

BIOTERRORISM WATCH

Preparing for and responding to biological, chemical and nuclear disasters

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Epidemiologic clues, alert clinicians key to detect covert chemical attack

But many obstacles still hinder early detection

Drawing upon a real-world lesson from the past, medical toxicologists recently recalled the 1983 Tylenol poisoning case in Chicago as an example of how a bioterrorism attack involving chemicals may begin to unfold. Though product-tampering protections have been improved, disturbing aspects of the case include how easy it was to accomplish and the fact that the perpetrator was never caught.

In 1983, seven sudden deaths occurred over a two-day period in several different suburbs of Chicago. At first, the deaths appeared to be unrelated. It was thought the first patient died of a stroke, and the second appeared to have suffered a massive heart attack. "But an astute physician at a Chicago area hospital grew suspicious when two family members of the first victim were admitted to the hospital with severe hypotension and unexplained acidosis," said **Martin Belson, MD**, a medical toxicologist at the Centers for Disease Control and Prevention (CDC) at a CDC satellite training broadcast. ". . . The physician reported the cases to the regional poison control center; and based on the signs and symptoms, cyanide was suspected and subsequently confirmed. The investigation into the deaths progressed when two observant off-duty firefighters made the connection of the deaths to Tylenol."

Subsequent investigation by law enforcement and public health agencies revealed that eight bottles of Tylenol had been removed from six different Chicago area stores over a period of weeks to months, and then placed back on the shelves of five different Chicago area stores. "Previous events, some very recent, involving intentional or inadvertent contamination of food or product tampering with chemicals have highlighted the need for physicians and public health officials to be at heightened alert for patients in their communities who have signs and symptoms consistent with chemical exposures." Belson said.

A priority in the Tylenol investigation was to determine the location where the tampering took place. Because the cyanide-laced Tylenol was discovered in shipments from more than one plant and

had only turned up near Chicago, investigators concluded that any tampering occurred at the retail level. More problematic would be a chemical poisoning of food, water, or consumer products at a location such as a distribution facility. "Unless detected early, the ongoing community-wide exposure may continue through the distribution chain," said **Manish Patel**, MD, MSc, a medical toxicologist at the CDC. "This might result in reports of illness to physicians over a long period and in various locations, such as grocery stores and pharmacies, through the city, state, or possibly across the country."

Patel and Belson were the principal faculty in the broadcast on recognizing and responding to

an intentional release of a chemical agent. Such an attack may be a covert or overt event.

"Examples of an overt event include a large explosion of a chemical container or a release of a nerve agent in a subway, such as the Tokyo sarin attacks in the 1990s," Belson said.

More insidious would be an unrecognized release in which the presentation of sick patients might be the first sign of an exposure. "An example of a recent covert event would include the ricin incidents where castor beans were ground up and ricin was extracted and put into the mail system with the specific intent of harming individuals," Patel said.

Another real-world example described during the program occurred in Michigan in January 2003, when 18 people from four families became ill after eating ground beef. Symptoms included nausea, vomiting, and a burning sensation in the mouth. One patient developed atrial fibrillation, but none had to be hospitalized. Officials recalled approximately 1,700 pounds of ground beef. Overall, 120 people returned the recalled product, and 36 more people reported being ill. It eventually was discovered that the product was contaminated at a single store rather than at the processing plant. The local health department alerted hospital emergency departments and local medical practices. In all, 92 people had an illness consistent with nicotine poisoning after eating the contaminated beef.

"An employee of the supermarket intentionally poisoned 200 pounds of beef with a nicotine containing insecticide," Patel noted. "He was subsequently arrested and indicted."

Prevention of such attacks is a challenge because of the large number of toxins and chemical agents and the infinite combination of agents and dissemination scenarios, Belson said.

"Despite some difficulties in recognizing illness from a covert exposure, there are ways to overcome the challenges. Early recognition of illness associated with these types of exposures is vital because early detection of an outbreak has the greatest potential for limiting the scope of the illness."

Obstacles to early detection

However, there are many obstacles to early detection of a chemical attack, including the possibility that initial symptoms will not be dramatic. "Chemicals do not always cause acute and obvious health effects," Patel added. "Immediate symptoms of chemical exposures might be nonexistent or mild despite the risk for long-term effects. Because

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of this lag time, it may be difficult for us to recognize the exposure source leading to the illness."

By the same token, some chemicals can cause nonspecific illness resembling other common natural illnesses. Chemical poisoning is notorious for resulting in signs or symptoms that resemble other common diseases, Belson noted. For example, arsenic is very likely to resemble viral gastroenteritis, he said.

"Acute lead poisoning may lead to neurologic emergencies such as status-epilepticus or encephalopathy that may be misdiagnosed initially as meningitis," Belson said. "Cyanide, a potent cellular poison, will lead to shock and acidosis, which could easily be mistaken for more common causes of shock such as acute cardiac failure and sepsis."

Many clinicians are not familiar with chemical-related illnesses, making initial diagnosis all the more problematic. "There are very few clinicians in the world, much less this country, who have ever seen a case of ricin poisoning," Patel said. "However, ricin is a potential agent of chemical terrorism. Poisoning from metals such as thallium, mercury, and arsenic also is not commonly seen."

Given that it is difficult to recognize an illness related to a single covert exposure, an attack involving more than one chemical agent might be all the more confounding. "Initially, I would recommend treating the patient's signs and symptoms at hand; however, for admitting physicians and public health officials, it may be prudent to consider a wider differential and make use of available environmental and biological screening tests to rule out other reasonable causes of illness," Patel said.

Despite some difficulties in recognizing illness from a covert exposure, there are ways to overcome the challenges, Belson said. "Ultimately, it involves familiarity with the epidemiologic clues and the syndromic presentations of chemical agents exposures," he said. For example, the first clue suggesting a covert release of a chemical agent might be an increase in the number of patients seeking medical care.

"These patients may seek care in clusters all in the same day or may be spread out over time, such as over a period of weeks," Belson said. Establishing thresholds of poison reports and other trigger mechanisms can be used in public health to sound the alarm.

"It's important to not only recognize this on the local level but also on a national level in order to identify trends or patterns of illness at other

locations throughout the country," he said. "This would be crucial in a potential widespread terrorist act."

Look for common exposure

Another epidemiologic point of investigation is determining whether a cluster of illness is occurring in people who have a common exposure. "The Michigan ground beef incident we discussed earlier is a perfect example," Patel said. "In this outbreak, there were four families with 18 people who initially became ill over a two-day period. As it turned out, all of the ill people ate beef purchased from the same store prior to becoming ill."

An epidemiologic clue suggesting covert release of a chemical agent is the unexplained death of plants, fish, or animals, either domestic or wild. "For example, just this past spring, CDC and state and local health officials investigated the death of several dogs shortly after the dogs swam in a lake in Nebraska," Belson said. "Their deaths were attributed to a toxin released from Microcystins, a blue-green algae, found on autopsy and in the lake water. Fortunately, no significant illness occurred in humans living around the lake, but the death of the dogs alerted public health officials to a potential human health threat."

Another clue that immediately should raise suspicions is death among young or healthy people. "In recognizing covert CT (chemical terrorism) events, the key message to remember is that it will really involve recognition of patterns rather than individual cases," Patel said. "The pattern to recognize will involve a combination of epidemiologic clues and clinical syndromes."

One classic example of a clinical syndrome that clinicians should be aware of is cellular hypoxia, he said. "When we talk of agents that cause cellular hypoxia, we are talking about chemicals that impair the ability of our body's cells to utilize oxygen," Patel said. "The hallmark of toxicity in this syndrome is acidosis, particularly unexplained acidosis. Again, an isolated case of unexplained acidosis is not something that would tip off clinicians; however, if combined with the epidemiologic patterns we discussed earlier, a CT event should be considered."

Indeed, Belson added, one reason the Tylenol cyanide outbreak in Chicago was detected early was because an astute clinician recognized the unusual pattern of unexplained acidosis in two family members. ■

Do you know where your alternate care site is?

'In Northern Montana, you want heating'

The Agency for Healthcare Research and Quality (AHRQ) has created a tool to help state and local officials quickly locate alternate health care sites if hospitals are overwhelmed by patients due to a bioterrorism attack or other public health emergency.

The alternate care site selection tool, produced by Denver Health, one of AHRQ's Integrated Delivery System Research Network (IDSRN) partners, was shared with emergency response planners at the 2004 Summer Olympics in Athens, Greece. The IDSRN program links the nation's top researchers with some of the largest health care systems to conduct fast-track research on cutting-edge issues in health care.

In the aftermath of a bioterrorist event or other public health emergency, hospitals may be overwhelmed by a sudden influx of patients, AHRQ explains. The new alternate care site selection tool is designed to allow regional planners to locate and rank potential alternative sites — stadiums, schools, recreation centers, motels, and other venues — based on whether they have adequate ventilation, plumbing, food supply, and kitchen facilities, for example.

Old West has new ideas

The effort to develop the tool began in October 2002, recalls **Stephen Cantrill**, MD, associate director in the department of emergency medicine at Denver Health Medical Center. "It started with a task order from AHRQ that dealt with regional planning for bioterrorism. We brought together partners from all of Federal Region 8 [Colorado, Utah, Wyoming, Montana, and North and South Dakota]." The team included representatives from state departments of health, medical societies, and all the large hospital groups in the Denver Metro area. Federal partners included the Public Health Service; the U.S. Northern Command in Colorado Springs, CO; the VA; and FEMA.

"We built on some of the earlier work that had been done by the command in terms of criteria," Cantrill says. "We enhanced those, developed a kind of a grading scale to be used to look at facilities to be able in a gross way to determine the

acceptability of potential alternative care sites — i.e., whether they fulfilled specific needs."

The tool includes a list of about 30 different attributes, such as availability of toilet facilities, availability of communication lines, availability of a food service area, and so on.

"Basically, it's a big spread sheet," Cantrill explains. "You go down, put your potential sites on one axis, your needs on another, rate them on a 0-5 scale (5 being the highest), add up your total, and see if it makes logical sense."

This process aids you in prioritizing different potential sites, to see which would be best to use, he says. "In an ideal situation, you do this as part of your advanced planning," he advises, so you are prepared if traditional health care sites are overwhelmed in a bioterror event and you need alternative sites to give limited care to patients.

While much of the data were specific to his region, Cantrill says the new tool demonstrates an approach of assessment of resources in any given region. "We tried to develop some generalized tools," he notes. "Naturally, there are variables, like the time of year, the nature of the incident. If it's summertime, you may not care if you have heating, but you will want air conditioning. In Northern Montana, you want heating."

Therefore, he notes, there is no magic number in terms of a total score for a given alternative site. "What the tool does," says Cantrill, "is give you the ability to do relative scaling."

(Editor's note: The alternate care site selection tool is available free of charge as an Excel spreadsheet on AHRQ's web site at www.ahrq.gov. It also is included in a report — Rocky Mountain Regional Care Model for Bioterrorist Events. Copies of this report are available on the AHRQ Web site at www.ahrq.gov/research/altsites.htm.) ■

Investment in bioterror refueling public health

But preparation is a journey, not a destination

The massive public health investment to prepare for bioterrorism is paying for itself in the widespread benefits of an improved public health infrastructure, said **Julie Gerberding**, MD, MPH, director of the Centers for Disease Control and Prevention.

"I do take some pride at times in boldly stating

that of all the investments we are making in homeland security in our country, it is the public health investment that is absolutely guaranteed to pay off," she said. "And in fact, it already has paid off, and it will continue to pay off even if we never have another terrorist attack. The reason it's paying off is because our public health infrastructure — at least our infrastructure's capability to respond to emerging threats — is evolving in the context of the investments that are being made."

Delivering the keynote address recently in Washington, DC, at the 1st National Congress on Public Health Readiness, Gerberding said bioterrorism preparations have helped break down the barriers between public health and clinical settings. The conference was cosponsored by the CDC and the American Medical Association, and fittingly, the theme was the increasingly strong

marriage between clinical and public health.

"We've got communication. We've got networking," Gerberding said. "We know how to identify clinicians. The system is much further evolved than it was three years ago. We have more to do, but we have made substantial progress."

But preparing for bioterrorism is more of a journey than a destination. "A lot of times people ask me 'Well, are we prepared?' And the answer to the question is, 'It's the wrong question,' because preparedness is not a black and white event. It's not yes or no, on or off. Preparedness is a process; and it is an ongoing process, and it will continue to be an ongoing process of improvement over time."

While much has been accomplished, "you can still always imagine a scenario that's one step beyond where you are today," she said. The CDC and state and local health departments have made

Biodefense company pitches novel virus binder to feds

Seeking Project Bioshield R&D money

Biodefense firm Aethlon Medical Inc. in San Diego has developed a hemopurifier cartridge is capable of binding and removing a wide variety of blood-borne pathogenic viruses before they can infect cells and organs, according to a report posted on the firm's web site.

The company is pursuing federal government funding under Project Bioshield, a \$5.6 billion program that President Bush signed into law July 21, for further development of the hemopurifier cartridge.

Aethlon Medical is pioneering the development of viral filtration devices to treat pathogens that are mass-casualty biological warfare candidates. In pre-clinical human blood studies, the device has demonstrated the ability to remove HIV, hepatitis C virus, and related protein toxins from infected blood, according to the report.

The report is co-authored by **Ken Alibek**, MD, PhD, DSc, a former researcher in the Soviet Union's biological weapons program who defected to the United States in 1992. The report's other author is also high profile: Charles Bailey, PhD, former commander of the U.S. Army Medical Research Institute of Infectious Diseases. The authors "currently serve unpaid on Aethlon Medical's Science Advisory Board, which they joined in the spring of 2004. It is possible that they may be compensated for future consulting work for the company," the report states.

Each treatment application employs the use of a proprietary technology known as the hemopurifier, which is designed to rapidly reduce the presence of

infectious disease and toxins in the body. The hemopurifier converges the established scientific principals of affinity chromatography and hemodialysis as a means to augment the immune response of clearing viruses and toxins from the blood before cell and organ infection can occur, the report states.

The new product is a modified hollow-fiber hemodialysis cartridge containing an affinity matrix comprised of antibodies, lectins, or antisense DNA that selectively removes pathogenic viruses, bacteria, and toxins from circulating blood, the report adds. The hemopurifier technology can be rapidly developed, tested, and deployed to remove new resistant strains of biological warfare agents from soldiers and civilians, the company claims. In contrast to the situation with drugs and vaccines, development and initial deployment times of a few months are feasible even for a new agent.

"For example, should a terrorist group develop a new vaccine-resistant strain of smallpox, Aethlon need only find or generate an antibody that reacts with the new virus or toxin," the report states. "Once an antibody is available, Aethlon can build, and test a new hemopurifier in a few weeks. In a recent test scenario, Aethlon made and tested a new binding agent in six days."

In civilian use, the hemopurifier treatment would most likely be implemented in intensive care facilities staffed by trained medical personnel. In the ICU, many patients currently are treated for acute renal failure as the result of trauma or surgery. Such facilities have the equipment and expertise to establish an extracorporeal circuit and pump the patients' blood through the Hemopurifier, according to the report.

(Editor's note: To view the full report, go to the company's web site at www.aethlonmedical.com.) ■

major strides in preparedness planning and readiness assessment, surveillance and epidemiological response, laboratory capacity, communications and information technology, risk communication, education, and training, she said. "The beauty of this investment is, of course, its multifactorial benefit."

A tsunami of federal bio money

The investment in bioterrorism preparedness includes Project Bioshield, a \$5.6 billion program that President Bush signed into law on July 21, 2004. "BioShield is a federal project to purchase and develop countermeasures on an emergency basis to more rapidly develop and, hopefully in some cases, take these threats off the table," Gerberding said. (See related story, p. 45.)

The federal government also has formed Biowatch, a system of environmental detection in several cities around the country that samples air for a certain category of agents. The samples are sent to the laboratory response network for evaluation and ultimately for triage if there is a need for a public health response, she noted.

"But we can't have Biowatch in isolation, or you'd have nothing but chaos in the system. So we have to support Biowatch with other means of threat assessment. And one of these is Biosense, which is our electronic capability to collect health information from existing resources and interpret trends in those data as additional points of information in the context of local health. Right now, we're getting about 500,000 laboratory reports everyday from national sources," Gerberding said.

The surveillance system culls data on over-the-counter drug purchases, nursing hotlines, and other sources that may signal an unfolding bioterrorism attack, she added. "Ultimately, this connectivity that CDC is building for detection and response is something that is very integrally tied to the medical community and hopefully will be a very useful tool for the entire health system."

Alert clinician still is the key

In that regard, no matter how evolved the infrastructure, the alert clinician remains the key aspect of bioterrorism response. The lessons learned dealing with the 2001 anthrax attacks and emerging infections like monkeypox underscore the critical role of the clinician, Gerberding added.

"We know that the prepared clinician is the frontline of defense for recognizing many of the emerging threats and terrorism threats that we're

concerned about. It was the infectious disease doctor in Florida who had the foresight to recognize that those gram-positive rods in the spinal fluid were not contaminants and clearly represented most likely anthrax," she notes.

Similarly, an alert clinician recognized that West Nile virus was causing encephalopathy in organ transplant recipients. An Italian physician, who ultimately died of severe acute respiratory syndrome, was the first to report the emerging infection posed grave risk to health care workers, said Gerberding. "And it was an alert clinician who recognized the small lesion on the hand of a child represented a pox infection and connected that pox infection with the sick prairie dog that the child was handling. . . . And it is the clinician who ultimately will be the arbitrator of the countermeasure delivery — these are medical products, these are medical assets, and they, in large part, will be managed by medical personnel."

In addition, frontline clinicians will make the decisions about management of patients, separating those who need treatment from the worried well. "We learned head on in the middle of anthrax [about] the worried well and the confusion about who needed prophylaxis and who didn't," she explained. "It's the clinician who has to stand in front of the patient and make those decisions." ■

Top-down bio plans err on public cooperation

People will be full of fear and distrust

Skeptical about government instructions and concerned about loved ones, many Americans would not follow established plans in the event of a real bioterrorism attack, according to a new study by the Center for the Advancement of Collaborative Strategies in Health at The New York Academy of Medicine.

Current plans have been created in a top-down style, telling people what to do in the event of an attack without considering all of the risks and concerns that drive people's actions, the investigators found. The study found that only two-fifths of people would follow instructions to go to a public vaccination site in a smallpox outbreak, and only three-fifths would stay inside an undamaged building other than their home after a dirty bomb explosion.

"It's not that the rest of the people want to be uncooperative," says lead investigator **Roz Lasker, MD**, director of the center and of the academy's division of public health. "The problem is that current plans unwittingly put them in extremely difficult decision-making predicaments. So even if first responders work out all of the challenging logistics, far fewer people would be protected than planners want or the public deserves."

Reducing the risk

Though current plans will put many people unnecessarily at risk, immediate actions can be taken to dramatically increase their effectiveness, said Lasker. "Our study shows that if planners listened to and learned from the public, they could protect many more people," he says.

Redefining Readiness: Terrorism Planning Through the Eyes of the Public was based on interviews with government and private-sector planners, group discussions with diverse community residents around the country, and a telephone survey of 2,545 randomly selected adults in the continental United States. Many people fear the smallpox vaccine more than the disease, possibly undermining vaccination efforts, the research found. The study also shows that two-thirds of respondents would try to avoid being with strangers in a smallpox outbreak, suggesting they would be reluctant to report to vaccination sites. Concern for their loved ones was the primary reason cited by people who said they would not fully cooperate with instructions to stay inside the building after a dirty bomb. The report includes model plans to bring the public in and prevent such problems.

For example, the study's proposed smallpox plans include specific strategies that protect both the people who are at risk of contracting smallpox and the people who are at risk of developing serious complications from the vaccine. The study's dirty-bomb response calls for the development of safe-haven plans in the broad array of places where people are likely to be when an attack occurs, such as work sites, shops, malls, schools, day-care centers, and entertainment facilities.

(Editor's note: The full report is available at www.cacsh.org/eptpp.html.) ■



JOURNAL REVIEW

Rusnak JM, Kortepeter M, Ulrich R, et al. **Laboratory exposures to staphylococcal enterotoxin B.** *Emerg Infect Dis* 2004. Web site: www.cdc.gov/ncidod/EID/vol10no9/04-0250.htm.

Outside the context of food poisoning, few physicians would have experience evaluating people with staphylococcal enterotoxin B (SEB) intoxication. However, an increase in lab exposures and intoxications with staphylococcal enterotoxins can be expected as more institutions work with them due to increased funding for biodefense research, the authors said. "Health care workers evaluating persons who work with SEB need to be aware of the full spectrum of toxicity symptoms associated with SEB to avoid misdiagnosis resulting in unnecessary treatment, to identify breaches in laboratory technique, and to educate persons at risk of the importance of personal protective measures in preventing SEB exposure and intoxication. These cases emphasize that personal protective measures such as biosafety cabinets, gloves, and eye protection are paramount when working with SEB."

They reported three cases of purulent conjunctivitis with localized facial swelling that occurred after ocular exposure to SEB in the lab. Two of the patients also complained of gastrointestinal symptoms. The symptoms in the three mucocutaneous-acquired cases, and summary of symptoms from 16 lab-acquired inhalational intoxications with SEB, may help define the clinical spectrum that might be expected after exposures. The full spectrum of clinical signs and symptoms of intoxication with SEB is important to health care workers evaluating people with potential exposures to these agents, including bioterrorism. This discussion is relevant to military practitioners, since SEB previously has been developed as an incapacitating biowarfare agent.

Three events that occurred during the now disbanded U.S. offensive biologic warfare program resulted in inhalational exposures to SEB and subsequent intoxication. During that program, a contractor report on the efficacy of biosafety cabinets noted toxic reactions in those performing SEB purification studies on open lab benches. Symptoms seen in six people: conjunctivitis, nondescript

COMING IN FUTURE MONTHS

■ Should bioterror research be done openly?

■ A historical primer on bioterror

■ GAO stamps postal service for anthrax response

■ When the patient may be the terrorist

chemical irritation of one eye, general skin reaction, severe facial skin reaction, dermatitis, and cold symptoms. Conjunctivitis and acute pharyngitis, plus vomiting and diarrhea in two cases, were observed in 23 people wearing surgical masks or face shields while working with SEB. Those working within a biosafety cabinet had no symptoms. ■

CE/CME questions

9. Obstacles to early detection of a chemical attack include:
 - A. Initial symptoms may not be dramatic.
 - B. Chemicals can cause nonspecific illness resembling natural illnesses.
 - C. Many clinicians are not familiar with chemical-related illnesses.
 - D. all of the above
10. In the aftermath of a bioterrorism event or other public health emergency, hospitals may be overwhelmed by a sudden influx of patients. A new tool is designed to allow local regional planners to locate and rank:
 - A. triage resources
 - B. mobile care units
 - C. alternative care sites
 - D. all of the above
11. According to Julie Gerberding, MD, MPH, the answer to "Are we prepared for bioterrorism?" is:
 - A. yes
 - B. no
 - C. maybe
 - D. It's the wrong question.
12. Skeptical about government instructions and concerned about loved ones, many Americans would not follow established plans in the event of a real bioterrorism attack, according to a new study.
 - A. true
 - B. false

Answer Key: 9. D; 10. C; 11. D; 12. A

Supplement goes on-line beginning January 2005

Starting with the January/February 2005 issue, *Bioterrorism Watch* will be on-line at www.hospitalemployeehealth.com and www.HIConline.com, exclusively for subscribers of *Hospital Employee Health* and *Hospital Infection Control*. The issues will be available in HTML and PDF formats for easy reading. Just log on to print out a copy. For more information, call customer service at (800) 688-2421. ■

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To clarify confusion surrounding any questions answered incorrectly, please consult the source material. **After completing this semester's activity with this issue, you must complete the evaluation form provided and return it in the reply envelope to receive a certificate of completion.** When your evaluation is received, a certificate will be mailed to you. ■

CE/CME objectives

After reading each issue of *Bioterrorism Watch*, the infection control professional will be able to do the following:

- identify the particular clinical, legal or educational issue related to bioterrorism;
- describe how the issue affects health care providers, hospitals, or the health care industry in general;
- cite solutions to the problems associated with bioterrorism, based on guidelines from the federal Centers for Disease Control and Prevention or other authorities, and/or based on independent recommendations from clinicians and bioterrorism experts. ■