

Bioterrorism and weapons of mass destruction 2004: Physicians as first responders

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“The single greatest threat to man’s continued existence on earth is the virus.”

—Joshua Lederberg
Nobel Scientist

If the anthrax events of 2001 taught us anything it was that an astute physician could save lives. Physicians who do not know the common signs of deadly, albeit uncommon illnesses, will lose lives.^{1,2}

A private practice infectious disease specialist in concert with an alert laboratorian—both of who had just received basic bioterrorism awareness training—diagnosed the sentinel case of inhalation anthrax in the United States. While the sentinel patient ultimately lost his life, the alarm was raised in time to prevent other deaths.

Another patient in a different region of the country with symptoms consistent with inhalation anthrax was misdiagnosed and subsequently died. Does training pay off? Absolutely! The issue ultimately is what type of training is appropriate for physicians living in a world of competing demands.¹⁻⁶

Emerging infectious diseases can pose as deadly a threat as the intentional dissemination of deadly toxins.^{1-3, 7-10} As osteopathic physicians we are all too aware of the influenza pandemic of 1918 where millions died. Recent flu-related deaths affecting children have raised public concern about influenza. Subsequently, stockpiles of flu vaccine have become depleted as demand increased dramatically. In the last few months we have seen the appearance of monkey pox, severe acute respiratory syndrome (SARS), and avian flu affecting humans.¹⁰ As recent as February

2004, the toxin ricin was found in the US Capitol.

The war in Iraq was largely based upon the threat of biological weapons. Two cases of bubonic plague occurred in New York City within the year. It was contracted naturally from the victims’ home in the Southwest. It could just as easily have been the result of biowarfare. The question we need to ask ourselves: Would we have been able to make a rapid diagnosis based upon our current skill levels?^{7,6}

The new reality of biological weapons led the United States to embark upon a smallpox vaccination program.^{7,11-14} Many current physicians were unfamiliar with vaccinia and inexperienced in the use of bifurcated needles. Diseases long since eradicated or quiescent may re-emerge. At the same time, the number of experienced physicians who have seen or treated such illnesses continues to dwindle. Time is fleeting and it is critical to tap into their experiences.

Emerging threats

As practicing physicians we will face a variety of emerging health threats ranging from smoking and adolescent diabetes to anthrax and SARS. Associated with each of these threats will be new research, practice guidelines and training.

Because we live in a global world, our Atlantic and Pacific shores no longer protect us from diseases that are rare on this continent but endemic or epidemic in many other parts of the world. With

Table 1
Characteristics of biological weapons

Although virtually any microbe capable of causing illness can be utilized, biological agents selected for use as bioweapons share specific characteristics. These include:

- 1. Can be aerosolized
- 2. Potentially undetectable
- 3. Easily stored
- 4. Can cause serious illness or death
- 5. Small amount can affect large numbers of victims
- 6. Easily dispersed
- 7. Possibility of human-to-human transmission
- 8. May affect humans and/or animals or plants
- 9. Few affective treatments
- 10. Possible vaccine or pretreatment to protect aggressor

transcontinental flights, the increase in cruise ships and the immigration from other countries, we can expect to see a variety of unusual illnesses.

We also face a global biological threat. Our adversaries know our vulnerabilities better than we do. In addition, there is a black market on pathogens—especially deadly ones.

The former Soviet Union employed over 60,000 scientists at their bioweapon institute Biopreparat. Many of these scientists are now working for other countries. Estimates suggest that more than 20 countries have some form of bioweapons program.

Tens of thousands of our servicemen and women will be returning from the Persian Gulf—many of whom may be infected with diseases endemic to the region or the result of undetected bioweapons. Will we diagnose them cor-

rectly or will their return be marked by another “Persian Gulf Syndrome?” This syndrome in the early postwar years became synonymous for post-traumatic stress disorder (PTSD). In reality, it represented a variety of etiologies ranging from chemical exposure, desert illnesses as well as PTSD. Therefore the threat of biological weapons or uncommon illness is no longer the stuff of Robin Cook novels, but the reality of our future practices.

Since the tragic events of September 11, substance use—illicit drugs and alcohol—has increased significantly. Daily lives have changed to reflect our concerns. The mail is opened with suspicion; personal examinations and increased security accompany air travel.

Even our conversations reflect issues of terrorism, weapons and foreign threats. Who would have believed the terms “anthrax,” “sarin” and “plague” would become household words? Individuals who are our patients are purchasing gas masks as well as safe-room kits for the home.

Considering this new environment, physicians need to ask: How often do we discuss with our patients current events and the anxiety associated with daily terrorism updates? Perhaps it’s time that we do.

Bioterrorism and WMD

The use of bacteria and viruses to wreak death upon adversaries dates back to antiquity.¹ Virtually any microbe capable of causing human illness is a candidate for a bioweapon. In 1984, a cult in Oregon used salmonella to cause food borne illness in a small community.¹⁵ By sprinkling a simple preparation over salad bars at local restaurants, over 700 people became affected. However most experts consider a true bioweapon to be a pathogen that is capable of causing significant illness or death, and is readily disseminated and challenging to treat (Table 1).

The Centers for Disease Control and Prevention (CDC) has categorized biologicals into three levels—A, B, and C—based upon pathogenicity, and likelihood of use.¹⁰ The CDC Category A Biological Warfare Agents include:

- *Bacillus anthracis*—Anthrax
- *Variola* - Smallpox
- *Clostridium botulinum* toxin—Botulism
- *Francisella tularensis*—Tularemia
- *Yersinia pestis*—Plague
- Viral hemorrhagic fevers (VHF)—includes Ebola

Weapons of mass destruction are usually described by the acronym “BNICE”—biological, nuclear, incendiary, chemical and explosive. All are capable of causing a mass casualty event (MCE).

An important vulnerability in our preparedness planning is the almost interchangeable nature with which the BNICE acronym is viewed. It could be argued to change the acronym to B-NICE, because the B category of agent has distinct and important differences from the NICE group.

Even though bioweapons can cause mass casualties, such activities would not necessarily occur as “an event” in the traditional and expected MCE. Unfortunately, in many preparedness-planning meetings, biological weapons are discussed and treated as if they would result in a HAZMAT event requiring massive mobilization of emergency medical services (EMS), field decontamination and personnel donning biohazard level A suits.

Bioweapons are not like the other WMD agents. First, in the case of biologicals, as opposed to the “NICE” group, it is unlikely there would be a bang, plume, cloud, or other announcement.

Bioweapons are stealth weapons. Fire and forget. Blow plague or anthrax into the air ducts or HVAC (heating, ventila-

tion, air conditioning), walk away and wait for the incubation period to end, resulting in many sick and potentially dying people.

Second, when a “NICE” or HAZMAT event occurs, there usually are several victims presenting in a similar time and location. Typical MCEs occur as one exposure, one event, resulting in a group of victims. An example of this is the release of a sarin nerve agent in a Tokyo subway in 1995. Thousands were affected directly or psychologically—in a similar time and place. Contrast this with the biological event, and you have an exposure that occurs at one place and time, resulting in victims who often present days or weeks later, at seemingly unrelated locations and stages of illness.

Patients may even serve as weapons themselves if the bioweapon is contagious, such as with smallpox. Instead of discussing decontamination facilities and EMS paradigms, issues such as converting hospital beds to intensive care or isolation units, identifying ways to transport, quarantine or hospitalize patients should be considered. There is nothing to decontaminate, except at the source of exposure, if that can be identified.

The victims may have to be isolated, even quarantined, but this is not the same as decontamination. Not to say decontamination and EMS preparedness are not essential in an MCE, but the roles of the stakeholders and participants in a bioweapon are significantly different than that required in an explosion or other MCE.

The emergency departments and EMS will ultimately be involved, both in the care of the worried well and real patients. None the less, it is just as likely that a school nurse, public health clinician or primary care physician will be called upon to identify the index patient. Propagated outbreaks are not traditional mass casualty events. They require communications and training across disciplines.¹⁶⁻¹⁸

Biological terrorism may also or alternatively involve animals or food supplies.^{2,8,9} How often do we get concerned about a patient or two who have what we consider food poisoning? Yet many bioweapon illnesses, especially in the early stages, can be misdiagnosed as food-borne illness or simple dyspepsia. Poison control centers often get calls about food poisoning concerns.

Physicians need to link with poison control centers, and veterinary and agricultural toxicologists as information resources. In addition, physicians must understand how to obtain feedback from public health departments in terms of food-borne outbreaks.

Our vulnerability remains in treating each BNICE category as equal, thus amenable to the same general preparedness paradigm. Early identification of bioweapon victims, communications across disciplines, and organizing hospital, EMS and local clinic responses should be key considerations. They require distinctly different command and control structures, leaders, training and resources than the typical MCE associated with WMD.

Bioweapon agents

As a first step, bioweapon agents^{1, 3, 8-14} need to be defined and identified. Anthrax is a worldwide infectious agent, an occupational illness usually associated with herbivores such as sheep, goats and cattle. Humans usually contract anthrax handling contaminated animals.

Bacillus anthracis is a gram-positive, rod-shaped, spore-forming bacteria (Table 2). Spores usually observed in gram stains performed on culture isolates, not clinical specimens. Clinically the disease presents in three forms—cutaneous, inhalational and gastrointestinal. An oropharyngeal form is possible, although uncommon.



Cutaneous Anthrax. Photo courtesy of the CDC

Table 2
Presumptive identification of bacillus anthracis

Specimen selection—Serum, blood, sputum, bronchial wash/lavage, vesicular fluid

NB: nasal swabs are utilized for epidemiologic purposes

Colony morphology on sheep blood agar (SBA) (35° C @ 12-24 hr)

Ground glass like appearance, 2-5 mm diameter, irregularly round, “sticky” consistency

Gram stain

Gram-positive, broad rod, spore-positive (culture isolate) or spore-negative (clinical specimen)

Hemolysis

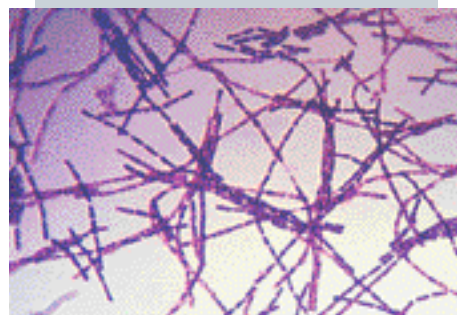
Nonhemolytic

Motility

Nonmotile

Catalase

Catalase positive



Photomicrograph of bacillus anthracis. Photo courtesy of the CDC

Table 3
Symptoms

Symptoms	Present x% per illness		
	Inhalation Anthrax	Flu	Influenza Like Illness (ILI)
Elevated Temp	70%	74%	73%
Fever/chills	100	86	85
Cough	90	90	90
Shortness of breath	80	6	6
Chest discomfort	60	35	23
Headache	50	88	85
Myalgia	50	88	88
Sore throat	20	80	80
Vomiting/nausea	80	12	12

Table 4
Mediastinal Widening—Etiology

- Ruptured Aortic Aneurysm
- Histoplasmosis
- Superior Vena Cava Syndrome
- Legionnaires Disease
- Psittacosis
- Coccidioidomycosis
- Sarcoidosis
- Anthrax
- Tularemia
- Other bioweapon illness

Cutaneous

Worldwide cutaneous anthrax is the most common clinical presentation, mostly occurring on the hands and forearms.

Cutaneous anthrax begins as a papule followed by formation of a fluid filled vesicle. This is usually painless, but characteristically associated with significant edema. Once the vesicle dries, a coal-black scab (eschar) forms. Although mortality is low even among untreated cases; cutaneous anthrax can disseminate into a fatal systemic infection.

Although the bite of a brown recluse spider is often included in the differential diagnosis, the presentation is different. The spider bite results in envenomation with a hemolytic toxin that can cause significant tissue breakdown, ranging from bullae to necrosis. Bites can be painless or



Inhalational anthrax. Photo courtesy of the CDC

very painful. However, profound edema like that found in cutaneous anthrax is not associated with the brown recluse.

Gastrointestinal

This form of anthrax is rare, and results from ingesting insufficiently cooked meat from infected animals. Untreated, this form is usually fatal. As with inhalation anthrax, central nervous system involvement is possible. Increases in the number of suspected food-borne illnesses (FBI) reported to the local health department should raise the index of suspicion for bioweapon-related illnesses.

Inhalational

Inhalational anthrax in the endemic or natural form, historically known as Wool-sorters' disease, results from the inhalation of anthrax spores in infected wool. This form presents the primary route of intentional infection and the most likely clinical presentation from weaponized aerosolized anthrax. The case fatality rate untreated is approximately 100 percent.

Since an early presumptive diagnosis will facilitate early treatment, the astute

clinician will obtain a thorough history, including occupational, travel and sequence of symptom presentation. While symptoms of early inhalation anthrax may resemble those of the flu, most patients will not present until the symptoms have advanced. The incubation period ranges from one to 60 days, although most recently estimated at one to six days.

In the initial stages the symptoms may be nonspecific. In such patients, there are clear differences in clinical presentation between anthrax and influenza-like illness (ILI) (Table 3).

Approximately 50 percent of inhalation anthrax patients have meningitis and/or neurologic involvement, and may present with altered mental status, seizures or coma. Chest radiographs (CXR) may reveal mediastinal widening (Table 4), a hallmark feature.

As the illness advances, dyspnea, stridor, cyanosis, increased chest pain, and chest wall edema occur, followed by shock and death within 24 hours. Once a case of inhalational anthrax is suspected, contact your local health department immediately. Realize any clinical samples from the patient are considered evidence in a crime scene. The laboratory and

chain of custody become part of the treatment plan.

Historically almost all cases in which treatment was initiated after patients became significantly symptomatic have been fatal as well. Therefore early diagnosis and treatment are essential to confer a survival advantage.

Naturally occurring strains are sensitive to penicillin, tetracyclines and most other antibiotic classes. However, resistance to the former two is not difficult and has already occurred through laboratory manipulation.

Since the case fatality rate among autumn 2001 victims was less than historical rates, these cases are being examined to study the antibiotic and medication combinations utilized.

Death results not from bacteria but from the toxins produced after the bacteria enter the alveolar macrophages. Studies are being conducted to assess if there is an antibiotic or combination of antibiotics that enhance the likelihood of survival by interrupting the protein synthesis or other pathological mechanism. Alternatively, does a treatment regimen predispose to an adverse outcome? Rifampin, vancomycin, clindamycin, azithromycin and other antimicrobials are being evaluated based upon their effects on cell walls, protein synthesis, and ultimately survival. Updates on antimicrobials will be presented. Current antibiotic recommendations:

■ Medical management of acute illness

Ciprofloxacin 400 mg IV q 12 hours or doxycycline—loading dose 200 mg IV followed by 100 mg IV q 12 hours. Duration of treatment should last 60 days; once the clinical condition improves, the patient can be switched to oral therapy.

■ Post exposure prophylaxis

Ciprofloxacin 500 mg by mouth twice a day as first line therapy. Alternatives include doxycycline 100 mg by mouth

twice a day. Duration of treatment is a minimum of four weeks plus vaccination or 60 days without vaccination.

■ Vaccine

Anthrax Vaccine Adsorbed is derived from an attenuated strain of anthrax using supernatant. Thus the vaccine does not contain live or dead organisms.

Data are insufficient in terms of effectiveness against inhalational anthrax; the vaccine has been shown to be effective against cutaneous anthrax.

The vaccine must be given as a series of .5 ml doses administered subcutaneously at zero, two and four weeks, followed by six, 12 and 18 months and subsequent yearly boosters.

Beyond mild discomfort at the injection site, according to military data, less than one percent experience more severe reactions, with systemic reactions being very rare.

Some personal protection and decontamination guidelines follow:

—Person-to-person transmission has not been reported.

—Isolation and quarantine are unnecessary.

—Universal precautions are sufficient when treating patients.

—Individuals exposed to anthrax should have their clothes removed, double bagged and saved as possible evidence of a crime.

—Soap and water should be used for people, sodium hypochlorite (10 parts water, one part household bleach) for nonhuman surfaces.

Francisella tularensis (Tularemia)

Tularemia was identified as causing a febrile, plague-like illness in San Francisco in the 1900s.

Tularemia is also known as “rabbit fever,” “deer fly fever,” “water-rat trappers disease,” and a host of other names de-



A tularemia lesion on dorsal skin of the right hand. Photo courtesy of the CDC

pending upon the region. Tularemia can be acquired via the dermal, gastrointestinal and inhalation routes.

Although there are six forms of human tularemia related illness, including ulceroglandular, glandular, typhoidal and pneumonic, the most likely would be the typhoidal form resulting from a weaponized aerosol and presenting much like inhalational anthrax illness.

The infective dose is estimated at 10-50 organisms (Table 1). The case fatality rate without treatment is 35 percent in naturally occurring typhoidal tularemia. Approximately 200 cases occur yearly in the United States.

■ Clinical diagnosis

Initial presentation includes fever, prostration and weight loss. The incubation period ranges from one to 14 days with an average of three to five days. The typical duration of illness is 14 days.

Person-to-person transmission has not been documented. Respiratory symptoms include chest discomfort, and progress to either a productive or non-productive fulminant pneumonia.

Patients with tularemia may exhibit a relative bradycardia. Fifty percent of chest radiographs show a pneumonia. Mediastinal lymphadenopathy (Table 4) is also common. Pleural effusions are possible, as are cavitory lesions. Septicemia is possible. Like anthrax, the

presumptive diagnosis is clinical.

Laboratory evaluations such as blood work and chemistries early in the illness are usually nonspecific. Specimens sent for analysis may aid in the diagnosis (Table 5), with definitive diagnosis made serologically with ELISA.

Antibodies appear within the first week of infection. Diagnosis should only be made if at least a four-fold increase in titer is observed. Maximal titers occur in four to eight weeks.

■ Medical management of acute illness

Tularemia is readily treated by aminoglycosides and Fluoroquinolones. Historically streptomycin has been the treatment of choice. Gentamicin 3-5 mg/kg IV for 10 to 14 days is an appropriate therapy. However current recommendations are to use Ciprofloxacin 400 mg IV every 12



Seen here are small hemorrhages on the skin of a plague victim. Photo courtesy of CDC.

hours during the initial illness, then switch to oral Ciprofloxacin 500 mg every 12 hours as the clinical course warrants. Total duration of treatment is 10 to 14 days. Tetracycline and chloramphenicol, as well as other antibiotics can be used, but relapse is not uncommon.

■ Personal protection and decontamination

Person-to-person spread of tularemia has not been documented. Universal precautions are sufficient when caring for patients with pneumonia or lesions. Isolation and quarantine are unnecessary.

Post-exposure prophylaxis (PEP)

When given within 24 hours of exposure from an aerosol attack, a two-week course of Ciprofloxacin 500-mg PO q 12 hours is appropriate. Unlike smallpox and other bioweapons, immune globulin is not available.

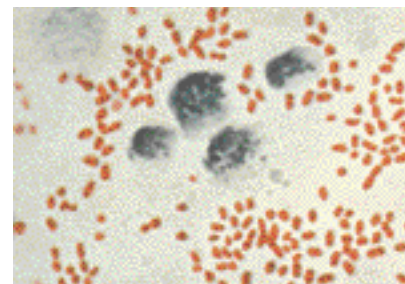
Vaccine:

Currently a live-attenuated vaccine is under investigation for the prevention of typhoidal tularemia.

Yersinia pestis (Plague)

“The Plague,” also known as the Black Death, caused the death of millions of Europeans during the Middle Ages.

Recently two tourists in New York City presented to the hospital with a rapidly progressive febrile illness; subsequently they were diagnosed with plague.



Photomicrograph of Yersinia. Photo courtesy of CDC.

They lived in New Mexico where studies isolated infected animals near their home.

In the United States, approximately a dozen cases of plague occur—it is a zoonotic disease, appearing mostly in the Southwest and usually affecting Native Americans.

Human plague illness appears in three forms—bubonic, septicemic and pneumonic. The causative agent—Yersinia pestis—is a rod-shaped, gram-negative, nonmotile, nonsporulating bacterium. Interest in plague as a bioweapon remains strong, with several nations attributed with weaponizing an aerosol version.

Unlike anthrax and tularemia, pneumonic plague is highly contagious, making it an especially worrisome potential bioweapon.

■ Bubonic

Worldwide this is the most common form, representing 85 percent of all cases. Usually a flea bite will introduce the bacterium into the patient, with the nearest lymph node being affected, ultimately enlarging into a “bubo.”

Table 5:
Laboratory identification tularemia

Poorly staining, tiny gram negative coccobacilli

Growth characteristics

At 24 hours on sheep blood agar (SBA)

- Gray-white, opaque colonies
- Too small to be seen individually

At 48 hours on SBA, Thayer-Martin or Chocolate Agar

- SBA: 1-2 mm white - blue-gray, opaque non-hemolytic
- TM/CA: 1-2 mm gray-white smooth and shiny

Tularemia will not grow on MacConkey.

Tularemia will opalesce on cysteine-rich medium

Biochemical

- Oxidase negative
- Catalase positive (weakly)
- Urease negative
- B-lactamase positive

Most commonly the inguinal nodes are affected since most flea bites occur on the lower extremity.

Bubonic plague has an incubation period of two to 10 days. High fever, myalgias, headache and malaise will accompany the beginning of a swollen, tender bubo.

The bubo is exquisitely painful. Fifty percent of patients have abdominal pain. Sometimes nausea and vomiting occur. The liver and spleen may become enlarged, palpable and tender. Secondary septicemia occurs frequently.

■ Septicemic

Primary septicemic form represents 15 percent of naturally occurring plague.

Plague septicemia presents much like other gram-negative septicemia. Primary septicemia presents without lymphadenopathy while secondary septicemia will have lymphatic involvement. Of concern DIC as well as thrombosis of the acral vessels can occur, resulting in necrosis or gangrene.

Endotoxemia can cause purpuric lesions. Hematogenous spread to the central nervous system and lungs is possible. High fever, chills, vomiting, and hypotension are common symptoms. Plague meningitis occurs in approximately 6 percent of septicemic and pneumonic cases.

■ Pneumonic

Only 1 percent of naturally occurring plague is pneumonic plague. However, as a weapon, this will be the most likely form.

Pneumonic plague can result from inhalation of organisms as spread by the weaponized aerosol (primary) or from hematogenous spread from septicemic plague (secondary).

The average incubation period is two to four days with a range of one to six days. Onset is abrupt. The patient may exhibit the three Hs—hemoptysis, hematemesis, and hemorrhagic diarrhea.

Bloody sputum is characteristic. Gastrointestinal symptoms such as nausea, diarrhea, and vomiting can occur. The CXR most commonly reveals bilateral infiltrates. However the findings can be varied. Pneumonic plague is rapidly progressive, and like inhalational anthrax results in shortness of breath, respiratory failure and death.

Heightened concern should arise if a rapidly progressive febrile illness similar to the syndrome of a gram-negative sepsis appears in a young, previously healthy individual. If increasing cases with similar symptoms occur, rapid consult with local health department is essential.

Plague diagnosis

Like other bioweapon illness, the diagnosis of plague must be made quickly and based upon clinical presentation.

Untreated bubonic plague has a case fatality rate of 60 percent, while untreated pneumonic plague is virtually always fatal. Laboratory testing may reveal a leukocytosis; total WBC count of 20,000 with more than 80 percent PMN.

Fibrin split products may indicate DIC. Increased liver enzymes and BUN/creatinine accompany multiple organ involvement. Antimicrobial therapy as well as appropriate symptomatic and supportive care must be initiated rapidly, and based upon a presumptive diagnosis. Definitive diagnosis is based upon culturing the organism from aspirates, cerebral spinal fluid, blood or sputum (Table 6).

Medical management

Aspirating the bubo is both therapeutic and assists in diagnosis by providing the organism.

As the bubo is exquisitely painful, removing the fluid will relieve much of the discomfort. Although incision and draining pose a risk to healthcare workers and

Table 6
Laboratory identification
plague (*Yersinia pestis*)

Essential specimen selection

■ Bubonic

Bubo—lymph node aspirate

■ Septicemic

Blood—organisms may be intermittent. Take three samples 10 to 30 minutes apart

■ Pneumonic

—Sputum
—Throat swab
—Bronchial washings

Testing procedures

■ Gram stain

Small, Gram-negative bipolar coccobacilli

■ Wayson, Wright, Geimsa stain

Pink-blue cells with closed safety pin look

■ Growth in Brain Heart Infusion Broth

Stalactites on side and bottom of tube—suspended clumps

■ Sheep Broth Agar (SBA)

24 hours

—Tiny, almost invisible
—Shiny gray translucent

48 hours

—One to two mm irregular colonies
—Fried egg appearance

■ Biochemical

Oxidase negative, Catalase positive, Urease negative, Indol negative

should be avoided, needle aspiration is a safe intervention when using universal precautions.

■ Treatment

Use symptomatic and supportive care to address hypotension, DIC and other systemic effects.

Streptomycin or other aminoglycosides, doxycycline and chloramphenicol are effective. Animal data suggest fluoroquinolones such as ciprofloxacin and ofloxacin may be effective in human treatment.

Streptomycin 30 mg/kg/day intramuscular twice a day for 10 - 14 days. Streptomycin can be obtained by calling the manufacturer Roerig Streptomycin Program at Pfizer Pharmaceuticals at (800) 254-4445. Doxycycline 200 mg IV loading dose followed by 100-mg q 12 hours IV for 10 to 14 days is a suitable alternative.

Ciprofloxacin can be given 400 mg IV BID for 10 to 14 days. For the treatment of plague meningitis, administer chloramphenicol 25 mg/kg IV loading dose followed by 15 mg/kg QID for 10 to 14 days.

■ Post-exposure prophylaxis

Regarding post exposure prophylaxis, antibiotics should be administered for seven days post exposure with a face-to-face contact of a pneumonic plague patient or aerosolized form of plague.

Doxycycline 100 mg PO BID or Ciprofloxacin 500 mg PO BID are appropriate. Tetracycline 500 mg PO QID or chloramphenicol 25 mg/kg PO QID are alternatives.

■ Vaccine

Although vaccine prototypes are under investigation, none are currently available to prevent plague.

■ Personal protection, decontamination

Suspected cases of pneumonic plague require respiratory droplet precautions and should be placed in strict isolation, preferably negative pressure rooms for a minimum of 48 hours of antimicrobial therapy, or for confirmed cases when sputum cultures are negative.

Vector tracing and control is required.

Soap and water is adequate for decontamination, while a 1:10 mixture of bleach to water is sufficient for surfaces.

Viruses

Viruses are the most simple of microorganisms. With the exception of very large DNA viruses like smallpox (Figure 1), most cannot be seen using light microscopy.

Essentially viruses are elegant in their simplicity and consist of a protein coat that contains genetic material, which can be either RNA or DNA.

Debate persisted for years about whether viruses were truly a life form. Viruses are parasites that depend upon the metabolic structures of their hosts to survive. Viruses require living cells to multiply based upon a complex interplay between host and virus.

Viruses are host specific—sometimes selective for humans only, other times able to infect primates. Viruses can infect plants, animals or bacteria. Pathogenicity occurs as a result of the changes in the host cell that accompanies viral infection.

The former Soviet Union employed tens of thousands of scientists at their viral bioterrorism facilities to study and possibly manipulate or alter pathogens.

The clinician should be vigilante about emerging threats, as well as aware that the clinical presentation of a viral illness may not demonstrate classic symptoms. This may be the result of natural evolution/adaptation—something viruses are capable of doing—or laboratory manipulation.

Smallpox (Variola)

The threat of Variola virus (smallpox)—the leading cause of infection—related death in history—has returned, and once again smallpox has become a household word. Smallpox infections have been rec-

ognized as far back as ancient Egypt, affecting pharaohs and peasants.

Unlike decades ago when smallpox was a naturally occurring infection, concerns are emerging that smallpox may become intentionally spread as a bio-weapon. Intelligence sources suggest Iraq and other terrorist-friendly nations may have access to or already weaponized Variola. Rumors persist that scientists in the former Soviet Union were trying to develop an Ebola/Variola hybrid virus.

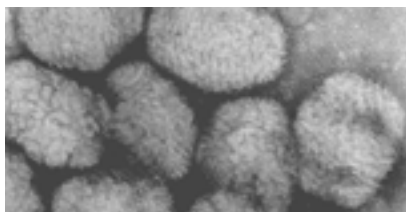
Smallpox is an Orthopox virus, which consists of the infectious agents that cause camelpox, smallpox, monkey pox and cowpox. Immunity to one member of this family confers protection against others, hence the use of vaccinia (cowpox) virus to immunize against Variola.

Vaccinia is a virus with minimal pathogenicity except in certain patients. Variola occurs as primarily two strains—variola major (smallpox) and the less pathological version variola minor, which causes a milder febrile rash, and is sometimes referred to as alastrim.

Smallpox presents a particularly serious risk because of a high case fatality rate estimated at 30 percent to 50 percent depending upon the strain, naive vaccine status of the exposed population and inconsistent availability of appropriate healthcare to prevent secondary bacterial infection.

Bioterrorism experts consider smallpox to be a significant threat because it is relatively easy to produce once starting material is obtained, the aerosol infectivity—contagiousness, widespread susceptibility of nonimmunized or under-immunized populations.

Contagion results from transmitting virus in airborne droplets or by contact with lesions. The last case of smallpox occurred during the 1940s in the United States, and the last naturally acquired case occurred in Somalia in 1977. Most clinicians have never seen this illness, so experienced diagnosticians are uncommon.



■ Initial presentation

Typically smallpox victims will experience a fever (100 to 105 degrees F) for several days before a rash develops. These people will be prostrated and complain of severe headache, chills, nausea and vomiting.

The typical skin rash may be preceded by an enanthem—a rash that appears within the oropharynx. Patients who have oral lesions are contagious, as are those who develop skin rashes.

Dentists and others who may be called upon to examine complaints of a febrile illness and mouth sores should be sensitized to the potential of smallpox. The distribution of the classic smallpox skin rash usually starts at the hands, feet and head, then works centrally, in contrast to the most similar disease in the differential diagnosis—chickenpox, whereupon the rash starts centrally on the trunk and works toward the periphery.

Smallpox lesions in the classic presentation are deep and dermal. The lesions are synchronous in their development—whatever location of the body a cluster of lesions appears on, they appear similar. The lesions progress from macula, papule, vesicle, pustule (pox) and ultimately to scabs. The time from exposure to symptoms ranges from seven to 17 days.

Chickenpox lesions are asynchronous in development—some are umbilicated, others are newly emerging, while the remainder may be ready to fall off. Unlike smallpox, chickenpox rarely affects the soles and palms. Other illnesses that may simulate chickenpox



on cursory appearance include coxsackievirus, leprosy, and syphilis.

The key distinguishing features between each illness is the history and differences in the rashes. Coxsackievirus usually affects adolescents and young adults, the patients do not appear ill, and the rash is superficial not dermal. Leprosy lesions are more confluent except in the tuberculous version, with possible neurologic symptoms, a clear history of the ailment. Again, especially if the patient has been treated, he/she will not appear ill. Smallpox patients will appear very sick and prostrated.

Syphilis patients will have lesions that tend to remain localized on the palms and soles, with may recollect a history of prior genital illness. Again such patients usually do not appear significantly ill.

Approximately 15 percent of smallpox victims will have delirium. Encephalitis is possible. Atypical forms of smallpox include the hemorrhagic variety, sometimes referred to as purpura variolosa, which is usually always fatal. It tends to occur more often in pregnant women and presents with epistaxis, hematemesis, hemoptysis, hematuria, subconjunctival hemorrhages, petechiae, echymosis and bloody pustules on the skin and mucosa. Other varieties include flat (malignant) smallpox whereupon a dense confluent macular rash occurs and carries a high mortality rate, and modified

or subacute—which may occur in previously immunized patients.

■ Medical management

Early suspicion, collaboration with experts from the health department and CDC to identify or rule out smallpox with subsequent contact tracing, vaccination and containment strategies are essential to contain a mass incident from this highly contagious disease.

Estimates of per person transmission rates vary from eight to 30 depending on the computer models utilized and the environment. Studies suggest that healthcare facilities are most likely to exhibit the highest transmission rates. Quarantine laws will probably be implemented under public health direction.

Symptomatic and supportive care is essential. Prevention of secondary infections is critical. If such exigency occurs, antibiotics must be quickly initiated. Because smallpox is spread from airborne droplets, respiratory and fluid precautions using appropriate personal protective equipment (PPE) are necessary. Patient isolation in negative pressure rooms equipped with special filter systems is important.

■ Vaccines

Post exposure vaccination within 72 hours with vaccinia vaccine should con-

fer significant protection for healthcare workers and others who have been exposed.

Vaccinia immune globulin (VIG) should be readily available to treat adverse events associated with the vaccine.

Vaccinia vaccine was generally considered a safe vaccine when given in the 1960s and 1970s, with relatively low adverse events recorded. Unfortunately with the increased number of immune-suppressed persons who have HIV, transplants or chronic illnesses and an aging society, there are subpopulations that may be at increased risk of adverse outcomes from the vaccine.

Although rare, encephalitis and death can occur. The most common adverse event is autoinnoculation—the patient scratches the vaccine site then rubs his or her eye, subsequently developing a lesion.

Patients with eczema are more likely to experience eczema vaccinatum. Realize that the risk of smallpox to these special populations is greater than the threat of vaccinia once exposure to variola occurs.

As of April 2003, vaccinations have been halted in many regions due to concerns over unexpected cardiac related deaths. Further studies should identify those individuals at risk or the mechanism by which such deaths have occurred.

Cidofovir (Vistide (r)) is an antiviral used for the treatment of cytomegalovirus (CMV) retinitis, especially in HIV patients. Other antivirals are being developed to treat smallpox.

Studies suggest cidofovir antiviral has some effectiveness against smallpox. However as of April 2003 it is not FDA approved for this indication. The side effects are renal toxicity and kidney stones. Some reports suggest coadministering probenecid with cidofovir may reduce the likelihood of these effects.

Clinical Diagnosis—smallpox

■ **Entry**—Airway

■ **Incubation**—~12 days

■ **Acute onset febrile illness with prostration**

■ **Classic rash**

- Appears 2-3 days after onset of fever.
- Synchronous development of lesions.
- Starts at head, hands, feet then progresses toward trunk.

■ **Death**

- 30% to 50% case fatality rate depending upon strain.
- Usually occurs between days 11 to 15.

Laboratory Diagnosis

- Rule out chickenpox (PCR).
- Specimen of choice is lesion material from pustules.
- Contact your State Public Health Laboratory for guidance.

Electron microscopy of vesicular scrapings = characteristic virions

- Light microscopy - Guarnieri bodies.
- Gispén's modified silver stain = cytoplasmic inclusions appear black.
- Characteristic growth on chorioallantoic membrane.
- PCR.

Viral Hemorrhagic Fevers (VHF)

Viral hemorrhagic fevers are a diverse collection of illnesses caused by a variety of RNA viruses (Table 1). The mere mention of VHF conjures up images of the movie *Outbreak*, with victims bleeding out of eye sockets and dying horrific deaths. While this is possible with some VHF, others are survivable with antivirals such as ribavirin (Lassa) or aggressive symptomatic and supportive care.

The most notorious is Ebola, but others include Dengue, Lassa and Crimean Congo. VHFs are endemic worldwide. Several cause common illnesses such as Dengue in Peru, Yellow Fever in South America, Lassa in West Africa and Ebola in Sub Saharan Africa.

The transmissibility of VHF varies with the causative virus: some are airborne or respiratory contagions while others can be contracted by contact with infected fluids or instruments. Several are mosquito-borne or tick-borne. Rodents may also be reservoirs.

In the Southwest United States, Hantavirus caused several deaths to victims exposed to rodent excreta. Owing to the large number of such illnesses, including the several varieties of Hantaviruses a discussion of general characteristics and key clinical clues that may be common to multiple VHFs will be presented.

All of these viruses target the vascular bed. Therefore evidence of derangements in vascular permeability should be expected.

In general VHFs are characterized as acute febrile illnesses accompanied by increased vascular permeability, endothelial damage, cutaneous flushing, bleeding from mucous membranes, conjunctival injection and hypotension.

Depending on the viral etiology, there is a wide range in severity. Some patients may appear critically ill with obvious bleeding diathesis, while others may demonstrate more subtle symptoms, such as mild epistaxis and ecchymosis. Other features include weakness, severe headache, shock, delirium, coma and seizures. Not everyone who is exposed to these viruses will develop VHF.

The presumptive diagnosis of VHF is clinical with confirmation by laboratory. A detailed travel and occupational history should be obtained.

VHF should be considered in patients presenting with fever, appearing

acutely ill, with evidence of bleeding derangement including easy bruising, as well as relative bradycardia, hypotension, thrombocytopenia, hematuria and possible DIC.

Some VHF's produce a clinical picture of jaundice; most such viruses affect the liver and will cause elevated hepatic enzymes. Some patients will have ARDS from pulmonary capillary leak. Multisystem organ involvement is possible. Patients may appear confused or have other neurologic signs and symptoms. Positive "cuff sign" or "tourniquet sign" is possible with Dengue and other VHF's.

Take a blood pressure cuff and pump it up to ~ 180 - 200 mm HG. After reading the blood pressure, which should be low in a VHF patient, remove the cuff. A VHF patient may show petechiae or echymosis somewhat circumferentially where the cuff was.

Relative bradycardia can also be caused by tularemia, plague or typhoid fever. Malaria is a more common illness in the differential diagnosis. It should be noted that in elderly, relative bradycardia, also referred to as pulse-temperature dissociation, may not be evident as older patients often do not manifest fevers and may be on heart rate suppressive medications such as beta adrene.

Identifying other patients with similar symptoms or family members also ill, may signal a possible widespread illness warranting involvement of infectious disease, hospital epidemiologist and public health. Personal Protective Equipment (PPE) must be utilized. Management must address bleeding. Often pressor agents are necessary. Aggressive symptomatic and supportive care is essential. Patients must be protected from unnecessary trauma, bruising or invasive techniques. Ribavirin may be useful for Lassa, Crimean-Congo and Rift Valley. Convalescent plasma may provide therapeutic benefit in some VHF. The nosocomial transmissibility of these viruses requires strict infection control.



Six-week old infant with botulism. Photo courtesy of CDC.

Viral Hemorrhagic Fevers

■ Arena Viruses

- Lassa fever
- Argentine hemorrhagic fever
- Bolivian hemorrhagic fever

■ Flaviviridae

- Yellow
- Dengue

■ Bunyaviridae

- Crimean-Congo fever

■ Filoviruses

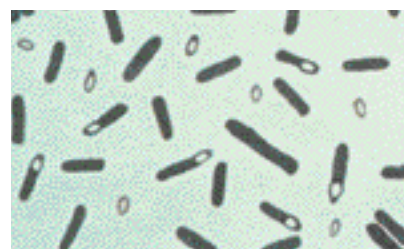
- Marburg Ebola hemorrhagic fevers

Botulism^{1,3,8-10}

Botulism is a toxin produced by the bacterium *Clostridium botulinum*, which is used as a medication, referred to as botox (r) and a CDC category A bioweapon.

On a milligram-per-milligram basis, botulinum toxin is the most lethal toxin known. It is estimated that one gram of botulinum could kill one million individuals.

Botulinum toxin has been used since the 1930s in the Japanese bioweapon facility known as Unit 731. *Clostridium* is an anaerobe, gram-positive, spore-forming bacillus. The toxin produces a two-chain polypeptide with seven distinct types identified, and named A - G. Usually humans are affected by types A, B and E.



Photomicrograph of clostridium botulinum. Photo courtesy of CDC.

There are three naturally occurring forms of botulinum toxicity: 1. Food-borne; 2. Wound contamination; and 3. Intestinal. Botulinum toxin blocks acetylcholine release from presynaptic motor neurons.

Category A bioweapons can cause a febrile upper respiratory illness. However, botulinum toxin, especially a weaponized form, can cause descending, flaccid paralysis preceded by bulbar palsy. Patients presenting with botulinum toxin should be afebrile, manifesting in tact sensation with the associated descending flaccid paralysis.

Patients may present with what is commonly referred to as the "4 D's"

- Dysphonia
- Dysarthria
- Diplopia
- Dysphagia

It should be noted that in the elderly, bulbar palsy might occur as a result of facial muscle paralysis. Since older patients may present with altered mental status, botu-

lism may be misdiagnosed in the early stages.

Guillain-Barre, myasthenia gravis are often confused with botulinum toxicity. Other neurological disorders including stroke must be considered as well. Botulism however results in bilateral paralysis whereas stroke is usually unilateral. Stroke patients may be confused; such would not be expected in botulism.

The key to effective treatment is early diagnosis. The mainstay of care is symptomatic and supportive, with aggressive airway management being of paramount importance.

Antitoxin is available from the CDC. However, the most available antitoxin is equine derived and thus poses a risk for a hypersensitivity reaction. The antitoxin is not an antidote, must be administered early and only addresses free toxin. Death usually is the result of respiratory muscle paralysis and thus mechanical ventilation—often long term—is life saving.

Role of physicians

“At the end of the day, primary care physicians are going to pick up most of any disease outbreak. Emergency rooms are going to be your first line of defense. You’re not going to create a massive capacity overnight.”^{16,16-18}

The current generation of healthcare professionals, especially community clinicians who may be among the first to identify potential bioweapon victims, remain inadequately prepared to address such events.^{1,2,5,6,16-18}

Physicians continue to express concern how to identify or manage victims of biological weapons. A recent study evaluating the knowledge of clinicians in terms of key issues related to WMD, and their interpretation of chest X-rays, raised some concerns. More than one-third could not identify gross mediastinal widening on chest X-rays, or distinguish between a normal chest X-ray from hilar enlargement.

Emphasis has largely been placed on training emergency medicine personnel.²

Healthcare providers affiliated with universities or medical centers are more likely to receive training than rural clinicians unaffiliated with teaching programs or well-financed health systems. However, in the event a bioweapon is used, pediatricians, (adolescent specialists¹⁹), geriatricians or other primary care clinicians are likely to be faced with the sentinel patient.

Since a bioweapon event might be a propagated epidemic, rural, urban and suburban patients would ensue. Are distance learning and computer-based courses enough to bridge the training gap that rural and independent clinicians may face?

Recently there was an episode about a possible smallpox event on the television show “ER.” Several children were brought to the emergency department obviously quite ill, with an unusual rash. They were placed in an overcrowded waiting room. What is wrong with that picture? How many of us remember going to the pediatrician as a child?

If you ever had a rash or potentially contagious illness, you, too, might have been taken to the back door instead of allowed to sit among other children in the waiting room. Some pediatricians had well-visit offices and waiting rooms distinct from sick child rooms. Is this ancient history? Perhaps, but we are rapidly becoming victims of our own healthcare success.

Many of our current physicians are unfamiliar with whooping cough, measles or mumps. Some cannot distinguish photographs of smallpox from chickenpox. Yet the very infection control practices we relied upon in the past have rapidly disappeared in the face of overcrowding and limited office space. Can we reinstitute such efforts in our practices? Do our receptionists and assistants receive training regarding which patients should be sequestered from the others? Do we take

the time to teach our staff about rashes, foreign travel, high fevers and other signs or symptoms of possibly contagious or unusual illness? Do we take a good travel and occupational history updating the information regularly? It can be surprising to note how often our patients change jobs, sometimes going from relatively safe occupations to ones fraught with risk.

Osteopathic physicians provide medical care to patients in many settings, from urban to rural, including regions that would otherwise be underserved³. The role of physicians, along with the type of infrastructure and support they can expect, will change depending upon the setting.

Regions with strong academic institutions, trauma centers and important governmental presence tend to be resource abundant. By contrast, rural areas may remain resource isolated. Yet the role of physicians in either setting remains constant: Maintain a high level of suspicion for unusual illness, learn about the diagnostic clues to emerging threats, and know whom to call when you suspect an unusual biological illness.

It is essential for physicians to identify vulnerabilities and resources in advance of a crisis. Physicians will need to work with the stakeholders to create and test preparedness plans. In many settings the physician is the only health officer in the area. As such, physicians may need to serve as diagnostician and treatment providers. Other responsibilities will include interacting with the media and helping to develop preparedness plans in concert with fire rescue, other governmental agencies and healthcare facilities.

In addition, physicians may be called on to identify local vulnerabilities and response partners. Physicians may not be accustomed to providing information through the media. However, as healthcare experts physicians are increasingly being called on to provide commentary and hopefully by extension calm. There-

for the skill sets of risk communications, public preparedness and clinical response to hazards must be acquired and practiced.

While physicians are the leaders in healthcare, they are not the only professionals and participants in healthcare facilities. Of concern, if physicians consider themselves under trained, what about the others on the team? Add to this the reality that surge capacity is all but nonexistent in the United States.

During a one-week period in Massachusetts, 67 out of 76 hospitals diverted patients away from emergency departments.¹⁸ Physicians may not be able to immediately repair the lack of surge capacity in our hospitals, but we can help identify temporary solutions and look at potential long-term strategies.

If we cannot handle the demands currently placed upon an already overstrained healthcare system, how will we adapt to a bioweapon illness or emerging disease that may affect hundreds simultaneously? Where will we diagnose and treat them? Will we have enough ventilators to support them? If not, who will provide ventilation?

Resource adaptation is critical and as physicians we must think out of the box for solutions. The Israelis, for example, train janitors to use ambubags.

Physicians as healthcare leaders in their communities will be called upon to address the psychosocial as well as medical issues associated with WMD. Yet recent studies reveal that physicians consider themselves to be undertrained to prepare for and respond to bioterrorism.

While it is clear that we must provide rapid, concise and practical training to our current physicians, the future leaders in healthcare—our students—cannot be allowed to face these new challenges as underprepared as we were in 2001.

The American Association of Colleges of Osteopathic Medicine (AACOM) and the Association of

American Medical Colleges (AAMC) have taken an important step in encouraging bioterrorism training in medical education, though few medical schools have developed a long-term strategy to accomplish this.

What follows is a review of the critical issues physicians should be aware of to appropriately attend to the needs of their patients and a discussion of opportunities to ensure the sustainability of such training.

Based on several task forces dedicated to developing competency-based training for healthcare providers, the following are identified as critical skills for physicians:

■ Identification

Through careful assessment, including obtaining a good history and focused examination, physicians should be able to identify a potential sentinel case of bioweapon illness or common presentation of uncommon illness or to distinguish a potential emerging disease from a common illness.

■ Initial management

Based on an index of suspicion, a physician should be able to initiate appropriate early treatment and testing, including proper infection control and use of PPE.

■ Referral

A physician should know the appropriate resources and the specialists to enlist for assistance and the proper public health authorities to collaborate with.

■ Follow-up

Patients infected with bioweapon illness may require long-term care, including psychological support.

Most bioweapon illness results in significant morbidity or mortality. Bioweapon illness is rarely subtle and the diagnosis is usually clinical. Laboratory testing is important for confirmation but the

patient's survival may well depend upon the bedside diagnosis.

If the physician suspects an emerging threat, unusual illness or bioweapon, it is essential to notify the laboratory immediately so as to alert personnel to utilize proper personal protective measures, obtain appropriate testing materials or enlist the assistance of the state laboratory network.

Through collaboration with federal funding and the CDC, most states have upgraded their laboratory capabilities to level three biohazard. In addition to notifying the laboratory of one's suspicions, the local or state public health department should be alerted so that their expertise and that of federal agencies can be prepared to respond.

Communication is critical and needs to involve physicians as well as governmental and medical organizations. Discussing unusual cases with colleagues may provide clues that an emerging problem exists.

Physicians should collaborate with preparedness coordinators in their communities and identify resources in terms of medications, PPE, locations where patients may need to be treated as alternatives to the hospital and vulnerable groups.

Stakeholders need to be made aware of the plans and their possible impact on the community. Communicating with the public that their community is preparing for bioweapons and what role they can play in emergency response will help ensure cooperation.

Special populations

As physicians we cannot afford to leave anyone behind in terms of bioweapon preparedness. Unfortunately certain populations have been marginalized, and awaited being included in funding initiatives or training programs. These populations include mental health patients,

children, students and school personnel, persons with disabilities, the chronically ill, those in nursing homes, the elderly, and ethnic subpopulations including Native Americans.

Schools are a significantly vulnerable and a place where our children spend much of their time. As physicians we treat a continuum of ages and a variety of patients with unique needs.

We need to consider the impact WMD will have on these special populations and the facilities they are most likely to visit or reside in. Many of the symptoms discussed in this article may not be evident.

Presentation of illness—bioweapon and community acquired—is often atypical and confounding. High fever—a common symptom of bioweapons—may not occur as predicted among older patients.

While several bioweapon illnesses cause alteration in mental status, the baseline cognition of an elderly patient may make this symptom—a valuable clue in the young—virtually unusable. Baseline dementia may also hamper the patient's ability to follow instructions or provide critical information.

A recent project funded by HRSA in collaboration with the National Association of Geriatric Education Centers (NAGEC) to address national training competencies in bioterrorism preparedness for the aging is underway and should provide needed training in geriatric health.

Children affected by bioweapons may not present with symptoms the way adults do. Our clinical experience is limited. They also may not respond to treatment as predicted. Of concern, many preparedness plans call for the use of schools as temporary treatment facilities or morgues. This presupposes the children won't be in school. But what if they are? Where shall they go? What will the impact be on children if their school is uti-

lized for bodies or profoundly ill, even disabled patients?

Have we considered the medical needs of school children with disabilities or chronic illness that might have to reside at schools during a WMD threat? The American Academy of Pediatrics and other national organizations dedicated to the health of children and adolescents have recognized the need to increase training among the respective specialties to properly prepare.¹⁹

Have we as physicians provided the leadership and support to school and nursing home staffs to implement better infection control or prepare for biological threats?

Persian Gulf veterans will be exposed to a variety of infectious illnesses including brucellosis, which can cause behavioral changes due to a neurotoxin associated with the pathogen. Such changes are often misdiagnosed as PTSD.

Careful evaluation of returning veterans is critical to avoid attributing a psychological illness as etiology when another cause, including pathogen endemic in the Middle East or other exposure might be the true diagnosis. As physicians we need to be sensitive to the stress veterans may experience in acclimating to American society after prolonged duty in a war zone.

General preparedness considerations

Key considerations for the toxicologist and clinician regarding bioterrorism and weapons of mass destruction:

1. Healthcare facility preparedness

- Professional training
- Medication and other resources
- Patient triage
- Early, presumptive diagnosis
- Patient placement

2. Smallpox, quarantine or special response designated facilities

3. Vaccination policy

Pre or post event strategy

- Vaccine candidate identification
- Transmission of vaccine related illness
- Vaccine candidate screening
- Immune globulin or other vaccine illness treatments
- At risk special populations

Does the vaccine pose specific risks?

Does the preparation, vehicle pose risks?

4. Antiviral therapy

5. Community education

As part of community preparedness, physicians should encourage their patients to obtain appropriate vaccines such as influenza, pneumococcal and varicella.

According to the CDC, more than 30,000 Americans die annually from influenza and pneumococcal pneumonia-related illness, two vaccine-preventable illnesses. A significant proportion of those deaths could be prevented if we as physicians improved our rate of vaccination and reached Healthy People 2010 goals.

We should also encourage our patients to learn cardiopulmonary resuscitation (CPR) and first aid. Now more than ever we all have a choice—to be part of the problem or part of the solution.

There are many sources for patient handouts. Do we make home preparedness information brochures available? Each region has natural disasters that we should all prepare for—in the South it is hurricanes, in the Northeast snowstorms.

Patients want to have useful information that is practical and valid for a variety of emergencies. Many agencies, including a variety of poison control centers (Long Island, Georgia) as well as the CDC offer bioterrorism and other poison information that can be downloaded, printed and placed in your offices.

We are all in this together as a community. As such, we should seek out additional training.

The AMA in collaboration with major medical centers has established Basic Disaster Life Support (BDLS) and Advanced Disaster Life Support Programs (ADLS).²⁰ The University of Arizona has developed an Advanced Hazardous Life Support (AHLS) training program.²¹ All of these programs having enormous early success, have been presented across the country and address public preparedness, bioweapons and other emerging threats. AACOM in concert with AOA is developing a Web-based interactive bioterrorism module that should be released shortly.

Final notes

The events of September 11 have demonstrated our vulnerabilities to terrorism. Bioterrorism and WMD present a very real threat to society. Up until recently, we have not adequately developed our healthcare infrastructure or prepared clinicians to respond to such threats.

To prepare for a WMD event, it will be necessary to train existing and future clinicians to diagnose bioweapon and emerging global illness, identify and treat local chemical threats, as well as participate in community preparedness.

In addition, we must advocate for greater HAZMAT (hazardous materials) legislation, strengthen the public health infrastructure, and promote coordination among the many organizations and professions that will need to be involved to protect society. Private physicians and public health need to work with fire rescue, law enforcement and stakeholder groups representing the public and various vulnerable entities like schools, houses of worship and facilities for the aged.

Physicians and other diverse organizations not accustomed to working together will have to train and conduct drills together to provide the best resources for the community. Such collaborations are essential. There are many questions that

remain unanswered and problems that must be solved in terms of WMD prevention, preparedness, and response.

People have always turned to physicians in times of stress and concern. We have a great opportunity to promote calm, enhance health and provide leadership in community safety. Continued training and education will hone our skills and allow us to provide the best possible care for our patients as well as strengthen our ability to be role models and valuable mentors to our students.

It is a daunting task to prepare for an unknown threat from an unknown assailant with an undisclosed timetable. None the less, the value to society in our leadership to promote calm, provide preventive strategies and reassure our patients that we are obtaining the most current training to deliver the best care is precisely what is needed. Hopefully we will never be called upon to diagnose ebola or smallpox, but we cannot afford to be unprepared for the sentinel case.

From our earliest days in medical school we were all taught "when you hear hoof beats, think horses before zebras." In a global world where borders no longer serve as barriers to disease, those hoof beats may in fact represent a zebra.

Regardless of the specialty we may be called upon to diagnose a patient presenting with an unusual set of symptoms. As physicians we must feel safe enough to err on the side of caution and think in terms of zebras as well as horses, worrying less that we are wrong in suspecting a bioweapon illness, while hoping in fact that we are!

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