

# BIOTERRORISM WATCH

Preparing for and responding to biological, chemical and nuclear disasters

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## Will an ancientcrippler find new legs through bioterror?

*As global eradication nears, questions arise about polio*

Disease eradication in the current age of bioterrorism inevitably raises the possibility of a defeated pathogen being weaponized. Thus, though smallpox has been eradicated in nature, it lives on as a potential bioweapon. Indeed, smallpox literally remains alive in the known world repositories to enable research that could limit its effectiveness in a bioterrorism attack. (See related story, p. 27.)

Now comes a similar scenario with polio. Some 125 countries had endemic polio cases in 1988, but now that number has been winnowed down to only six nations. The number of cases of paralytic polio — which was 1,000 per day in 1988 — occurred less than 800 times all of last year, according to **David Heymann, MD**, executive director for communicable diseases at the World Health Organization (WHO) in Geneva.

"Today in the world, there are actually more [countries] that were polio-free and had polio importations than there are countries with endemic polio," he says. "It is the first time that has occurred."

There are six countries that have continuing polio transmission that has never been interrupted: India, Pakistan, Afghanistan, Egypt, Nigeria, and Niger.

"The epidemiology of polio in all of these countries is changing," Heymann says. "If they have effective campaigns to raise immunization coverage in susceptible children — children under 5 — we believe they will be able to interrupt transmission."

Unfortunately, Nigeria stopped immunizing in some of its northern states last year due to unfounded rumors that the polio vaccine could cause infertility in females. "Those rumors have continued to circulate, and as a result, Nigeria had over half of the 800 cases of polio that occurred last year in the world," he adds. "In addition, Nigeria has exported polio to eight neighboring countries. Those countries had interrupted transmissions in about the year 2000, but they didn't keep their immunization coverage levels high with polio vaccine. So we see a phenomenon where an endemic country has exported polio to neighboring countries."

The eradication campaign continues in the key regions with immunization plans for vaccinating 63 million children younger than 5. Polio, the ancient crippler, seems to be finally losing its legs. With global eradication now on the horizon, is it foreseeable that vaccinations will end and — as occurred with smallpox — herd immunity will gradually become herd susceptibility? More to the point, could polio possibly become a bioterrorism weapon of the future?

### **Little attraction or the ideal weapon?**

“No self-respecting terrorist is ever going to use the polio virus,” says **William Sergeant**,

chairman of the International Polio Plus Committee of Rotary International in Oakridge, IL. “Do you realize that of every 200 people who are infected, [only] one of them is paralyzed? I don’t know that any terrorist wants to use a bullet that 199 times [does not do] any good. As a terrorist weapon, it has little attraction.”

One could argue that a one in 200 risk of being paralyzed would be sufficient to terrorize people, but it certainly is true that polio is not at the top of the bioterrorist’s weapons wish list. However, that could change as vaccination ends and global immunity wanes.

One article notes that “in a city of 10 million unvaccinated individuals, a rough estimate would be that a single release of virus could result in 7,000 paralytic cases.”<sup>1</sup> Indeed, **Alan Dove**, PhD, the co-author of that paper, argues further on his web site [Polio Information Center Online (PICO)] that “as a terrorist weapon, poliovirus is nearly ideal: It is highly contagious, easily released into food or water supplies, and virtually impossible to detect until the damage has already been done.”

In any case, both the theoretical threat of bioterrorism and the possibility of reintroduction of wild poliovirus will mean continuing vaccination in some countries for many years.

Inactivated (Salk) poliovirus vaccine (IPV) was licensed in 1955 and was used extensively from that time until the early 1960s. In 1961, type 1 and 2 monovalent oral poliovirus vaccine (MOPV) was licensed, and in 1962, type 3 MOPV was licensed. In 1963, trivalent oral poliovirus vaccine (OPV) was licensed and largely replaced IPV use. OPV has been the vaccine of choice in the United States and most other countries of the world since 1963. OPV contains live attenuated strains of all three serotypes of poliovirus.

Live attenuated polioviruses replicate in the intestinal mucosa and lymphoid cells, and in lymph nodes that drain the intestine, according to the Centers for Disease Control and Prevention (CDC). When OPV is used, vaccine viruses are excreted in the stool of the vaccinated person for up to six weeks after a dose. Maximum viral shedding occurs in the first one to two weeks after vaccination. Vaccine viruses may spread from the recipient to contacts. People coming in contact with fecal material of a vaccinated person may be exposed and infected with vaccine virus. For these reasons, the OPV vaccine will no longer be used once polio eradication is declared.

“If a country decides to use vaccine after eradication, it will have to use inactivated polio

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#### **Editorial Questions**

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vaccine," Heymann says. "Countries will make that decision [to continue vaccinating] based on the information that they have. That information will include whether or not they consider polio an agent that could be used in bioterrorism. It has never been used in the past. It has never been placed on the list of pathogens that may be used in bioterrorism by the international group in Geneva. But there will be countries, I am sure, that will consider that it might be a risk; and they will want to consider continuing vaccination."

There is a problem, however, that differentiates poliovirus from smallpox virus. With the latter,

researchers do not need the virus to make the vaccine, which is comprised of vaccinia (cowpox). Thus debate has continued about destroying the remaining stocks of smallpox virus. In contrast, stocks of live poliovirus must be available to create the inactivated polio vaccine.

"That is a major difficulty. There are two things that are being done. One is that the companies that produce inactivated vaccine are developing maximum-security areas where they can grow the virus and produce the vaccine," Heymann says. "The second thing is to see if it is possible to produce inactivated polio vaccines from the Sabin [attenuated] virus. There has been vaccine produced from

## Smallpox on death row, but research is yielding fruit

*"If smallpox is outlawed, only outlaws will have smallpox."* Peter Jahrling, civilian advisor to the United States Army Medical Research Institute of Infectious Diseases.<sup>1</sup>

Once very near execution, smallpox remains on death row. Eradicated in nature, the infamous killer survives in two official repositories in the United States and Russia.

After the global eradication of smallpox was confirmed by the World Health Organization (WHO) in 1980, a series of philosophical and scientific discussions began about the fate of the remaining stocks of live virus. In the mid-1980s, the WHO consolidated the world's known stocks of live virus in two locations: the Centre of Virology and Biotechnology (VECTOR) in Koltsovo, Russia; and the Centers for Disease Control and Prevention (CDC). At that time, the first recommendations to destroy the stocks came forward, sparking the aforementioned debates about the research value of keeping the virus alive.

In 1990, a WHO ad hoc committee recommended the destruction of the smallpox stocks by Dec. 31, 1993. As debate continued about the wisdom of the action, the deadline was extended repeatedly. In May 2002, the WHO approved resolution WHO55.15, the most recent clemency granted for the live viral stocks of smallpox. The resolution called for "temporary, retention of the existing stocks of live *Variola virus* at the current locations . . . [with] the understanding that steps should be taken to ensure that all approved research would remain outcome-oriented and time-limited and periodically reviewed and a proposed new date for destruction should be set when the research accomplishments and outcomes allow consensus."

Though the virus famously described as the "demon in the freezer" has been close several

times to being thawed and killed, it appears the research agenda is bearing fruit. The most recent progress report on smallpox research was presented at the fifth meeting of the WHO Advisory Committee on Variola Virus Research, November 2003.<sup>2</sup> The current variola virus stocks at CDC include 451 isolates, of which 49 have been selected for viability studies. Of those, 45 isolates could be propagated in tissue culture.

Of the 120 samples at VECTOR, 55 were tested for viability and 32 could be propagated. The WHO committee recommended that isolates shown to be non-viable should be destroyed and removed from the inventories, with DNA being isolated if this was considered useful for future studies. The committee recommended that the WHO should approach the responsible authorities within the collaborating centers to implement the recommendations concerning the destruction of these virus isolates.

The WHO committee reported progress in developing a primate model for smallpox in the United States using macaque monkeys. Essential research on an animal model of smallpox is needed to meet the efficacy rules for the licensing of new antiviral compounds. In additional research with the smallpox virus, antiviral treatment with cidofovir was shown to protect monkeys against variola-induced death if given 24 hours before infection. The WHO committee acknowledged "the need for continued research" toward treatments and better vaccines, meaning that for the foreseeable future smallpox lives to fight another day.

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that that is effective, but the question remains whether this can become the procedure which industry will use. We know that some companies don't want to change their procedures because then there is a whole new licensing [requirement]. So there [probably] will be wild polio virus that is used in vaccine production."

### **Biosecurity on the front burner**

Thus biosecurity at vaccine production and storage facilities will be a major concern as immunizations halt after eradication is achieved.

"One of the things that has been done is inventorying laboratories in anticipation of us getting to the end on polio eradication," explains **James Hughes**, MD, director of the CDC center for infectious diseases.

"We've been involved in helping inventory labs in the United States so that we know, first, where polio virus is. We will be in a position to take whatever action the global community decides is appropriate when the time comes," he adds. "Polio is a disease where the infection is usually asymptomatic, so it is possible that in addition to polio stocks that might be around in laboratories, there might be stool specimens harboring poliovirus. All of that inventorying has to be done as we begin preparing to — at a minimum — consolidate the residual [live virus] stocks in a few places."

Even then there is some question whether the disease will truly be eradicated, particularly since researchers have shown that poliovirus can be genetically created in the lab.<sup>2</sup> Regardless of origin, the WHO has contingency plans for the reappearance of polio.

"As we finish the job of interrupting polio transmission, we are also developing mechanisms, which can be used after polio eradication to intervene should there be polio," Heymann says. "Those mechanisms will include a stockpile of oral polio vaccine. It will probably be a monovalent vaccine, but that has to be licensed. There will be a response mechanism that is based at WHO — a global alert and response network that will respond to polio should it occur."

Ultimately, it appears — just as with smallpox — poliovirus will be defeated in the wild but live on under lock and key in designated laboratories.

"Most countries are now doing their inventories — that's the first phase," he explains. "The second phase is consolidating the specimens, and the third is putting them under maximum security. So it will be treated just as the smallpox virus."

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2. Cello J, Paul AV, Wimmer E. Chemical synthesis of poliovirus cDNA: Generation of infectious virus in the absence of natural template. *Science* 2002; 297:1,016-1,018. ■

## **Expert says terrorists eventually will go nuclear**

*'I don't know how we are going to stop it'*

In a grim but frank assessment, a leading national security expert tells *Bioterrorism Watch* that it is only a matter of time before terrorists detonate a nuclear warhead in the United States. You read that correctly.

The prediction is not a dirty bomb device releasing radiation through a conventional explosive but an attack with a tactical nuclear warhead that could be placed in a vehicle.

"That's my prediction, and I believe it will occur at some point," says **Cham E. Dallas**, PhD, director of the University of Georgia Interdisciplinary Toxicology Program in Athens and civilian national consultant for weapons of mass destruction for the U.S. Air Force Surgeon General. "Eventually, I think it is inevitable that they are going to get a warhead in the back of a van or an SUV, and I don't know how we are going to stop it," he notes.

An era of "buffoon" terrorism marked by crude attempts with poorly understood agents eventually will be followed by terrorist possession of a nuclear weapon, says Dallas, who also is the director of the Center for Leadership in Education and Applied Research in Mass Destruction Defense (CLEARMADD), which is funded by the Centers for Disease Control and Prevention as a specialty center in public health.

"Then somewhere down the line, one of them will hit pay dirt," he explains. "[If] they are intense enough in the dedication to the twisted cause they serve."

One of the world's leading experts on the Chernobyl nuclear plant disaster in the former Soviet Union, Dallas is not given to hysterical forecasts. Suffice it to say, he hopes he is wrong. But in the even tones of a scientist and security expert, he assesses the threat and calls it as he sees it. For example, the much publicized dirty bomb threat is highly overrated, Dallas adds.

“When you get right down to it, a dirty bomb is only a hazard to human health really for the most part relative to its explosive capacity,” Dallas says. “You take the people out of the area and treat them for injuries. But as far as contamination, you simply wash them off. You monitor them over time, but more than likely, the people that would be contaminated by a dirty bomb, I would predict less than 1% of those individuals would have any health effect. Now, if they ingested or inhaled anything at the time, that’s where your 1% risk goes up. As yet, we don’t have effective strategies for removing radioactive materials from the body. But as long as they are decontaminated, clothes disposed of, and skin thoroughly scrubbed, the risk probably is very low.”

What about the feared dead zone of reactivity, where the plume was dispersed? Having seen the real thing in the Chernobyl area, Dallas does not think a dirty bomb will create a similar problem. “It is possible to decontaminate an area,” he says. “With most dirty bombs, the area is going to be small. You are not talking about a nuclear crater here. It is a low-risk scenario, but it is not a good one. The panic and the economic loss are not to be underestimated. People have a deep-seated fear of radiation. But dirty bomb incidents — that is far down the list of what I think about. That is not one of the ones that keeps me awake at night.”

No, sleepless nights come in contemplation of the sheer number and proliferation of nuclear weapons throughout the world. “The major risk is a fact that is not commonly known,” Dallas notes. “There is not 1 ounce of plutonium in any of these nuclear weapons that has been deactivated and destroyed. The Soviet arsenal had over 17,000 tactical nuclear warheads; the ones that could be fired in a cannon, dropped from a plane, or carried in a brief case. They deactivated many of those. They take the warheads out and the plutonium pits out of the warheads, but they don’t destroy the plutonium pits. They are stored in warehouses, and there are thousands and thousands of them.”

Frequent visits to Russia in the aftermath of the Chernobyl disaster have not been reassuring. “I don’t have a lot of confidence in the quality control within that system,” he says. “I can only hope that they are keeping their eyes on those nuclear warheads. There are all sorts of stories about so-called loose nukes. I assume that the enemies of this country have nuclear weapons.”

Dallas’ concerns were echoed by a recent report and analysis conducted for the Nuclear Threat Initiative, which was founded by former Sen. Sam

Nunn, D-GA. (See key points, p. 30.) “Because disputes over access to sensitive sites and other bureaucratic obstacles have been allowed to fester, the amount of nuclear material secured in the two years immediately following the 9/11 attacks was actually *less* than the amount secured in the two years immediately before the attacks,” the report states. “An attack using an explosive — either a stolen nuclear weapon or an improvised terrorist bomb made from stolen nuclear material — would be among the most difficult types of attacks for terrorists to accomplish. But the danger is real.”<sup>1</sup>

### ***The lessons of Chernobyl***

Dallas’ warning carries weight because he has visited Chernobyl many times as a research toxicologist and seen the direct effect of a radiological disaster. Some of the lessons about radiation were surprising in the aftermath of Chernobyl, he says.

“Many of the things that we were expecting to see, didn’t occur — for instance, birth defects,” he says. “There was 100 million curries of radioactivity released, more than a 100 times the radioactivity released from Hiroshima and Nagasaki combined. It was the largest airborne dispersal of radioactivity in history.”

As the nuclear reactor fire efficiently dispersed radiation over the region for several days, there was wide expectation of birth defects. Of an estimated 90,000 pregnant women in the exposure area, some 30,000 decided to terminate their pregnancies. But birth defects related to radiation were not found in the babies that were brought to term, Dallas says. The babies apparently were safely shielded in the womb.

“Radiation is a factor of time, distance, and shielding,” he adds. “The problem is ingestion and inhalation of radioactive particles. The Soviets did not tell their people what was going on for three days. If you take an iodine tablet within 12 hours of exposure to radiation, you will prevent 100% of thyroid cancer. It is the preventable cancer from radiation. I mean it will be zero.”

Since that was not done in a timely fashion, there was an explosion of thyroid cancer in the years that followed the Chernobyl disaster. The primary victims were children who were ages 4 to 12 when they were exposed to the radiation, Dallas adds. “In that group, we saw thousands of thyroid cancers, and not all of them were next to the reactors. Many of them were hundreds of miles away. The thyroid cancer incidence was clustered along the rail line from Chernobyl to

Moscow. It was not related to the radioactive plume, the airborne dispersion. It was correlated with the rail line, which we hypothesize had to do with food consumption. They get their food right off the train."

Dallas has stood on top of an empty skyscraper and looked out across the abandoned city of Prtivia, which sits near the Chernobyl site. "It was a town of 70,000 people, a very modern town by Russian standards because it was a nuclear industry town. It is abandoned, and it will be

abandoned for quite for some time, for a long time. Because Prtivia was directly in the plume of the reactor burn, people stood on their balconies for three days and watched the fire burn."

The area most directly contaminated by the disaster is called the exclusion zone, and a respirator must be worn to enter it, he says. "You can still go through it for short periods of time without hazard, as long as you don't eat or breathe anything," he says.

Some Russians are now farming and moving

## Nuclear acquisition a real threat in Russia, Pakistan

If the world's existing stockpiles of nuclear weapons and weapons-usable nuclear materials can be secured reliably, nuclear terrorism can be prevented. Simple enough, but therein lies the challenge. A recent analysis of the situation commissioned by the Nuclear Threat Initiative concludes that "a fast-paced global partnership is urgently needed to secure the world's nuclear stockpiles before terrorists and thieves get to them. This must be a global effort, as the essential ingredients of nuclear weapons exist in more than 40 countries, on every inhabited continent."<sup>1</sup>

Key issues and areas for action cited in the report are summarized as follows:

- The United States and Russia bear a special responsibility for leading this effort, as they possess more than 95% of the world's nuclear weapons and more than 85% of the world's weapons-usable nuclear material, and in many cases, were the suppliers for weapons-usable nuclear material in other countries around the world.
- The Russian government and economy have stabilized; nuclear workers and guards are now being paid a living wage on time; and the most glaring security deficiencies have largely been fixed. But serious security problems remain.
- Experts who visit Russia's nuclear sites continue to report broken intrusion detectors; nuclear-material accounting systems never designed to detect the theft of nuclear material; and security culture problems ranging from guards turning off detectors when they are annoyed by the false alarms to security gates propped open for convenience.
- At the same time, threats to these facilities appear to be growing: Russian official sources report four incidents of terrorist reconnaissance on Russian nuclear warheads from 2001 to 2002. The Russian state newspaper reports that the 41 heavily armed terrorists who seized hundreds of hostages at a Moscow theater in October 2002 first considered

seizing a Moscow site with enough highly enriched uranium (HEU) for dozens of nuclear weapons. A 2003 criminal case revealed that a Russian businessman had been offering \$750,000 for stolen weapon-grade plutonium for sale to a foreign client — and had succeeded in making contact with residents of the closed nuclear weapon city of Sarov, to attempt to arrange the purchase.

- Pakistan's nuclear stockpiles are very small compared to those of Russia and the United States, and its facilities are believed to be heavily guarded. But the threat in Pakistan is very, very high — both from nuclear insiders sympathetic to extreme Islamic causes and from the large armed remnants of al Qaeda.
- Some 20 metric tons of HEU — enough for hundreds of nuclear weapons — exist as fuel for civilian research reactors around the world. More than 130 research reactors still use HEU as their fuel, in more than 40 countries. Most of these facilities have very modest security — in many cases, no more than a night watchman and a chain-link fence.
- Research-reactor fuel elements are small enough for a thief to put several of them into a backpack and carry them to a waiting vehicle. Chemical processing would be needed to extract the HEU from these fuel elements — but the processing required is reasonably straightforward, and all the details of the necessary processes are published in the open literature.
- When both fresh and unirradiated fuel are included, there are probably dozens of locations around the world where enough material for a bomb exists at a single site — and given the terrorists' demonstrated ability to carry out multiple coordinated attacks, the danger that they might strike more than one site to get their material cannot be discounted.

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1. Bunn M, Wier A. *Securing the Bomb: An Agenda for Action*. Washington, DC: Nuclear Threat Initiative and the Project on Managing the Atom, Harvard University; May 2004. ■

back within about 20 miles of the exclusion zone, Dallas explains. "The good news is that the contamination [there] was not as bad as we thought it would be. We had this moonscape mentality, but it is was just not true."

Unfortunately, that ghastly vision may well be true if a nuclear weapon is exploded in a city. "A single medium-range nuclear weapon would fill every burn bed in the eastern United States," he says. "You could lose 1 million people at once. That is the real threat. It's one we've all grown up with, but it is very different now. We are not talking about a nuclear exchange with another power."

## Reference

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## NIH assembles team to end smallpox vaccine threat

If it was ever necessary to conduct mass smallpox immunizations to protect the general populace, millions of people with atopic dermatitis would have to weigh the risk of smallpox vs. their potential fatal reaction to the vaccine.

The condition is called eczema vaccinatum (EV), a severe and potentially deadly complication of smallpox immunization. EV occurs almost exclusively in people with a history of atopic dermatitis (AD), a chronic, itchy skin condition commonly referred to as eczema. While uncommon, EV can develop when AD patients are given the smallpox vaccine or come in close personal contact with people who recently received the vaccine.

If untreated, EV can kill between 1% to 6% of those affected. In children younger than 2, EV has been estimated to kill up to 30%.

To address the problem, the National Institute of Allergy and Infectious Diseases (NIAID) has formed a nationwide research group. The recently formed network is comprised of three integrated components: a clinical studies consortium, an

**CE/CME questions**

1. In contrast to smallpox, stocks of what substance must be available to create the inactivated polio vaccine?
  - A. live polio virus
  - B. killed polio virus
  - C. lymphoid cells
  - D. all of the above
2. Cham E. Dallas, PhD, said the most serious nuclear threat to the U.S. is the massive radiological contamination caused by a dirty bomb.
  - A. true
  - B. false
3. Which type of cancer is prevented by taking an iodine tablet within 12 hours of a radiation exposure?
  - A. lung
  - B. leukemia
  - C. thyroid
  - D. colon
4. Which of the following is a severe and potentially deadly complication of smallpox immunization?
  - A. atopic dermatitis
  - B. eczema vaccinatum
  - C. varicella vaccinia
  - D. uncommon psoriasis

**Answer Key:** 1. A; 2. B; 3. C; 4. B

animal studies consortium, and a statistical and data coordinating center.

"Previous studies suggest that both innate and adaptive immunity are impaired in patients with atopic dermatitis, but the specific defects that increase the likelihood of eczema vaccinatum have yet to be explained," says **Daniel Rotrosen**, MD, director of NIAID's division of allergy, immunology and transplantation. "The information generated by this network will improve our understanding of the immune responses of these patients and should greatly influence the design of a safer smallpox vaccine."

The Atopic Dermatitis and Vaccinia Network (ADVN) will try to determine why people with AD have such severe reactions to smallpox vaccine by evaluating their immune responses after natural exposure to less harmful skin viruses such as

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herpes simplex. The ADVN Animal Studies Consortium will establish animal models of AD and investigate their immune responses to vaccinia — the virus used in smallpox vaccine and other skin viruses such as varicella, which causes chickenpox and shingles. The ADVN Statistical and Data Coordinating Center will support these clinical and animal studies by analyzing research data, coordinating trials and regulatory activities, and developing and maintaining a registry of AD patients.

The institutions in the ADVN Clinical Studies Consortium and principal investigators are:

- National Jewish Medical and Research Center, Donald Leung, MD, PhD.
- Oregon Health and Science University, Jon Hanifin, MD.
- Children's Hospital Boston, Lynda Schneider, MD.
- University of California at San Diego, Richard Gallo, MD, PhD.
- Johns Hopkins Asthma and Allergy Center, Lisa Beck, MD.
- University of Bonn, Germany, Thomas Bieber, MD, PhD.

The institutions in the ADVN Animal Studies Consortium and principal investigators are:

- Children's Hospital Boston, Raif Geha, MD, and Hans Oettgen, MD, PhD.
- National Jewish Medical and Research Center, Donald Leung, MD, PhD, and Erwin Gelfand, MD.
- Harvard Skin Diseases Research Center, Thomas Kupper, MD, and Robert Fuhlbridge, MD.
- University of Illinois at Chicago, Lawrence Chan, MD.
- La Jolla Institute for Allergy and Immunology, Toshiaki Kawakami, MD, PhD.

The Statistical and Data Coordinating Center will be operated by Rho Federal Systems Division. The principal investigator is Susan Lieff, PhD. ■

## Supplement goes on-line beginning January 2005

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## CE/CME instructions

Physicians and nurses participate in this CE/CME program by reading the issue, using the provided references for further research, and studying the questions. Participants should select what they believe to be the correct answers, then refer to answer key to test their knowledge.

To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this semester's activity, you must complete the evaluation form that will be 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. ■