and flooding events have occurred in the United States, such as after extensive Mississippi River flooding in Iowa in 1993.[10] From 100 to 200 cases of LS are reported every year in the United States with most cases reported from Hawaii, where the incidence is increasing during the rainy seasons and on Kauai, the wettest Hawaiian island.[8,9] LS is also endemic in Louisiana with reservoirs in both rodents and insectivores.[11] Ichinose et al.[11] reported one of the earliest clusters of six fatal cases of LS-caused Weil's disease with hepatorenal failure in Louisiana in 1963. As more than half of LS cases are mild-to-moderate, the hospitalization rate for severe LS and Weil's disease would be anticipated to be less than the incidence rate.[5] In a retrospective study of LS-associated hospitalization in the United States during the period, 1998-2009, Traxler et al.[5] at the CDC reported an annual LS hospitalization rate of 0.6 hospitalizations per 1,000,000 persons with hospitalization rates highest for males aged more than 20 years. In addition to rural flooding victims, the authors also identified two new risk groups for LS in their descriptive analysis including inner city, urban residents and recreational event participants.[5]

Once considered an occupational disease of abattoir and sewer workers, LS outbreaks are now being increasingly reported worldwide among flood survivors, white water rafters, adventure travelers, soldiers, and triathlon and *Ironman* participants.[12-14] The largest US outbreak occurred during a combination of two international triathlon events with more than 1,500 registered participants that featured 1.5 mile lake swims held in consecutive months in Illinois and Wisconsin during the unseasonably rainy summer of 1998.[13] Of 639 single or combined event participants interviewed by telephone, 74 had illnesses consistent with the CDC case definition of LS that included fever with or without chills, headache, myalgia, abdominal pain, eye pain, red eyes, or diarrhea during the month-long period encompassing the two events for an attack rate of 12 percent.[13] The median age of probable cases was 36 years; 80 percent were males; and 54 of 74 case-patients sought medical attention (73 percent), of whom 21 (39 percent) were hospitalized.[13] Among hospitalized patients, two patients manifested jaundice and acute renal failure requiring hemodialysis (Weil's disease), and two underwent exploratory laparotomies for acute abdomens.[12] Acute-phase serum samples from several triathletes

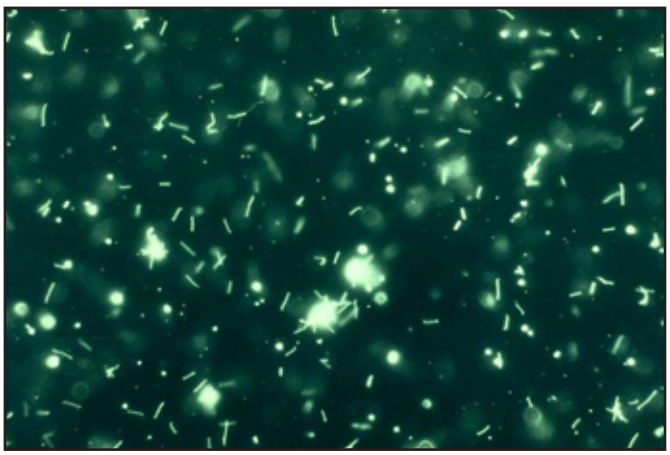

Figure 1. Photomicrograph of a positive leptospiral microscopic agglutination test (MAT) with live antigen using dark-field microscopy. *Source*: US Centers for Disease Control and Prevention. No copyright permission required. Available at *http://www.phil.cdc.gov/phil/details/.asp*.

were positive for LS by enzyme-linked immunosorbent assay (ELISA)-based IgM dipstick tests.[13] As a result of the outbreak, public health authorities temporarily closed the lake in which triathletes participated to swimming, water skiing, and personal watercraft use for further testing.[13]

In 2013, Mendoza et al.[3] described the clinical features and complications of moderate-to-severe LS among patients admitted to nine referral hospitals in the Philippines following a typhoon in September 2009. Of 650 cases of possible LS, only 259 (44 percent) were confirmed by the microscopic agglutination test (MAT) and/or culture (Figure 1).[3] Of the confirmed cases, the mean age was 38.9 ± 14.3 years; and most cases occurred in males (82 percent) who had waded through floodwaters (98 percent).[3] Most patients presented with a nonspecific febrile illness (98.5 percent) with myalgias (78.1 percent), malaise (74.9 percent), and conjunctival suffusion (59.3 percent).[3] Significant complications included renal failure (82 percent), pulmonary hemorrhage (8 percent), meningitis (5 percent), and myocarditis (4 percent).[3] The case fatality rate (CFR) was 5 percent, primarily due to pulmonary hemorrhage.[3]

Socolovschi et al.[4] examined the interaction effects of climatic conditions, socioecological factors, and *Leptospira* prevalence in rodents on the reemergence of LS in Marseilles, France, over 30 years. Three new cases of LS were reported over the study period with the index case occurring after heavy rainfall with flooding.[4] Rats were trapped in the flooded alleys where patients may have acquired LS, and *Leptospira* DNA was detected in two of 11 rats.[4] In addition to heavy rainfall with flooding, the authors identified garbage collection strikes and street-side refuse accumulation as associated with LS outbreaks and concluded that human exposures to floodwaters and the contribution of uncollected garbage to an expanded, well-fed *Leptospira*-infected rat population were the key factors responsible for the reemergence of LS in Marseilles during the study period.[4]

In summary, outbreaks of LS, a reemerging zoonosis in infected, but asymptomatic rodents, have been reported during warm and rainy seasons, such as the monsoon and typhoon seasons in Asia and Polynesia, and the tropical storm and hurricane seasons in the Caribbean and the southeast United States.[3,8-10] The climatic and ecologic factors which can precipitate LS outbreaks have now been defined as seasonal heavy rainfall often with flooding, garbage collection cessation, an endemic *Leptospira*-infected and expanded rodent population, and human exposures to floodwaters or contaminated recreational freshwater bodies. The descriptive epidemiology of LS has also been defined as a febrile infectious disease of adult males with recent freshwater exposures that is subclinical-to-mild in half of the cases and moderate-to-severe in the remaining cases with potentially fatal Weil's disease in 5 percent.[9,13,14]

Epidemiology of Hantavirus outbreaks

Like the leptospires, the Hantaviruses (family Bunyaviridae, genus Hantavirus) are rodent- and insectivore-borne pathogens with a worldwide distribution, except in Antarctica.[15] However, unlike LS, Hantavirus infections may range from hemorrhagic fevers with renal or cardiopulmonary failure and high CFRs to mild flu-like and asymptomatic cases.[15] Among the Old World Hantaviruses (Hantaan, Dobrava-Belgrade, Seoul, Puumala, and others), Hantaan virus was first described as the cause of the HFRS in US soldiers returning from the Korean War

Table 1. Representative species of the Old World and New World Hantaviruses (family Bunyaviridae, genus Hantavirus)			
	Rodent reservoir (common name)	**Rodent reservoir (Latin name)**	**Geographic distribution**
Old World Hantavirus species*			
Hantaan	Striped field mouse	*Apodemus agrarius*	Korea, China, Russia
Seoul	Black rat, Norway rat	*Rattus rattus, Rattus norvegicus*	Asia, Eastern Europe
Thailand	Bandicoot rat	*Bandicota indica*	Southeast Asia
Thottapalayam	Musk shrew	*Suncus murinus*	Pakistan, India, Nepal, Sri Lanka
Puumala	Bank vole	*Myodes glareolus* (formerly *Clethrionomys glareolus*)	Scandinavia, Russia, Europe
Dobrava-Belgrade	Yellow-neck mouse	*Apodemis flavicollis*	Eastern Europe (Balkans), Russia
Tula	European common vole	*Microtus arvalis*	Europe, Russia
New World Hantavirus species†			
Sin nombre	Deer mouse	*Peromyscus maniculatus*	Canada, United States, Mexico
Bayou	Marsh rice rat	*Oryzomys palustris*	Texas, Louisiana
Black Creek Canal	Cotton rat	*Sigmodon hispidus*	Southeast United States, Florida
New York	White-footed mouse	*Peromyscus leucopus*	Canada, US New England States
El Moro Canyon	Western harvest mouse	*Reithrodontomys megalotis*	Canada, Western United States, Mexico
Rio Segundo	Mexican harvest mouse	*Reithrodontomys mexicanus*	Mexico, Costa Rica, Panama
Andes‡	Long-tailed pygmy rice rat	*Oligoryzomys longicaudatus*	Argentina, Chile

*The Old World Hantaviruses are the causative Hantaviruses of hemorrhagic fever with renal syndrome (HFRS).
†The New World Hantaviruses are the causative Hantaviruses of Hantavirus cardiopulmonary syndrome (HCPS).
‡The Andes Hantavirus is the only Hantavirus for which person-to-person transmission has been confirmed.

in the early1950s.[15] All of the Old World Hantaviruses target the kidneys and can cause HFRS (Table 1).

All of the New World Hantaviruses target the heart and lungs and can cause HPS (Table 1). Only Andes virus, which is endemic in South America, is capable of human-to-human transmission.[15] Although the US Hantaviruses cause HPS and not HFRS like the Old World Hantaviruses, both of the Southeastern US Hantaviruses, Bayou virus and Black Creek Canal virus, may cause HPS associated with clinical findings similar to Eurasian strain-caused HFRS including severe myositis, renal insufficiency with elevated creatinine and blood urea nitrogen (BUN) levels, and intra-alveolar hemorrhage.[16-23]

China has the highest incidence of Old World Hantavirus-caused HFRS reported worldwide.[6,7] In 2013, Xiao et al.[6] reported the results of their log-link linear regression model designed to study the impact

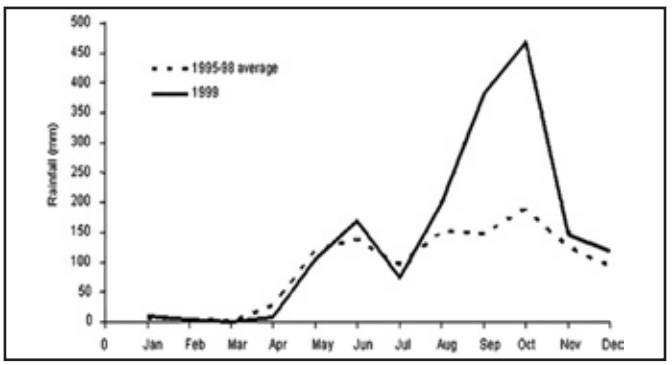

Figure 2. A graphic comparison of the monthly rainfall amounts (mm) in Los Santos Province, Panama, in 1999 (solid line) with the average monthly rainfall during the period, 1995-1998 (dashed line). Atypical heavy rainfall resulted in flooding throughout the dry and deforested region and an increase in the observed rodent population with more frequent contact between rodents and humans. A Hantavirus pulmonary syndrome (HPS) outbreak began in Los Santos in December 1999 and ended in January 2000 with 11 cases and three deaths. *Source*: Ref. 26. Available at *http://www.cdc.gov/eid*.

of atmospheric moisture variability on the transmission of HFRS in mainland China over the study period, 1991-2010. The investigators found a significant correlation between an increasing incidence of HFRS cases and increasing moisture conditions associated with the El Niño Southern Oscillation Index.[6] In addition to the significant association between atmospheric moisture and HFRS incidence, there were statistically significant positive correlations between increasing annual precipitation rates and mean absolute humidity and increasing HFRS incidence.[6] The authors concluded that their atmospheric moisture variability model provided accurate forecasts of new HFRS cases and could be adopted as an early warning surveillance system for HFRS outbreaks in mainland China, where several species of Old World Hantaviruses remain hyperendemic (Table 1).[6]

In 2014, Xiao et al.[7] reported the results of their polynomial distributed-lag model designed to study the impact of natural and socioeconomic variations on the transmission of HFRS in a large city in mainland China over the study period, 2006-2010. They found statistically significant correlations between increasing monthly cases of HFRS and several disease emergence-promoting factors including increasing overall rodent population density, increasing monthly average rainfall and relative humidity, increasing gross domestic product, and increasing urbanization rate.[7] In addition to confirming increased rainfall and humidity as precipitating factors for HFRS outbreaks in China, Xiao et al.[7] identified a new and unanticipated high-risk group for HFRS, specifically middle-income, urban residents.

Over the past 20 years in the United States, 624 cases of HPS have been described with most cases (n = 612, 98 percent) caused by the *Sin nombre* virus (SNV) with its rodent reservoir in deer mice, *Peromyscus maniculatus*, in states west of the Mississippi River.[15,24,25] Although the deer mouse ranges throughout the western United States, it is not indigenous to the southeastern United States or to the Atlantic seaboard states.[15,24,25] The few cases of HPS described in these areas (n = 12) were caused by other species of Hantaviruses each having different, preferred, regional rodent reservoirs (Table 1).

Among the New World Hantaviruses (SNV, Andes, Bayou, Black Creek Canal, New York, and others), SNV was first described in 1993 as the cause of a cluster outbreak of severe pneumonia with respiratory failure or HPS in 24 young patients, 18 of whom died (CFR = 76 percent), in the Four Corners region of the southwestern United States where the borders of Arizona, Colorado, New Mexico, and Utah meet.[24] Engelthaler et al.[25] studied the environmental patterns associated with the initial HPS outbreak in the Four Corners region in 1993. The investigators concluded that the dramatic increase in high-desert rainfall associated with the 1992-1993 El Niño Southern Oscillation contributed to the risks of SNV exposure in the region; and that annual precipitation predictions would be of value in designing disease prevention campaigns.[25]

Following months of heavy rainfall and flooding, the first outbreak of HPS in Central America occurred in late 1999 and early 2000 in Los Santos Province on the Pacific Coast of Panama with 11 human cases, nine confirmed serologically, and three deaths (Figure 2).[26] Unlike the HPS outbreaks described earlier in North and South America, the Panamanian outbreak

was characterized by atypical epidemiological features and clinical manifestations.[26] Atypical epidemiological features included 1) a significantly lower CFR (25 percent) than in other New World HPS outbreaks; 2) household surveys of previously infected persons that confirmed frequent direct contact with rodents or their excreta; 3) rodent trapping of a Hantavirus seropositive rodent, *Oligoryzomys fulvescens*, the fulvous pygmy rice rat, in the household of a confirmed HPS case-patient that was infected with a new strain of Hantavirus, the *Choclo* virus; and 4) a significant increase in rainfall compared to previous years that preceded the HPS outbreak and was associated with unusually large numbers of confirmed rodent sightings by the residents (Figure 2).[26]

Compared to the typically symptomatic manifestations of fever, cough, myalgia, hypotension, dyspnea, and pneumonia that characterized North and South American HPS case-patients, only five (12.5 percent) of 40 antibody-positive participants in the Los Santos household survey recalled having fever or myalgia during the outbreak period of December 1999 to January 2000; most only reported mild flu-like symptoms of rhinorrhea (45 percent), sore throat (35 percent), and cough (22 percent); and two seropositive participants were virtually asymptomatic with one reporting cough only.[26] Therefore, not all Hantavirus infections are symptomatic, and mildly symptomatic and asymptomatic, but seropositive, infections have now been described.[26]

In summary, the climatic and ecologic factors that can precipitate Hantavirus outbreaks have now been defined as increasing monthly average rainfall and humidity often associated with flooding, increasing rodent population density for both HFRS and HPS, and increasing gross domestic product and urbanization rate for HFRS in mainland China. The descriptive epidemiology of Hantavirus infections has been stratified into two regionally distinct presenting syndromes: 1) regional HFRS caused by the Old World Hantaviruses and 2) regional hemorrhagic fever associated with pneumonia and cardiorespiratory failure caused by the New World Hantaviruses (Table 1). The person-to-person transmission of HPS has only been confirmed in Andes virus infections in South America.

Discussion

Leptospires are motile spirochetes of the family Leptospiraceae with nearly 300 serotypes divided into human pathogenic strains and saprophytic strains. The larger group of pathogenic leptospires comprises the *Leptospira interrogans sensu lato* complex with more than 200 serotypes. Although many wild and domestic mammals serve as reservoir hosts for leptospires in their kidneys, rodents, primarily rats and mice, are the most common reservoirs worldwide. Asymptomatically infected rodents excrete leptospires in their urine which proliferate in freshwater, mud, moist soil, and wet vegetation and remain viable and infectious for months.[8-10] As heavy rains and flooding saturate soil and surface vegetation, leptospires percolate into ground and surface waters contaminating large inland freshwater systems, including lakes and rivers.

Human LS infections are transmitted most commonly by direct or indirect contact of mucous membranes, including conjunctivae, or abraded or broken skin with urine from infected rodents or contaminated surface waters.[13,14] Less common modes of transmission include rodent bites, ingestion of rodent-urine contaminated water or food, inhalation of infectious aerosols of rodent excreta, congenital transmission, and transmission following breast feeding, blood transfusions, and organ transplants.[13,14] Person-to-person transmission is possible, but rarely described.[14]

After an incubation period of 1-30 days (mean 7-14 days), LS displays a wide spectrum of clinical manifestations ranging from a mildly symptomatic, almost subclinical, infection as in most cases; to a constellation of abrupt fever, headache, myalgias, nausea, vomiting, diarrhea, and an occasional maculopapular rash that resolves in a week; to a biphasic illness that starts with fever, myalgias, and conjunctival suffusion in the first week, and in 5-10 percent of cases progresses to icteric LS or Weil's disease (LS *icterus hemorrhagica*).[8] Weil's disease is characterized by jaundice, thrombocytopenia, acute renal failure, respiratory distress, and cardiac arrhythmias. Weil's disease occurred in two patients in the triathlon outbreak and has a 5-10 percent CFR with males experiencing more severe illnesses and fatalities than females.[13]

The differential diagnosis of LS is broad and includes most febrile infectious diseases including HPS and relies on a careful exposure history and clinical suspicion supported by serologic testing. Dipstick screening tests using ELISA to detect serum IgM antibodies to leptospires are quick and easy to perform but do not cover all serotypes of pathogenic *L. interrogans*. The MAT is the most reliable test for LS but is more time consuming, and only offered by reference laboratories, such as the CDC (Figure 1). As IgM antibodies cannot be detected until 5-7 days into the illness, acute serologic tests may be negative initially and positive later in the illness and during convalescence. Cultures of leptospires from blood or urine are time consuming and of limited value in management. Antibiotic therapy with oral doxycycline, ampicillin, amoxicillin, erythromycin, or azithromycin is recommended for mild cases; with intravenous therapy with ceftriaxone or penicillin G recommended for severe cases. Chemoprophylaxis with doxycycline, 200 mg/wk, has an efficacy rate of 95 percent and should be considered for soldiers on training maneuvers and for triathletes participating in competitive swimming or paddling events in LS-endemic regions.[13]

Although vaccines are under development for LS, none are universally available today; the best preventive strategies for LS include drinking boiled or bottled water and minimizing exposure to rodent-urine contaminated environments by wearing waterproof boots and clothing. All cuts and abrasions should be covered with waterproof dressings. Triathletes participating in distance swimming events, kayakers, and whitewater rafters should wear waterproof goggles to prevent transconjunctival transmission and avoid submersion in and ingestion of river water.[12,13] All healthcare providers should maintain high levels of suspicion for LS after flooding events and freshwater immersions; and public health officers should immediately promote heightened awareness of LS outbreaks among all flood-affected populations.

Unlike most LS cases, Hantavirus cases are typically symptomatic and characterized by fever and respiratory distress. Humans become infected by inhalation of aerosolized Hantavirus virions from rodent excreta, or, less commonly, by rodent bites (one of 10 cases in the Yosemite HPS outbreak), often during sweeping and cleanup of rodent habitats within closed spaces.[27] Following an incubation period of 9-33 days (median = 14-17 days), patients with HPS develop a prodromal febrile syndrome with chills, headache, myalgias, and vomiting followed within 3-7 days by a cardiopulmonary phase with hypotension, cough, dyspnea, pulmonary edema, and respiratory failure requiring mechanical ventilation. At present, the person-to-person transmission of HPS has only occurred during outbreaks caused by the Andes virus in South America (Argentine and Chile).[15] HFRS follows similar prodromal patterns to HPS and manifests similar initial presenting manifestations followed within 3-7 days by rapidly progressing renal insufficiency. Thus far, the person-to-person transmission of Hantaviruses causing HFRS has not been demonstrated. Associated hematological findings in HPS include hemoconcentration, thrombocytopenia, and left-shifted granulocytosis. An early, pathognomonic immunological response in HPS is the appearance of circulating immunoblasts which herald the end of the prodromal phase and the onset of the cardiorespiratory phase. Hypoalbuminemia, elevated hepatic enzymes, and hyperbilirubinemia with jaundice may occur in HPS and HFRS.

As all available serologic tests for the diagnosis of HPS are broadly cross-reactive with all of the New and Old World Hantaviruses, specific Hantavirus identification requires polymerase chain reaction (PCR) with sequencing with acute specimens collected early in the illness and shipped to reference laboratories frozen to preserve RNA for analysis. As there is no vaccine or specific antiviral therapy, including ribavirin, for HPS or HFRS, only early diagnosis and intensive supportive care, potentially including extracorporeal membrane oxygenation (ECMO) and inhaled nitric oxide (NO) administration will reduce the high CFRs from HPS.[27] HFRS is managed supportively with a variety of extracorporeal renal replacement therapies, including hemodialysis. Clinicians should always consider a diagnosis of HPS or HFRS in persons with febrile illnesses that progress rapidly to respiratory or renal insufficiency following rodent exposures in enclosed spaces.

Eradicating all rodent reservoir hosts for both pathogenic leptospires and Hantaviruses is both impractical because of the widespread distribution of rodents and undesirable because of the importance of rodents as competent insectivores and prey for larger predators in the ecosystem.[28] The best and most effective strategies for the control and prevention of rodent-borne infectious diseases include storing all unrefrigerated foods including pet foods in thick plastic, glass, or metal containers with tight-fitting lids; limiting contact with all wild and peridomestic rats and mice; avoiding all contact with rodent excreta; safely disposing all rodent excreta; and modifying the built environment to deter rodents from frequenting and colonizing households and workplaces.[28] Only spring-loaded traps that kill rodents should be deployed as live and sticky traps do not kill rodents which can bite humans during disposal transmitting Hantaviruses and creating open wounds for potential LS transmission.[27] While struggling to get free of nonlethal traps, rodents chronically infected with leptospires or Hantaviruses may urinate and/or emit infectious aerosols contaminating enclosed spaces.[28] All areas inhabited by rodents should be cleaned with mops wetted with dilute bleach solutions rather than swept or vacuumed which could create infectious aerosols. Interested readers are referred to the *Morbidity and Mortality Weekly Reports* (*MMWR*) *Recommendations and Reports* Series Number 9, 2002, for a listing of all CDC-recommended strategies to limit household and outdoor exposures to rodents, to rodent-proof households and workplaces, to select the best disinfecting solutions to clean up rodent excreta and nesting materials, and to safely dispose of dead rodents and their nests.[28]

Conclusions

Healthcare providers should maintain high levels of suspicion for LS in patients developing febrile illnesses after contaminated freshwater exposures during flooding disasters or freshwater recreational events and military maneuvers; public health officers should immediately promote heightened awareness of LS outbreaks among all flood-affected populations. Clinicians should consider a diagnosis of HPS in all persons with febrile illnesses that progress rapidly to respiratory insufficiency in New World Hantavirus-endemic regions following rodent exposures in enclosed spaces. Clinicians should consider a diagnosis of HFRS in all persons with febrile illnesses that progress rapidly to renal insufficiency in Old World Hantavirus-endemic regions following rodent exposures in enclosed spaces. Public health educational strategies should encourage limiting human contact with all wild and peridomestic rats and mice; avoiding all contact with rodent excreta; safely disposing all rodent excreta; and modifying the built environment to deter rodents from colonizing households and workplaces. The causative agents for LS and Hantavirus are widely distributed worldwide and will continue to cause sporadic outbreaks of potentially fatal illnesses often precipitated by cyclical climatic conditions associated with heavy rainfall and flooding.

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James H. Diaz, MD, DrPH, Environmental/Occupational Health, LSU School of Public Health, New Orleans, Louisiana.

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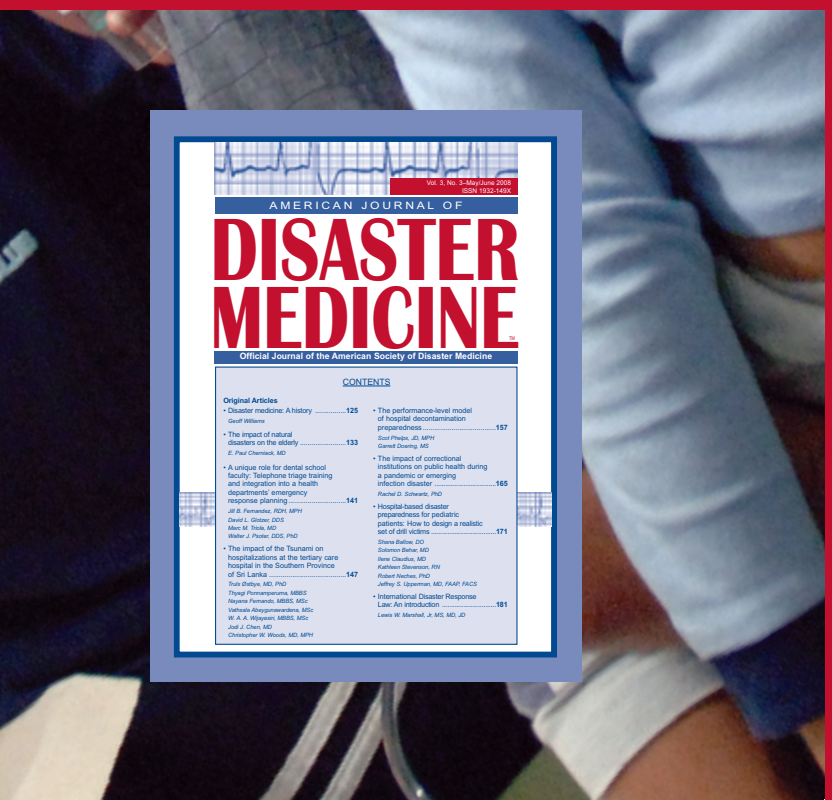

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